No. 4889
Date: March 11 1993 2:45 p.m.
Approved: Baltasar Corrada del Río
Secretary of State
By: Lourdes de Piñeiro
Assistant Secretary of State

COMMONWEALTH OF PUERTO RICO
DEPARTMENT OF LABOR AND HUMAN RESOURCES
office of the Secretary
Hato Rey, Puerto Rico

R E S O L U T I O N

I, Cesar Juan Almodóvar Marchany, Secretary of Labor and Human Resources, pursuant to the authority conferred by Section 8 of the Puerto Rico Occupational Safety and Health Act, Number 16 of August 5, 1975 as amended (29 LPRA) 361 et seq.,) hereby amend the Puerto Rico Occupational Safety and Health Regulation, Number Twelve (Part 1915,1916,1917 and 1918) approved on February 1st, 1978 and amended on March 23, September 30, 1983, March 16, 1987, April 8, September 28, 1988 and February 13, 1990 by adopting the following amendment:

Occupational Exposure to Cadmium; Final Rule as published in the Federal Register Volume 57, Number 178 of September 14, 1992 (42102-42463) and Volume 57, Number 211 of October 30, 1992 (49272)

The adoption of this amendment shall be effective immediately after its approval.

Given on this 10 day of March of 1993.

CESAR JUAN ALMODOVAR MARCHANY

Federal Register

Monday
September 14, 1992

4889

Part II

Department of Labor

Occupational Safety and Health Administration

29 CFR Part 1910, et al.

Occupational Exposure to Cadmium; Final Rules

DEPARTMENT OF LABOR

Occupational Safety and Health Administration

29 CFR Parts 1910, 1915 and 1926

[Docket No. H-057a]

RIN 1218-AB16

Occupational Exposure to Cadmium

AGENCY: Occupational Safety and Health Administration (OSHA), Department of Labor.

ACTION: Final rules.

SUMMARY: The Occupational Safety and Health Administration (OSHA) hereby publishes a new standard for occupational exposure to cadmium, applicable to general industry and agriculture and maritime. A separate standard regulating exposure to cadmium in the construction industry was also developed, because the differences in job duration, exposure and worksite conditions warrant unique treatment. OSHA is publishing the construction standard at 29 CFR 1926.63.

The basis of this regulation is a determination by the Assistant Secretary that employees exposed to cadmium face a significant risk to their health from lung cancer and serious kidney damage at the current permissible exposure limits and that promulgating this standard will substantially reduce that risk. The information gathered during the rulemaking demonstrates that employees chronically exposed to levels of cadmium well below existing permissible exposure limits are at increased risk of developing kidney dysfunction and cancer.

The new standard establishes a single 8-hour time weighted average permissible exposure limit (TWA PEL) of 5 micrograms of cadmium per cubic meter ($\mu g/m^3$) of air for all cadmium compounds, including dust and fumes. Employers are required to comply with this limit primarily by means of engineering and work practice controls. For a small number of industries, OSHA has also established a separate engineering control air limit (SECAL) of 25 $\mu g/m^3$ as the lowest feasible level above the PEL that can be achieved by engineering and work practice controls. Like the PEL for other industries, the SECAL, where applicable, must be achieved by engineering and work practice controls except to the extent that the employer can demonstrate that such controls are not feasible.

EFFECTIVE DATE: The new standards published today take effect December 14, 1992.

ADDRESSES: For additional copies of these final standards, contact: OSHA Office of Publications, room S-4203, U.S. Department of Labor, 200 Constitution Avenue NW., Washington, DC 20210. Telephone 202-523-8151.

FOR FURTHER INFORMATION CONTACT: Mr. James F. Foster, Director, Office of Information and Consumer Affairs, OSHA, U.S. Department of Labor, room N-3647, 200 Constitution Avenue NW., Washington, DC 20210. Telephone (202) 523-8151.

SUPPLEMENTARY INFORMATION:

Table of Contents

I. Introduction
II. Pertinent Legal Authority
III. Regulatory History
IV. Chemical Identification, Production, and Use of Cadmium
V. Health Effects
VI. Quantitative Risk Assessment
VII. Significance of Risk
VIII. Regulatory Impact Analysis
IX. Summary and Explanation of the Final Standard (General Industries, agriculture, and maritime) (Construction Industry)
X. Authority and Signature
XI. Final Standard (General industries, agriculture, and maritime) (Construction industry)

References to the rulemaking record are in this text, and the following abbreviations have been used: 1. Ex.: Exhibit, with accompanying number in Docket H-057a, which is located in room N-2625 at the Department of Labor. 2. Tr.: Transcript, with accompanying date and page number.

I. Introduction

A. General

The preamble to this standard on occupational exposure to cadmium discusses the events that led to the development of the proposal, cadmium's physical properties, manufacture and use, the health effects associated with exposure to cadmium, and the degree and the significance of the risk. In addition, an analysis of the regulatory impact and technological and economic feasibility of the proposed standard and the rationale behind the specific provisions set forth in the regulatory text are also presented.

OSHA is acting to regulate a hazard widely recognized by other Federal agencies, health experts, and the general public. These standards will be codified at 29 CFR 1910.1027 for general industry and at 29 CFR 1926.63 for the construction industry. Pursuant to sections 4(b)(2), 6(b), 8(c) and 8(g) of the Occupational Safety and Health Act of 1970 (the Act) (84 Stat. 1592, 1593, 1596, 1599; 29 U.S.C. 653, 655, 657), the Construction Safety Act (40 U.S.C. 333), the Longshore and Harbor Workers' Compensation Act (33 U.S.C. 941), the Secretary of Labor's Order No. 1-90 (55 FR 9033), and 29 CFR part 1911, these final standards hereby amend and revise the current cadmium standards.

This action follows publication of a proposed rule on February 6, 1990 (55 FR 4052) and holding of public hearings from June 5-13, 1990 in Washington, DC and July 17-19, 1990 in Denver, Colorado to provide the public with an opportunity to comment on OSHA's proposed rule on cadmium. Approximately 2000 pages of testimony and 100 comments were received into the record of this rulemaking and have been analyzed by the Agency in creating this final standard.

B. Construction

OSHA has decided to issue two separate standards regulating occupational exposure to cadmium; one that applies to workplaces in general industry and agricultural and maritime industries, and another covering construction worksites. By doing so, OSHA is acting in accordance with the recommendations of the Advisory Committee for Construction Safety and Health (ACCSH), which has reviewed and commented on the proposal and has submitted changes in that proposal to the record of the rulemaking.

Additional reasons that support a separate standard for construction can be summarized briefly as follows:

(1) The construction industry is characterized by nonfixed worksites that are temporary in nature and differ from those in general industry in regard to the need for a designated competent person as well as significant differences between workplaces in terms of site conditions, size and scope of tasks, methods of operation, and environmental conditions.

(2) Employees in the construction industry often do not remain in construction or in the employ of the same employer for a long period of time, in contrast to employees in fixed-site manufacturing facilities.

(3) The special characteristics of construction operations made it necessary to tailor some of the requirements traditionally included in OSHA health standards to the specific needs of the construction industry.

OSHA has tailored the requirements of the final construction standard to reflect differences in operations of various types within the construction industry itself. In recognition of this

wide diversity in construction projects, the Agency has specifically identified in the final rule those additional requirements that apply to such construction operations. The record demonstrates, with a few exceptions, the generally low exposures and well-controlled conditions prevailing in construction operations involving the use of cadmium.

II. Pertinent Legal Authority

A. Purpose

The primary purpose of the Occupational Safety and Health Act (the Act) (29 U.S.C. 655 et seq.) is to assure, so far as possible, safe and healthful working conditions for every American worker over the period of his or her working lifetime. One means prescribed by the Congress to achieve this goal is the mandate given to, and the concomitant authority vested in, the Secretary of Labor to set mandatory safety and health standards. The Congress specifically mandated that:

> The Secretary, in promulgating standards dealing with toxic materials or harmful physical agents under this subsection shall set the standard which most adequately assures, to the extent feasible, on the basis of the best available evidence, that no employee will suffer material impairment of health or functional capacity even if such employee has regular exposure to the hazard dealt with by such standard for the period of his working life. Development of standards under this subsection shall be based upon research, demonstrations, experiments, and such other information as may be appropriate * * *. In addition to the attainment of the highest degree of health and safety protection for the employee, other considerations shall be the latest available scientific data in the field, the feasibility of the standards, and experience gained under this and other health and safety laws. Whenever practicable, the standard promulgated shall be expressed in terms of objective criteria and of the performance desired [section 6(b)(5)].

B. Action Needed

The issuance of this final standard is authorized by sections 6(b), 8(c), and 8(g)(2) of the Occupational Safety and Health Act of 1970 (the Act), (84 Stat. 1593; 29 U.S.C. 655(b), 657(g)(2)). Section 6(b)(5) governs the issuance of occupational safety and health standards dealing with toxic materials or harmful physical agents. Section 3(8) defines an occupational safety and health standard as:

> * * * A standard which requires conditions, or the adoption or use of one or more practices, means, methods, operations, or processes, reasonably necessary or appropriate to provide safe or healthful employment and places of employment.

The Supreme Court has held that under the Act the Secretary, before issuing any new standard, must determine that it is reasonably necessary and appropriate to remedy a significant risk of material health impairment. *Industrial Union Department* v. *American Petroleum Institute*, 448 U.S. 607 (1980). The court stated that "before he can promulgate any permanent health or safety standard, the Secretary is required to make a threshold finding that a place of employment is unsafe in the sense that significant risks are present and can be eliminated or lessened by a change in practices" (488 U.S. at 642). The Court also stated "that the Act does limit the Secretary's power to requiring the elimination of significant risks" (448 U.S. at 644, n. 49).

The court indicated, however, that the significant risk determination is "not a mathematical straitjacket," and that "OSHA is not required to support its finding that a significant risk exists with anything approaching scientific certainty." The court ruled that "a reviewing court [is] to give OSHA some leeway where its findings must be made on the frontiers of scientific knowledge * * * [and that] the Agency is free to use conservative assumptions in interpreting the data with respect to carcinogens, risking error on the side of overprotection rather than underprotection" (448 U.S. at 655, 656). The court also stated that "while that Agency must support its finding that a certain level of risk exists with substantial evidence, we recognize that its determination that a particular level of risk is 'significant' will be based largely on policy considerations." (448 U.S. at 655, 656, n. 62).

After OSHA has determined that a significant risk exists and that such risk can be reduced by the proposed standard, it must set a standard "which most adequately assures, to the extent feasible on the basis of the best available evidence, that no employee will suffer material impairment of health" (section 6(b)(5) of the Act). The Supreme Court has interpreted this section to mean that OSHA must enact the most protective standard possible to eliminate a significant risk of material health impairment, subject to the constraints of technological and economic feasibility. *American Textile Manufacturers Institute, Inc.* v. *Donovan*, 452 U.S. 490 (1981). The court held that "cost-benefit analysis is not required by the statute because feasibility analysis is." (452 U.S. at 509). The Court stated that the Agency could use cost-effective analysis and choose the least costly of two equally effective standards. (452 U.S. 531, n. 32).

C. Regulation

Authority to issue this proposed standard is also found in section 8(C) and (g) of the Act. Section 8(c)(3) gives the Secretary authority to require employers to "maintain accurate records of employee exposures to potentially toxic materials or harmful physical agents which are required to be monitored or measured under section 6." Section 8(g)(2) gives the Secretary authority to "prescribe such rules and regulations as he may deem necessary to carry out * * * [his] responsibilities under this Act."

In addition, the Secretary's responsibilities under the Act are amplified by its enumerated purposes, which include:

> * * * Encouraging employers and employees in their efforts to reduce the number of occupational safety and health hazards at their places of employment, and to stimulate employers and employees to institute new and to perfect existing programs for providing safe and healthful working conditions; * * *
>
> Authorizing the Secretary of Labor to set mandatory occupational safety and health standards applicable to business affecting interstate commerce * * *.
>
> Building upon advances already made through employer and employee initiative for providing safe and healthful working conditions; * * *
>
> Providing for the development and promulgation of occupational safety and health standards; * * *
>
> Providing for appropriate reporting procedures with respect to occupational safety and health which procedures will help achieve the objectives of the Act and accurately describe the nature of the occupational safety and health problem; * * *
>
> Exploring ways to discover latent diseases; * * *
>
> Establishing causal connections between diseases and work in environmental conditions * * *;
>
> Encouraging joint labor—management efforts to reduce injuries and disease arising out of employment * * *
>
> And * * * developing innovative methods, techniques, and approaches for dealing with occupational safety and health problems * * *.

Because the final cadmium standard is reasonably related to these statutory goals and because the Agency's judgment is that the evidence satisfies the statutory requirements and that the final standard is feasible and substantially reduces a significant risk of cancer and other adverse health effects, the Secretary finds that this standard is necessary and appropriate to carry out her responsibilities under the Act.

D. Information Collection Requirements:

5 CFR Part 1320 sets forth procedures for agencies to follow in obtaining OMB clearance for information collection requirements under the Paperwork Reduction Act of 1980, 44 U.S.C. 3501 et seq. The final cadmium standard requires the employer to allow OSHA access to various records including the employers' compliance and training plans; and the employees' exposure monitoring, medical and training records. In accordance with the provisions of the Paperwork Reduction Act and the regulations issued pursuant thereto, OSHA certifies that it has submitted the information collection requirements of this standard to OMB for review under section 3504(h) of that Act.

Public reporting burden for this collection of information is estimated to average 5 minutes to allow OSHA compliance officers access to the employer's records. Send comments regarding this burden estimate, or any other aspect of this collection of information, including suggestions for reducing this burden, to the Office of Information Management, Department of Labor, room N-1301, 200 Constitution Avenue NW., Washington, DC, 20210; and to the Office of Management and Budget, Paperwork Reduction Project (Cadmium Standard), Washington, DC, 20503.

E. Federalism

This final standard has been reviewed in accordance with Executive Order 12612, 52 FR 41685 (October 30, 1987), regarding Federalism. This Order requires that agencies, to the extent possible, refrain from limiting State policy options, consult with States prior to taking any actions that would restrict State policy options, and take such actions only when there is clear constitutional authority and the presence of a problem of national scope. The Order provides for preemption of State law only if there is a clear Congressional intent for the agency to do so. Any such preemption is to be limited to the extent possible.

Section 18 of the Occupational Safety and Health Act [OSH Act], expresses Congress' clear intent to preempt State laws with respect to which Federal OSHA has promulgated occupational safety or health standards. Under the OSH Act, a State can avoid preemption only if it submits and obtains Federal approval of a plan for the development of comparable State standards and their enforcement. Occupational safety and health standards developed by such Plan States must, among other things, be at least as effective as the Federal standards in providing safe and healthful employment and places of employment.

Those States which have elected to participate under Section 18 of the OSH Act would not be preempted by this regulation and would be able to deal with special, local conditions within the framework provided by this performance-oriented standard while ensuring that their standards are at least as effective as the Federal standard.

F. State Plans

The 25 states and territories with their own OSHA-approved occupational safety and health plans must revise their existing standards within six months of the publication date of this final standard. These states or territories are: Alaska, Arizona, California, Connecticut, Hawaii, Indiana, Iowa, Kentucky, Maryland, Michigan, Minnesota, Nevada, New Mexico, New York, North Carolina, Oregon, Puerto Rico, South Carolina, Tennessee, Utah, Vermont, Virginia, Virgin Islands, Washington, and Wyoming. (In Connecticut and New York, the plan covers only State and local government employees.) Until such time as a state standard is promulgated, Federal OSHA will provide interim enforcement assistance, as appropriate.

III. Regulatory History

A. OSHA's Existing PELs

OSHA's existing permissible exposure limits for cadmium were originally developed by the American National Standards Institute. In 1941 the American Standards Association (now American National Standards Institute, or ANSI) set as guidelines an American Defense Emergency Standard of 1000 $\mu g/m^3$ for cadmium and its compounds. This was done to reduce discomfort from exposures to cadmium and to reduce the incidence of acute health effects. ANSI revised its standard to current levels (ANSI Z37.5, 1970) which OSHA adopted in 1971 as a national consensus standard under section 6(a) of the Occupational Safety and Health Act of 1970 (29 U.S.C. 655). These PELs, as specified in 29 CFR 1910.1000, Table Z-2 are an 8-hour time-weighted average (TWA PEL) of 100 $\mu g/m^3$ for cadmium fume with a ceiling concentration of 300 $\mu g/m^3$ and an 8-hour TWA of 200 $\mu g/m^3$ for cadmium dust with a ceiling concentration of 600 $\mu g/m^3$. OSHA's existing PEL in the construction industry is 100 $\mu g/m^3$ for cadmium oxide fumes and 200 $\mu g/m^3$ for metal dust and soluble salts (29 CFR 1926.55).

B. Other Agency Findings

In preparing this document, OSHA reviewed the existing regulations for occupational exposures in other countries worldwide. The range of existing PELs runs from the ban of all non-essential uses of cadmium in Sweden to OSHA's existing TWA PEL of 200 $\mu g/m^3$ for cadmium dust.

Sweden also established a PEL of 20 $\mu g/m^3$ for all existing uses of cadmium along with a PEL of 10 $\mu g/m^3$ for all new workplaces. Australia has a PEL of 50 $\mu g/m^3$ for both dust and fume but is presently proposing a level of 10 $\mu g/m^3$. China and the former USSR follow a PEL of 10 $\mu g/m^3$. Finland established a fume PEL of 10 $\mu g/m^3$ and dust PEL of 20 $\mu g/m^3$, while France allows cadmium oxide dust to be 50 $\mu g/m^3$. Japan's PEL is set at 50 $\mu g/m^3$. The regulations in the United Kingdom are under review, but the current allowable exposure level is 50 $\mu g/m^3$ except for the respirable cadmium sulfide level which is set at 40 $\mu g/m^3$ (Ex. L-140-50).

The German government bans the use of cadmium chloride and has also been intent on changing its cadmium exposure levels for all other cadmium compounds based on the MAK carcinogenic classification "A2" which defines cadmium as "unmistakably carcinogenic in experimental animals only" (ACGIH documentation of TLV, 1991).

Agencies and institutions other than OSHA have revised their air quality standards for cadmium. In 1976, the National Institute for Occupational Safety and Health (NIOSH) recommended that exposures to any form of cadmium should not exceed a concentration greater than 40 $\mu g/m^3$ as a 10-hour TWA or a concentration greater than 200 $\mu g/m^3$ for any 15-minute period. This recommended limit was intended to protect against renal damage and pulmonary disease. In 1984, NIOSH issued a Current Intelligence Bulletin (CIB), which recommended that cadmium and its compounds be regarded as potential occupational carcinogens based on evidence of lung cancer in workers exposed to cadmium in a smelter and that exposures should be reduced to the lowest possible level.

The Environmental Protection Agency (EPA) issued a Health Assessment Document (HAD) for cadmium in 1981 which presented the health effects and potential risk to human health associated with environmental exposure to cadmium. An update of the HAD in 1985 concluded that the epidemiologic evidence is suggestive of a significant risk of lung cancer from exposure to

cadmium. According to the EPA's 1984 Proposed Guidelines for Carcinogenic Risk Assessment, cadmium is classified as a Group B1 substance and is thus considered to be a "probable" human carcinogen (Ex. 4–04).

In 1987, the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) summarized the results from tests for genetic and related effects of a large number of compounds thought to be potentially carcinogenic. The IARC working group of experts evaluated these data as well as epidemiologic and animal studies and concluded that cadmium and cadmium compounds should be classified in Group 2A—"probably carcinogenic to humans" (Ex. 8–681). Since 1946, the American Conference of Governmental Industrial Hygienists (ACGIH) has recommended that exposures to cadmium be controlled. In 1946, ACGIH recommended a Maximum Allowable Concentration (MAC) of 100 $\mu g/m^3$ for cadmium. After 1948, the MAC was called the Threshold Limit Value (TLV). In 1956, a TLV of 100 $\mu g/m^3$ was assigned to cadmium oxide fume. In 1965, a value of 200 $\mu g/m^3$ for cadmium (metal dusts and soluble salts) was proposed; it was adopted as a recommended value in 1967. In 1970, the ACGIH TLV of 200 $\mu g/m^3$ for cadmium dust and salts remained unchanged, but the TLV for cadmium fume was changed to a ceiling. In 1973, the ACGIH announced its intent to change the TLV for cadmium fume to 50 $\mu g/m^3$ and in 1974 announced its intent to extend this TLV to cadmium dusts and salts. A note was added in 1975 indicating that cadmium oxide production involved carcinogenic or co-carcinogenic potential.

Recently, the ACGIH has recommended further changes in air quality standards for cadmium. They have classified cadmium as a potential human carcinogen and published a *Notice of Intent* to lower the TLV to 10 $\mu g/m^3$ for total dust and 2 $\mu g/m^3$ for respirable dust to protect workers from lung cancer and renal dysfunction. ACGIH justified this latest change in part by noting:

> In consideration of the strength of the white rat inhalation studies and with some additional support from the retrospective human mortality study by Thun *et al.*, an A_2 designation as an industrial substance of carcinogenic potential for man is given to cadmium and its compounds (Ex. 8–664).

The Mine Safety and Health Administration (MSHA) publishes air quality standards which include cadmium. MSHA frequently incorporates, by reference, the ACGIH TLVs as permissible exposure levels. Currently, MSHA is in the process of updating its PELs to take account of proposed ACGIH changes in the TLVs. MSHA published a notice of proposed rulemaking (*NPRM*, 8/29/89) proposing alternative TWA PELs of 10 $\mu g/m^3$ and 5 $\mu g/m^3$ for cadmium. The record for this notice closed on August 30, 1991 and internal review is now underway with an anticipated final standard publication date of February 1993.

Since 1987, the National Center for Health Statistics (NCHS), Department of Health and Human Services, Center for Disease Control, has included cadmium-in-urine measurements in its current third National Health and Nutrition Examination Survey (NHANES III). This survey, originally started in 1974, provides national estimates of diagnosed and undiagnosed medical conditions, as well as information on normal and abnormal conditions in the general population of the U.S. Such information is used by government agencies to obtain a more complete picture of national health and medical needs (Ex. 8–679). OSHA considers the inclusion of cadmium by NCHS to indicate a high level of concern regarding cadmium-related health effects among the general population of the United States. This emphasizes the importance of promulgating a final cadmium standard since general cadmium exposures among the U.S. population are much lower than cadmium exposures among most occupational groups.

C. Unified PEL

In keeping with the recommendations of other agencies like NIOSH, EPA and the ACGIH, this standard does not differentiate between exposure to cadmium fumes or dust. Since the early 1940's, acute inhalation of cadmium fumes from soldering or welding was known to cause severe health effects such as chemical pneumonitis and death (Ex. 8–678). These properties led researchers to readily accept the possibility of adverse health effects associated with exposure to fumes. It is now generally accepted that overexposures to cadmium in any form results in the same final chronic endpoints of cancer and kidney dysfunction (Exs. 4–27, 4–28, 4–68, and 4–19). By 1970, when ANSI republished their original guidelines, it acknowledged that exposures to cadmium fumes or dusts cause irreversible lung damage, proteinuria, and kidney damage. In the mid-1970's the ACGIH announced an intent to change the TLV for all forms of cadmium (fumes, dust, and salts) to 50 $\mu g/m^3$, and the differentiation between fumes and dusts was set aside.

D. Chronology of Cadmium rulemaking

OSHA's decision to reduce the PELs for cadmium exposures is, in part, in response to a petition, of June 18, 1986, from the Health Research Group (HRG) of Public Citizen, joined by the International Chemical Workers Union (ICWU), which requested OSHA to issue an Emergency Temporary Standard (ETS) for cadmium providing for a permissible exposure limit (PEL) of 1 $\mu g/m^3$ as an 8-hour TWA and 5 $\mu g/m^3$ as a ceiling limit. In support of their position the petitioners cited several studies which they believed provided evidence that workers were in grave danger from occupational exposure to cadmium at and below current PELs.

The major human study cited was that by Thun et al. (Ex. 4–68), which found significant increases in lung cancer in cadmium smelter workers. The petitioners also cited several animal studies which demonstrate the carcinogenic potential of cadmium. The most notable of these was an inhalation study cited in which rats exposed to cadmium chloride at levels below OSHA's PEL, developed lung cancer while the unexposed controls developed none (Ex. 4–67). Other human studies cited by the petitioners showed statistically significant increases in prostate cancer among battery factory, smelter, and alloy factory workers exposed to cadmium. Other human studies cited by the petitioners also showed evidence of renal damage and non-malignant respiratory disease among workers exposed to cadmium at levels below the PEL. The exposure limits requested by HRG and ICWU were aimed at ensuring that workers would not be at excess risk of cancer and kidney disease.

On July 1, 1987, OSHA denied the petition for an ETS on the grounds that the record did not support findings that cadmium posed a "grave danger" as defined by the courts. However, OSHA determined that the existing PELs at that time are not sufficiently protective and that the Agency should proceed with permanent rulemaking under section 6(b) of the Act to reduce cadmium exposure. In July of 1989, petitioners, alleging unnecessary delay on OSHA's part, filed a petition for a Writ of Mandamus in the U.S. Court of Appeals for the D.C. Circuit seeking to compel the Agency to issue the proposed and final standards by specified dates. On October 20, 1989, the court ordered the case held in abeyance and ordered

OSHA to file a report within three months on the status of the proposed rule and the date by which the Agency expected to issue a final rule. OSHA duly filed its status report, projecting publication of the proposal around the end of January 1990 and publication of the final cadmium rule within 24 months thereafter.

On February 6, 1990 OSHA published its proposed rule to regulate occupational exposure to cadmium (55 FR 4052). The main health effects targeted by the Agency were lung cancer and kidney damage. Based on the Agency's review of major epidemiological studies of lung cancer and renal dysfunction among workers exposed to cadmium, and based on the Agency's quantitative risk assessment, OSHA proposed establishing a PEL of 1 $\mu g/m^3$, or in the alternative, a PEL of 5 $\mu g/m^3$.

In proposing two alternative PELs, OSHA acknowledged that either PEL would be difficult to achieve in some sectors through engineering controls alone. In these particular industry and occupational sectors reliance upon respirators would be considerable.

Thereafter, on February 12, 1990, the Court of Appeals indicated that it was satisfied with OSHA's compliance to date but noted: (1) That OSHA's projection of 24 months for publishing a final standard exceeded by six months the 18-month period previously projected by the Agency, and (2) that all parties agree that exposure to cadmium poses a serious risk to workers and that OSHA should therefore proceed expeditiously. Consequently, the court ordered that the case continue to be held in abeyance, pending further review, and further ordered OSHA to file with the court, every six months until the final rule is issued, a report indicating the status of the rulemaking and the date by which the Agency expects to issue a final rule.

A public hearing on the proposal was held in Washington, DC on June 5–13, 1990, and in Denver on July 17–19, 1990. In response to significant public and expert comment on the proposed medical surveillance provisions, OSHA on July 2, 1990 sent a memo to all hearing participants, requesting further information, testimony, and comments on medical surveillance and smoking in the workplace (Ex. 46). OSHA made this request to hearing participants in order to maximize their participation in the development of the final requirements for medical surveillance and in light of substantial comment in expert and other testimony at the hearings in Washington, DC, and in pre-hearing written comments.

In the memorandum, OSHA summarized the submissions to the record as follows:

(a) Employer action generally should not be triggered on the basis of a single biological parameter;

(b) Prior to the onset of kidney disease, cadmium levels in urine provide the most practical indication of cadmium body burden;

(c) Concurrently high values in tests for both cadmium in urine and beta-2-microglobulin in urine provide the best early indicator of kidney dysfunction;

(d) A pre-placement (initial) medical examination is necessary for all employees previously, as well as currently exposed to cadmium above the action level to establish their health status;

(e) A termination of employment examination is also necessary to establish the health status of all employees previously exposed above the action level and to facilitate prognosis;

(f) Medical exams may not be necessary annually so long as periodic biological monitoring results are within normal ranges;

(g) Physician's discretion should be an important part of any medical surveillance program;

(h) A physician's decision that an employee must be medically removed from exposure to cadmium above the action level may mean that the employee cannot be returned to work in facilities with cadmium exposure;

(i) Multiple physician review may be an appropriate mechanism to assure the quality of medical determinations; and

(j) OSHA should directly address the issue of smoking among cadmium exposed workers.

In response to these submissions OSHA presented updated medical surveillance provisions and sought further testimony and comment.

In addition, in the memo, OSHA requested information and comments on several issues relating to smoking, including but not limited to: Whether smoking is likely to increase the smoker's body burden of cadmium; whether smoking is likely to contribute to cadmium-induced disease; whether OSHA should require the examining physician to inquire about the patient's smoking history and status, and; whether OSHA should require the examining physician to advise the patient that smoking is a source of cadmium exposure that is cumulative with whatever occupational exposure the patient absorbs and that the patient therefore should stop smoking. Comment and information was requested to be provided in testimony at the Denver hearing site and/or in post-hearing comment.

After the Denver hearing of July, 1990, a post-hearing comment period of 90 days was established by the hearing officer, Administrative Law Judge Julius A. Johnson. On September 18, 1990, SCM Chemicals, Inc., a cadmium pigment manufacturer, moved to extend the post-hearing comment period. SCM sought the extension to allow submission to the record of studies that were about to be initiated regarding the possible confounding effect of the photo-decomposition (solubilization) of cadmium sulfide on the results of an important long term inhalation study of rats exposed to cadmium sulfide and other cadmium compounds (Glaser, U., et al., "Carcinogenicity and Toxicity of Four Cadmium Compounds Inhaled by Rats," *Toxicological and Environmental Chemistry*, Vol. 27, pp. 153–62, 1990). That study by Glaser et al. showed cadmium sulfide to be a lung carcinogen of approximately equal potency with other cadmium compounds. The follow-up studies were to test whether the evidence of equal potency might be attributable, in whole or in part, to the existence of more toxic compounds in the inhaled cadmium sulfide aerosol. Industry representatives asserted that the toxic compounds were produced by the photo-decomposition of cadmium sulfide prior to inhalation by the test animals. The SCM motion was denied by Judge Johnson, but OSHA indicated that if significant new evidence soon became available, the Agency would consider reopening the record. The post hearing comment period ended on October 18, 1990.

On April 22, 1991, the Dry Color Manufacturers' Association (DCMA), representing cadmium pigment manufacturers and users, filed a motion with Judge Johnson to reopen the hearing to allow cross examination of OSHA witnesses regarding the carcinogenicity of cadmium sulfide in light of the results of the follow-up studies which had been completed, or alternatively to remove cadmium pigments from the current rulemaking. In its opposition to the motion, OSHA indicated that, in the interest of fairness and fully developing the record, the Agency would carry out a limited reopening of the record to allow submission of the results of the follow-up studies and written public comment on the studies and underlying issues. DCMA's motion was denied by the judge on May 13, 1991. On May 24, 1991, Judge Johnson certified the record for the public hearing as closed. Thereafter, on June 17, 1991, DCMA moved for

reconsideration of its previous motion. On July 5, 1991, OSHA denied the motion to reconsider. In its letter of denial, OSHA reiterated that the Agency would reopen the record for the limited purpose of receiving the final reports of the two recent studies and updated assessments of those reports and to seek public comment on the new evidence and the underlying issues concerning cadmium sulfide. OSHA then contracted with one of its experts at the hearing, Dr. G. Oberdörster, who is a co-author of one of the follow-up studies, and with one of the co-authors of the other study, Dr. U. Heinrich, to assess cadmium sulfide's solubility, bioavailability, toxicity, carcinogenicity and potency relative to other cadmium compounds in light of all the evidence, including their own studies.

The record was reopened for 45 days on September 18, 1991 and closed on November 4, 1991. OSHA submitted the reports of the additional studies of cadmium sulfide and the assessments by Drs. Oberdörster and Heinrich. New data had to be submitted by October 18, 1991, and other comments could be placed in the record until the record closed.

On February 12, 1992 OSHA filed its required status report to the court requesting a six-month extension due to unanticipated difficulties in developing specific portions of the final standard and the complexities of the issues that need to be addressed.

The International Chemical Worker's Union (ICWU) and Public Citizen's Health Research Group (HRG) moved to have the court impose a deadline of August 31, 1992, for OSHA to publish the final standard. Although OSHA expected to have completed the standard by this date, the Agency opposed a court imposed deadline. On March 20, 1992, the court ordered OSHA to issue the final rule by August 31, 1992 (*International Chemical Workers Union, et al.*, v. *Strunk and Martin*, No. 89-1357, March 20, 1992).

On June 5, 1992, DCMA filed another motion with the Agency to remove cadmium pigments from consideration in the final rule due to evidence adduced subsequent to the public hearings alleging that cadmium pigments are less toxic than other cadmium compounds (Ex. 171; and see Ex. 172). OSHA denied the motion for reasons stated in previous responses to DCMA and in this preamble (Ex. L-173).

In this rulemaking, OSHA has developed two final standards, one for general industry, maritime, and agriculture, and a separate one for the construction industry. In both standards, the Agency has concluded that excess exposure to cadmium in any form does pose a significant threat to the health of workers, whether it is from material impairment of kidney function, lung cancer or other cadmium-related illnesses. OSHA determined that the TWA PEL should not be set above 5 $\mu g/m^3$ based on the record of evidence and its own quantitative risk assessment. The Agency found that the animal and human data show strikingly similar evidence of cadmium toxicity. The decision to establish the PEL at 5 $\mu g/m^3$ was made on the basis of feasibility as well. OSHA's quantitative risk assessment does not take account of the reductions in risk attributable to the ancillary provisions. Although OSHA's risk assessment indicates that some risk may remain at a TWA PEL of 5 $\mu g/m^3$, the Agency has relied upon the ancillary provisions to eliminate significant risk at the new PEL.

IV. Chemical Identification, Production, and Use of Cadmium

Cadmium (Chemical Services Registry Number 7740-43-9) is a soft, blue-white, malleable, lustrous metal or a grayish-white powder. It is insoluble in water and reacts readily with dilute nitric acid. It reacts slowly with hot hydrochloric acid and does not react with alkalies. It is slowly oxidized by moist air to form cadmium oxide. Cadmium occurs in nature in ores, and is obtained as a by-product from the extraction, separation and recovery of those metals in refinery plants.

According to the Mine Safety and Health Administration (MSHA), cadmium ore does not exist since cadmium is a by-product of ores mined for other metals. In fact, cadmium is considered a "contaminant" in mining because it simply is not profitable for industries to mine for it solely. Cadmium is always found with other elements such as zinc, lead, copper or arsenic. An ore must contain at least a trace of a mineral or an aggregate of minerals; however to be considered valuable, it must contain a certain percentage of a desired mineral(s), which is cost-effective and profitable for the mine to process out of the ore. Generally, an ore is named after the minerals it contains which are being recovered. It usually follows that the ore is named in the order of the percentage of the elements present. For example, if an ore is mainly zinc then selenium and finally cadmium, it would be called zinc-selenium-cadmium-ore [personal communication 4/27/90, Mine Safety and Health (MSHA)]

Cadmium metal is produced by three basic processes: Fractional precipitation and distillation of roasted zinc ores; direct distillation of cadmium-bearing zinc; and, electrolytic zinc processing. Presently, there are four sites where cadmium is processed: ASARCO Incorporated in Denver, Colorado and Corpus Christi, Texas, where cadmium is recovered from lead smelter baghouse dust; Big River Zinc in Sauget, Illinois; Jersey Miniere Zinc Company in Clarksville, Tennessee; and Zinc Corporation of America in Bartlesville, Oklahoma where cadmium is recovered as byproduct of smelting zinc concentrates. ("Mineral Industry Surveys * * * Cadmium in 1991", Bureau of Mines, Department of Interior, 4/9/92).

A primary use for cadmium metal is as an anticorrosive, electroplated onto steel. Cadmium may serve as an electrode component in alkaline batteries and may be used in alloys, silver solders, and welding. Cadmium exposures in general occur in refining and smelting operations. Relative to the metals with which it is found, cadmium volatilizes readily during these processes because of its low boiling point (765 °C) and high vapor pressure. The cadmium then condenses to form fine airborne particles that react almost immediately with oxygen to form respirable cadmium oxide. Other general industry groups where exposure to cadmium may occur include electroplating, battery manufacturing, and pigment and plastics manufacturing. In addition, cadmium exposure is associated with welding, brazing, and painting operations in many other industries.

Cadmium exists in +2 valence state, and does not form stable alkyl compounds or other organometallic compounds of known toxicologic significance. Although all cadmium and cadmium-containing compounds are covered under this standard, OSHA is focusing in this section on those compounds most commonly associated with industrial processes in the United States of America which pose potentially serious health effects: cadmium oxide, cadmium sulfate, cadmium chloride, and cadmium sulfide (Ex. 8-671).

Cadmium oxide (CdO; Chemical Services Registry No. 1306-19-0) occurs as dark brown infusible powder or cubic crystals. It is practically insoluble in water but is soluble in dilute acids. It is also slowly soluble in ammonium salts. It is used as an electroplating chemical; as a component of silver alloys, phosphors, and semiconductors; and, in glass and ceramic glazes. It is also used as a vermicide and is a starting material for polyvinyl chloride (PVC) heat

stabilizers. Cadmium oxide is used as a second polarizer in silver-zinc storage batteries and in plastics such as Teflon to improve their high-temperature properties.

Cadmium oxide fumes are formed when cadmium compounds are heated and cadmium ions are driven off. As these ions cool, they condense out of the air as cadmium oxide. Cadmium oxide exposures can occur in a variety of industries where cadmium-containing compounds are heated, such as smelters, refiners, and copper-cadmium alloy manufacturing plants. Workers who perform welding on automobile parts in manufacturing plants, using cadmium containing solders, can be exposed to cadmium oxide fumes.

Cadmium chloride ($CdCl_2$; Chemical Services Registry No. 10108–64–2) is also widely used in industry. It is hygroscopic and occurs as rhombohedral crystals. It is freely soluble in water and acetone but slightly soluble in methanol and ethanol. It is used: In fungicides, in the manufacture of cadmium yellow pigments, in galvanoplasty, as an ice-nucleating agent, in laboratory analyses of sulfides to absorb H_2S, as a test for pyridine bases, and in electroplating. It is also used as an addition to tinning solutions, as a mordant in the dyeing and printing of textiles, as a component of metal finishing baths and aerosols, as an agent in photocopying, as an agent in the manufacture of coatings for electronic vacuum tubes, as an agent in the manufacture of special mirrors, as a solid film lubricant, as a catalyst, as a fog inhibitor in photographic film emulsions, as a chemical intermediary for cadmium sulfide, as a colorant for pyrotechnics, and in pesticides. Workers can be exposed to cadmium chloride dusts and aerosols in: battery manufacturing, electroplating, alloy and solder production, ceramics and vapor lamps production, and in welding.

Cadmium sulfate ($CdSO_4$; Chemical Services Registry No. 10124–36–4) also has many applications in industry. It occurs as odorless monoclinic hydrate. It is freely soluble in water but is almost insoluble in alcohol and ethyl acetate. It is used: In fungicides; as an intermediary in recovery of cadmium from zinc ore; in the electrodeposition of cadmium, copper, and nickel; in analytical tests as a catalyst for determining for arsenic, hydrogen sulfide and fumaric acids; in the manufacture of cadmium salts of longchain fatty acids; for stabilizing plastics, especially polyvinyl chloride; in the production of vacuum tubes, fluorescent screens, and phosphors; as an electrolyte in standard cells; in CdS, cadmium lithopone and cadmium sulfoselenide pigment production as a chemical intermediary; in cement formation, as a chemical accelerator; and in the manufacture of standard cadmium elements. In addition, cadmium sulfate has the ability to absorb hydrochloric acid from waste gases from chemical plants.

Cadmium sulfide (CdS; Chemical Services Registry No. 1306–23–6) also has many industrial uses. It occurs in nature as the mineral greenokite. It occurs as light-yellow or orange-colored cubic or hexagonal crystals. Its solubility in water is approximately 0.13 mg/100g at 18 °C. Some applications include: As a pure, inorganic photoconductor; as a pigment which is colorfast against light in glass; as a colorant for soaps, textiles, paper and rubber; in printing inks, ceramic glazes and fireworks; in x-ray fluorescent screens; in body temperature detectors; in rectifiers, transistors, photovoltaic cells, and in solar cells; in pigments which include phosphors; and, in lead-sealing glass-binders to provide smooth glass enamel surface that is durable and resistant to damage from development, cleaning and handling. Cadmium sulfide also provides stability against oxidation and UV radiation in specific industrial products.

A substantial amount of cadmium sulfide and cadmium sulfoselenide is used in pigments to yield colors ranging from yellow to deep red. These pigments have a high tolerance to heat and to light and are used primarily in coloring plastics, ceramics and paints. Cadmium stearate is used as a stabilizer in plastics because it inhibits the deterioration of the product. Cadmium compounds are also used in smaller amounts in electric batteries and electronic components. Of the many inorganic cadmium compounds, several are quite soluble in water.

V. Health Effects

A vast amount of literature exists which documents the adverse health effects from acute and chronic exposure to cadmium in both humans and animals. The primary adverse health effects which have been observed are lung cancer and kidney damage. This section on health effects will not attempt to describe every study ever conducted on cadmium toxicity. Instead, the most important studies will be reviewed and the testimony and comments submitted to the record of the rulemaking will be presented. For greater detail, the cited reviews and articles should be consulted.

A. Metabolism

Cadmium enters the human body by inhalation, by ingestion, and perhaps by absorption through the skin. Inhaled cadmium is more readily absorbed into the body than is ingested cadmium. Intake of cadmium by ingestion and skin absorption are considered to be of relatively less importance in occupational settings.

In occupational settings cadmium is inhaled in the form of either small particles of fume or larger particles of dust. The extent of deposition depends on the particle size. It is estimated that ten percent of the particles of approximately 5.0 micrometers mean mass diameter (MMD) are deposited in the lung, whereas 50 percent of the particles of 1.0 micrometer MMD are deposited in the lung. Of the proportion deposited, 20 to 25 percent is systemically absorbed. (Exs. 8–619; 8–086a, p. 107). Limited data on smokers indicate a high rate of absorption (10% to 50%) of inhaled cadmium (Exs. 8–86 and 29). Animal experiments have shown an absorption rate of between 10% to 60% of inhaled cadmium (Ex. 29). Thus, smoking habits and personal hygiene are of great importance as a source of indirect exposure in a cadmium-contaminated environment.

Many of the effects of cadmium are systemic. After initial exposure, inhalation, and absorption, cadmium is transported by the blood plasma, although the majority of the cadmium is bound to the blood cells. According to Clarkson et al.:

> Cadmium in blood is distributed between blood cells and plasma * * *. In persons with industrial exposure to cadmium and in cadmium-exposed experimental animals, cadmium in blood is found mainly in erythrocytes * * *. (Ex. 14–18, pp. 160–161)

Cross-sectional studies of workers who had varying durations of exposure at varying levels of exposure have yielded little definitive information about the kinetics of blood cadmium and the distribution of cadmium between the plasma and blood cells. Therefore, cadmium in blood is most accurately measured in whole blood.

After a sudden increase in exposure, cadmium in blood increases rapidly during the first three to four months and then reaches an apparent steady level which is likely to reflect the average exposure during those months. When high exposures cease, blood levels of cadmium decrease with two distinct half-time components. One component has a half-time of a few months and probably reflects the turnover rate of red blood cells. The other half-time

component is several years long and is likely to reflect body burden, presumably consisting of several components with half-lives varying from about one year in blood to about five years in other soft tissues (De Silva, Ex. 8–718; and Friberg, Ex. 8–068–B). Therefore, the transport of absorbed cadmium in blood is of crucial importance.

Cadmium transported to the liver induces the synthesis of metallothionein, a low molecular weight metal-binding protein. Cadmium becomes bound to this protein, forming a metal-protein complex which is then released back to the blood and transported to the kidney. In the kidney, the cadmium-metallothionein complex passes through the glomeruli and is reabsorbed by the proximal tubules. This complex can then be broken down by lysosomes, releasing unbound cadmium which can induce renal synthesis of metallothionein. In workers with only short-term exposures to low levels of cadmium, the cadmium will be bound again in the kidney to the locally produced metallothionein providing a protective effect from cadmium. However, after prolonged exposure, the binding process in the kidney becomes saturated leading to an increase in unbound cadmium which can result in toxic effects (Dr. Goyer, Tr. 6/6/90, pp. 129, 131).

Unlike other heavy metals such as mercury and lead, cadmium occurs in only one valence state, +2, and does not form stable alkyl compounds or other organometallic compounds of known toxicologic significance (Casarett, 1980, Referenced in Ex. 8–735, Casarett, 1986). Thus, it is elemental cadmium that is the toxic agent. In his testimony, Lars Friberg, M.D., Professor Emeritus at the Karolinska Institute in Stockholm where he was formerly Chairman of the Department of Environmental Health, an international expert and pioneer in the field of cadmium-induced kidney disease, past Chairman of the WHO task group on cadmium, and senior editor of a number of comprehensive monographs on cadmium, discussed the mechanisms by which cadmium is taken up by the human body and how cadmium ultimately affects the kidney. Dr. Friberg stated:

> One has firm epidemiological evidence, thanks to the data from Ellis and Roels * * * that there is an association between total cadmium in kidneys and effects * * *. (Tr. 6/6/90, p. 100)

The studies by Ellis and Roels are discussed below.

Regardless of the route of absorption or the type of cadmium compound, approximately one half to one third of the body burden of cadmium is found in the kidneys after chronic low-level exposure, with the highest concentrations found in the renal cortex (Ex. 8–086a, p. 168). After long-term exposure, one sixth and one fifth of the body burden are found in the liver and muscles, respectively. As exposure level increases, a greater proportion of the body burden of cadmium will be found in the liver relative to the kidney. Also, upon the onset of renal dysfunction, the level of cadmium in the kidney will decrease (Friberg, Tr. 6/6/90, p. 84). The half-life of cadmium in the liver, kidney and muscles is 5 to 15 years, 10 to 30 years, and more than 30 years, respectively. (Ex. 8–086a, p. 168).

B. Non-Carcinogenic Health Effects

1. Acute Effects

a. *Evidence in humans.* A variety of adverse health effects may result from acute exposure to cadmium compounds. The most widely recognized effects are seen in the respiratory system from the inhalation of cadmium fumes and dust. Acute pneumonitis occurs 10 to 24 hours after initial acute inhalation of high levels of cadmium fumes with symptoms such as fever and chest pain (Exs. 30, 8–086b, p. 4). In extreme exposure cases pulmonary edema may develop and cause death several days after exposure. Such symptoms have been reported among workers exposed to high concentrations of cadmium. For example, after a day's exposure to cadmium fumes, workers developed severe weakness, dyspnea, coughing and tightness of the chest. Chest radiographs showed signs of pulmonary edema (Ex. 8–41).

As in the case above, the exposure levels at which the adverse effects occurred were not recorded in many investigations of acute health effects from high cadmium exposures. Estimation of the exposure levels associated with acute respiratory effects has relied on measurements of the amount of cadmium found in the lung after death modified by assumptions about the proportion of cadmium fumes retained in the lungs. At one time, a lethal concentration of cadmium is considered to be not higher than (and probably lower than) 5 mg/m^3 over a period of eight hours (Exs. 8–41 and 29). This number was estimated by assuming that 11% of the cadmium fumes were retained in the lungs. Given that the victims were exposed for 5 hours, the average concentration was estimated to be 8.6 mg/m^3. This is equivalent to an 8-hour exposure of approximately 5 mg/m^3. Because this estimate rests on a number of assumptions used to derive this exposure level, however, there is some uncertainty as to the accuracy of this estimate. Also, the amount of cadmium measured in the lung of the fatal cases may have been higher than the amount necessary to cause death. It should also be noted that this type of estimate is for lethal concentrations, and that lower concentrations may give rise to acute symptoms and significant lung damage without resulting in death.

Little actual exposure measurement data are available on the level of airborne cadmium exposure that causes such immediate adverse health effects. More recent studies have revealed that an eight hour exposure to 5 mg/m^3 should not be regarded as the lowest concentration that can give rise to a fatal poisoning. It is reasonable to believe a cadmium concentration of approximately 1 mg/m^3 over an eight hour period is "immediately dangerous" (Exs. 8–86B; 29). Such exposures can ultimately be life-threatening. In response to questions during the hearing, George Kazantzis, M.D., Emeritus Professor of Occupational Medicine at the University of London, Honorary Consultant Physician at the Middlesex Hospital in London, and a member of the WHO task group on environmental health, testified that he found a statistically significant excess of worker deaths due to chronic bronchitis in his 17 plant cohort study in the U.K. These deaths were, in his opinion, directly related to high cadmium exposures of 1 mg/m^3 or more (Tr. 6/6/90, pp. 156–157).

Although there are little data on the lowest cadmium exposure level that may trigger an acute effect, it is known that a few days of cadmium exposure in excess of 200 μg/m^3 will result in elevated levels of cadmium in the blood and urine. Based upon his experience, Dr. Friberg said that an eight-hour time-weighted-average (TWA) exposure of 75–100 μg/m^3 should never be exceeded in order to prevent adverse health effects (Ex. 144–15).

Experimental animals exposed to various cadmium compounds through various routes of exposure have experienced acute pulmonary effects. In a number of studies reviewed by Friberg (Ex. 8–086b, p. 2), NIOSH (Ex. 4–02) and EPA (Ex. 8–619), cadmium exposures ranging from 5 to 10 mg/m^3 over 15 to 120 minute periods were sufficient to induce significant increases in lung weights indicative of pulmonary edema. Also, rats exposed to cadmium aerosol at 60 mg/m^3 for 30 minutes died within 3 days from pulmonary edema (Ex. 8–402). Multiple experimental studies confirm

these findings of acute pulmonary effects. In addition, animals injected with cadmium compounds have exhibited acute effects in the testes, ovaries, liver and blood (Exs. 8–420, 8–86B, 8–370, and 8–668).

2. Renal Effects

a. *Evidence in humans—introduction.* The human kidney is a filtration mechanism for the blood. It has three major functions that are vital to maintaining normal health: Removing wastes; preventing leakage of essential elements and chemical compounds from the body; and providing homeostasis. According to Robert A. Goyer, M.D., Professor and Chairman of the Department of Pathology at the University of Western Ontario, Chairperson of the World Health Organization (WHO) Task Force on Environmental Health Criteria for Cadmium in 1989 and coauthor of the WHO Environmental Health Criteria Document on Nephrotoxicity (1989), these:

* * * are the ones by which we measure the health of the kidney and the health of the person * * *. (Tr. 6/6/90, p. 123.)

The kidney cortex including the nephrons is the anatomic division of the kidney of most concern when considering cadmium's toxicity. Each nephron is a functional filtration unit of the kidney and is composed of glomeruli and tubuli. Each glomerulus is a collecting system made up of capillaries that filter the blood and prevent leakage of all large particles with a molecular weight greater than 30,000. The molecular weight of a molecule is the weight that is equal to the sum of the atomic weights of its constituent atoms. Normally, as blood passes through the kidney, high molecular weight proteins such as albumin, immunoglobulin G, and a variety of glycoproteins do not cross an intact glomerular basement membrane into the kidney tubule. The function of the proximal tubule is to filter out small organic compounds. These include essential electrolytes, metals, and elements that are essential to life, such as calcium, potassium, sodium, and magnesium, among others. The size of low molecular weight proteins and small essential compounds allows them to cross an intact glomerular basement membrane into the kidney tubule where they are routinely reabsorbed by the proximal tubule of the nephron. Only very small quantities of these are excreted in the urine.

Further down the tubule, in the distal portion, water balance is adjusted and urine is either concentrated or diluted. There are very fine capillaries along the tubule for the exchange of essential substances between the blood and the urine. It is in the tubule that the cells are most active metabolically and where most of the electrolyte exchange occurs. For example, the biologically active metabolites of vitamin D are produced primarily in the tubules, and altered vitamin D metabolism may result from cadmium-associated renal tubular dysfunction (Ex. 8–086).

The earliest form of cadmium toxicity occurs in the proximal portion of the tubule. According to Dr. Friberg:

The first sign of cadmium induced renal damage is tubular proteinuria with increased urinary excretion of low molecular weight serum proteins, such as beta-2 microglobulin * * *. At the same time there is a dramatic increase of cadmium in the urine * * *. (Tr. 6/6/90, p. 72)

Any of several small proteins in urine may be monitored as markers of kidney function: Retinol Binding Protein (RBP), Beta-2-Microglobulin (β_2-M), N-Acetyl-β_D-Glucosaminidase (NAG), and Metallothionein (MT). In the absence of elevated levels of these analytes, the kidney is considered to be functioning normally.

Retinol Binding Protein (RBP) is a low-molecular weight vitamin A transporting protein which is cleared from serum into glomerular filtrate and resorbed into renal tubular cells. β_2-M is a low molecular weight protein that is normally reabsorbed by the proximal tubule. Metallothionein (MT) is a metal-binding protein that correlates with cadmium and β_2-M levels. N-Acetyl-β_D-Glucosaminidase (NAG) is an analyte that may correlate well with cadmium levels under 10 micrograms per gram creatinine (μg/g Cr) (Ex. 30), but this finding is disputed (Ex. 148).

Only β_2-M is widely used as an early indicator of cadmium-induced kidney dysfunction. Carl-Gustav Elinder, M.D., Chairman of the Department of Nephrology at the Karolinska Institute, testified that measurements of β_2-M in urine constitute a very sensitive indicator of tubular damage. This is because a small decrease in tubular reabsorption from the normal 99.9% to 99% would result in a tenfold increase in the urinary excretion of this protein (Ex. 55).

Dr. Kazantzis, testifying for the Cadmium Council, stated that the earliest indicator of any effect of cadmium on the kidney is the increased excretion in the urine of a number of low molecular weight plasma proteins, and that this effect can be monitored by estimating the β_2-M or RBP concentrations in the urine (Ex. 19–43A).

As indicated by Drs. Friberg and Goyer, the finding of excess β_2-M proteins in urine in conjunction with findings of an elevated cadmium body burden, as indicated by elevated levels of cadmium in urine (CdU) and cadmium in blood (CdB), helps establish that kidney disease exists and that it is probably associated with cadmium toxicity. For example, Dr. Goyer testified that if both β_2-M is below 300 μg/g Cr and CdU is below 2 μg/g Cr, workers are likely to have no damage. Glomerular proteinuria, another form of cadmium-related kidney dysfunction, refers to the presence of high molecular weight proteins in the urine due to the increased permeability of the glomerulus (a "leaky" glomerulus) which allows the passage of the high molecular weight proteins into the proximal tubule. When high molecular weight proteins are not reabsorbed by the proximal tubule, the proteins are excreted in the urine. Glomerular proteinuria is considered to be a clinically significant form of kidney dysfunction that differs from tubular proteinuria (Exs. 8–080b, p. 63, 4–54). In some cases, glomerular and tubular damage can occur at the same time resulting in a mixed type of proteinuria.

The concept of a "critical concentration" of cadmium in the kidney has been used repeatedly throughout the medical literature on cadmium-induced kidney dysfunction. A critical concentration is a threshold which when crossed leads to adverse health effects. When the concentration of cadmium in the kidney exceeds the critical concentration, the effects of cadmium-induced kidney dysfunction start to occur in individuals (Ex. 144–3–C).

Dr. Goyer testified that according to his review of the literature, there is a:

* * * commonly coded critical concentration of cadmium for people for the so-called [population critical-concentration], where 50 percent of the working population that has a kidney concentration of 200 micrograms per gram of tissue would have detectable renal disease. And this seems to be about the same level in rats * * * in people there's a much wider variation in what that level * * * because there are people with different states of ability to make metallothioneine and different essential iron intakes * * * the variations that are reported by Roels and by Ellis in their human studies by neutron activation are from one to 300 or more micrograms * * *."(Tr. 6/6/90, pp. 130–131)

Despite individual variability, the concept of an individual's critical concentration of cadmium in the kidney has been well established. There is general agreement that the critical concentration in the renal cortex is about 200 μg/g of kidney cortex wet

weight. On the basis of autopsy studies, the WHO task group concluded that the critical level in the renal cortex necessary for the appearance of proteinuria ranged from 100 to 300 μg cadmium (Cd) with the likely estimate being 200 μg Cd/g wet weight, or 200 mg/kg, (Exs. 4–12, 8–440). Similarly, a review of autopsies and *in vivo* measurements, made through neutron activation analysis of human kidney tissues, showed that adverse effects first occur in the range of 170 to 200 μg Cd/g wet weight (Ex. 8–086b, p. 99). Roels et al., concluded that the "critical concentration" for renal cadmium cortex is found in the range 160 to 285 μg Cd/g. Above 285 μg Cd/g renal cortex, the probability is very high that all persons will show signs of renal dysfunction (Ex. 57–K). In animals, the concentration of cadmium in the renal cortex at which dysfunction first appears ranges from 100 to 300 μg Cd/g wet weight, with most species showing proteinuria at 200 μg Cd/g (Ex. 8–086b, p. 97). According to Clarkson et al.,:

> * * * the critical concentration of cadmium in renal cortex for a substantial (but unspecified) proportion of an exposed group of individuals has been estimated to be around 200 (μK/g) mg/kg (1.78 mmol/kg) both in animals and in humans * * *. Calculations for humans based on *in vivo* neutron activation analyses * * * [indicate] that about 10 percent of a population develops renal effects at concentrations of Cd in kidney cortex lower than 200 mg/kg wet weight * * * (Ex. 14–18, p. 157).

In a study by Ellis (Ex. 4–27), the cadmium body burden for each worker was determined through the direct measurement of the level of cadmium in the kidneys of workers with and without kidney damage. As noted by C.H. Hine, M.D., Medical Director of ASARCO, this technique, however, is "not of practical use" for routine monitoring (Ex. 107). A simpler, more commonly used method to evaluate whether a worker has approached this individual "critical concentration" is to use cumulative exposure to cadmium as a proxy for concentration of cadmium in the kidney cortex. Cadmium exposure histories and personal sampling data can be used to calculate a cumulative exposure level, as was done for members of the Ellis cohort. Despite the uncertainty inherent in estimating cumulative exposures from work histories, Ellis found a significant correlation between exposure and cadmium body burden as measured in the liver and the kidney.

b. *Review of the literature.* The authors of at least seven studies including Ellis sought to examine the relationship between cumulative cadmium exposure and kidney dysfunction. Rather than relate the concentration of cadmium in the kidney cortex to incidence of tubular proteinuria, these authors related cumulative cadmium exposure to incidence of tubular proteinuria. Exposures and responses in all seven studies have been well characterized. The seven major studies reviewed in depth below are: Kjellstrom et al. (Ex. 4–47); Falck et al., (Ex. 4–28); Ellis et al., (Ex. 4–27); Jarup et al., (Ex. 8–661); Elinder et al., (Ex. L–140–45); Mason et al., (Ex. 8–669–A); and, Thun et al., (Ex. 8–670). The data from these studies provide strong evidence that occupational exposures to all forms of cadmium are associated with kidney damage at similar cumulative exposure levels.

The seven primary studies cover five populations of cadmium-exposed workers. Excesses of low molecular weight proteins in urine were observed in all of these occupationally exposed populations. In each of these studies, the authors defined kidney dysfunction on the basis of biological markers prior to collecting and analyzing the data, and response was a dichotomous variable with workers separated into two categories: those with abnormal kidney function (i.e. dysfunction) and those with normal kidney function.

The findings of each study are dependent on the manner in which each researcher defined renal dysfunction; the tests used to identify the presence or absence of dysfunction; and the reference methodology used by each laboratory. In general, few studies of kidney function among occupationally exposed cohorts have relied upon RBP, NAG, or MT. Of the seven major epidemiological studies reviewed here, only one (Mason et al, Ex. 8–669–A) relied upon RBP as a marker of kidney function. In Mason's study, β_2-M was also measured. In the other six studies, β_2-M was the analyte used to distinguish between normal and abnormal kidney function.

The results from the studies are strikingly similar. The authors found that the type of abnormality and the prevalence of abnormality was similar, at similar exposure levels, regardless of the type of cadmium compound to which workers were exposed. These results, from difference worker populations in different countries, demonstrate that the kidney is one of the major target organs of cadmium toxicity. The studies also imply that there is agreement on what constitutes abnormality.

i. *Kjellstrom et al. (Ex. 4–47).* Kjellstrom conducted a study of kidney dysfunction among 240 workers in a Swedish battery factory. The cohort was comprised of 197 men and 43 women. The factory had two separate plants: the material plant that manufactured raw material for the battery electrodes and the assembly plant that made the complete electrodes and batteries. The primary exposures at the factory were to cadmium oxide (CdO) dust and nickel hydroxide [$Ni(OH)_2$] dust. A group of 87 lumbermen and shipyard workers belonging to the same occupational health clinic served as controls.

A spot urine sample was collected from each study participant, and the pH and specific gravity were immediately determined. Twenty of 327 urine samples collected for the dose-response study had pH <5.6 and had to be buffered with a phosphate buffer with pH of 7.6 to increase the pH over this level. Then the samples were frozen. β_2-M in urine was measured using the Phadebas β_2-M microtest from Pharmacia.

Kidney dysfunction was determined by the level of β_2-M in urine because increased urinary excretion of β_2-M would be caused by cadmium, not nickel hydroxide dust exposures (Friberg, 1950, referenced in Kjellstrom). Kjellstrom classified a worker as having abnormal proteinuria if the level of β_2-M exceeded 290 μg/liter, the upper 95% tolerance limit for the control population. Among men in the assembly plant, 25% exceeded this limit, a significantly higher proportion than the 3.4% of controls who exceeded this limit ($p<0.001$). The proportion of men in the material plant who exceeded the limit was 50%, also statistically significantly greater than the proportion in the control group ($p<0.001$). Among women, only 2.3% of those in the assembly plant exceeded the limit.

Exposure estimates based on area samples were provided by the battery factory management for the years 1949 to 1972. Kjellstrom estimated that cadmium exposures in the assembly plant had been about 50 $\mu g/m^3$ since 1963. Area and personal air sampling data in the material plant were sparse. The first data available were from 1968 when two area samplers found cadmium exposures to be 7 and 31 μg Cd/m^3. Some personal sampling data were also available from 1972. Information on the continuity of exposure, time of first employment, and exposure duration was provided by the safety engineer of the factory.

Workers were classified into four categories according to exposure histories. The non-exposed group consisted of six workers who worked on the premises of the plant but were found to have virtually no exposure to

cadmium. The intermittently exposed group consisted of forty-nine workers. Finally, there were two groups of workers who had spent time in jobs where exposure to cadmium was continuous. These two groups were comprised of 15 workers from the material plant and 170 workers from the assembly plant.

The 185 people in the continuously exposed groups were the primary subjects of this study. Nine of these workers were from Yugoslavia. Their results were analyzed separately from the other exposed workers because in some parts of Yugoslavia, Bulgaria, and Rumania, tubular proteinuria is endemic (Balkan nephropathy). Forty-eight workers (26%) had started employment in 1974, three years before this study was conducted. Fifty-two workers (28%) had been employed since before 1952. The majority of these 52 had been moved to "cadmium-free" work before the study was conducted.

Workers exposed continuously to cadmium at levels of 50 $\mu g/m^3$ for 6 to 12 years showed a higher prevalence of proteinuria than controls (19% vs. 3.4%). For the continuously exposed groups, prevalence of proteinuria increased with length of time since first employment; the prevalence was 6.2%, 18%, and 57% among workers with less than 6 years, 6 to 22 years, and greater than 22 years of exposure, respectively.

Using data on 129 exposed workers who responded to a smoking questionnaire and for whom β_2-M levels and length of employment information was available, the effects of smoking on kidney function were evaluated. The prevalence of proteinuria among non-smokers was 13.3 percent, while among current smokers it was 32.4 percent. Thus, the prevalence of kidney dysfunction among current smokers was about two and one-half times higher than among non-smokers. The authors noted that the total dust concentrations in workroom air may have been high enough to cause substantial contamination of the workers' hands and bodies, and that tobacco products contaminated by a worker's hands could account for the higher prevalence of tubular proteinuria among smokers. The authors' conclusion that the increased incidence of dysfunction among smokers was not attributable to the cigarettes themselves is supported by findings from the Falck study, (Ex. 4–28), described below.

ii. *Falck et al. (Ex. 4–28).* Falck studied 33 male workers in a refrigeration compressor plant in the U.S. The plant produced refrigeration compressors with silver brazed copper fittings. These fittings were brazed either by hand or on an automated line. Falck reported that according to plant managers, neither process has changed since the automatic assembly line was installed in 1968. Air monitoring data for this plant had been collected by the Michigan Department of Industrial Health since 1961. All samples used for estimating exposures for individual workers were from the worker's breathing zone. The mean calculated exposure on the automatic line for an 11 year period was 39 $\mu g/m^3$, $\pm$7.6 (SE). Mean exposures on the manual line, 110 $\mu g/^3$, $\pm$25.5 (SE), were significantly higher.

Work histories were obtained for each subject participating in the study, and time on each of the production lines was calculated for each worker. Cumulative cadmium exposure was calculated for each worker by multiplying the mean cadmium exposure of a line with the number of years a worker spent on that line.

A spot urine sample was collected for each worker, and an aliquot of urine was analyzed for β_2-M. The pH was recorded and adjusted above 5.5 where necessary. All samples were then frozen. β_2-M in urine was measured using the Phadebas microtest by Pharmacia. Blood samples were collected, and blood and urine cadmium levels were measured using a flameless atomic absorption spectrophotometer (Varian). Three workers had histories of diabetes, kidney infection, or hypertension and were eliminated from the statistical analyses. Descriptive statistics on the workers are presented in Table V–1.

TABLE V–1.—DESCRIPTIVE STATISTICS FOR A COHORT OF 30 EMPLOYEES AT A REFRIGERATION COMPRESSOR PRODUCTION PLANT [a]

	Normal kidney function mean (95% CI) [b]	Abnormal kidney function mean (95% CI)	P Value [c]
N	23	7	
Age (years)	49 (47, 51)	53 (51, 55)	.13
TWE [d] ($\mu g/m^3$ years)	459 (332, 634)	1137 (741, 1737)	.02
Smoking Habits (pack-years)	14 (9, 19)	24 (14, 34)	.07
Urine Ratios			
Protein/Creatinine (mg/g)	34 (26, 43)	246 (132, 456)	<.001
β_2-Microglobulin/Creatinine (μ/g) [e]	53 (31, 90)	6375 (1115, 36463)	<.001
Cadmium/Creatinine ($\mu g/g$)	11 (10, 13)	16 (8, 36)	0.07
Serum Ratios			
Creatinine/Serum (mg/100ml)	1.1 (1, 1.2)	1.4 (1.2, 1.1.7)	0.003
β_2-Microglobulin/Serum ($\mu g/ml$)	2 (1.6, 2.4)	2.3 (1.8, 2.8)	0.32

[a] Data taken from Falck et al (Ex. 4–28).
[b] Mean and 95% confidence intervals are presented. Means for age and smoking habits are arithmetic means; all others are geometric means. Confidence intervals are constructed from arithmetic standard deviations for age and smoking; all others are from the geometric standard deviations.
[c] P-value is associated with a test of differences between group means.
[d] Time-weighted inhalation exposure estimate (i.e. dose).
[e] β_2-Microglobulin measured in urine, based on spot samples.

Forty-one males who were not known to be exposed to cadmium were selected to serve as controls. Reference values calculated from the spot urine and serum samples collected from the controls, were established at: glucose >130 mg/g Cr; total protein >173 mg/g Cr; or β_2-M >629 $\mu g/g$ Cr. Eight workers' results exceeded the reference values, and for these eight, a 24 hour urine sample was obtained. Reference values for 24 hour samples were established at glucose >250 mg/24 hour; total protein >188 mg/24 hour; or β_2-M >400 μg/liter urine from 24 hour samples from 7 controls.

Seven workers out of 33 were found to have abnormal kidney function (21%).

This was significantly higher than the 7% of controls who had abnormal spot urine results. The average cumulative time-weighted exposure for workers with abnormal renal function was 1,137 $\mu g/m^3$-yrs, significantly higher than the average cumulative time-weighted exposure of workers with normal renal function (p=.02). Furthermore, as cumulative exposures increased, the prevalence of kidney dysfunction increased.

According to the authors, the change in renal function observed in the workers was not age related since there was no statistically significant difference in age between workers with abnormal and normal renal function (p=.13). Information on smoking habits was collected from questionnaires and medical histories. The authors found that the difference in pack-years smoked between the workers with abnormal and normal renal function was also not statistically significant (p=.07). Despite this the authors stated that ingestion of cadmium was not likely to be significant given the manufacturing process and plant layout. If Kjellstrom's hypothesis that contamination of smoking products was a likely explanation of increased proteinuria among smokers in his study, it would explain why no differences were noted in renal function between smokers and non-smokers in this study by Falck.

iii. *Ellis et al. (Ex. 4–27).* Ellis conducted a study of 82 male workers at a U.S. cadmium smelter. The cohort was comprised of 51 active workers and 31 retired workers employed in production, non-production, office, and laboratory work. Each cohort member completed a health history questionnaire, took a physical exam, gave specimens for blood and urine tests, and provided 24-hour urine samples. Urine samples were pH adjusted and frozen. Kidney function was judged to be abnormal if urinary levels of β_2-M exceeded 200 $\mu g/g$ Cr or if total urinary protein levels exceeded 250 mg/g Cr. These limits were chosen to comply with those reported by Roels *et al.* (Ex. 57–K). In addition, the cadmium content of the left kidney and the liver was measured directly by the *in vivo* prompt-gamma neutron activation technique. Information on smoking habits was not available.

Eighteen active workers (35%) and twenty-three retired workers (74%) were classified as having abnormal kidney function. Descriptive statistics for the entire cohort are presented in Table V–2.

TABLE V–2.—DESCRIPTIVE STATISTICS FOR A COHORT OF 82 ACTIVE AND RETIRED CADMIUM SMELTER EMPLOYEES [a]

	Normal kidney function mean (SD) [b]	Abnormal kidney function mean (SD)
Active Workers		
N	33	18
Age (years)	42.6 (13.3)	53.6 (6.8)
Duration of Exposure (months)	141 (118)	264 (105)
TWE [c] ($\mu g/m^3$-years)	105 (9.0)	1690 (2.7)
Renal Cadmium [d] ($\mu g/g$)	125 (2.8)	230 (2.0)
Liver Cadmium (ppm)	11.3 (2.8)	63.9 (1.5)
Retired Workers		
N	8	23
Age (years)	69.0 (8.3)	67.9 (6.9)
Duration of Exposure (months)	342 (75)	329 (103)
TWE [c] ($\mu g/m^3$-years)	379 (3.3)	3143 (3.6)
Renal Cadmium [d] ($\mu g/g$)	148 (2.1)	169 (1.7)
Liver Cadmium (ppm)	14.0 (3.1)	33.6 (2.9)

[a] Data taken from Ellis et al (Ex. 4–27).
[b] Mean (Standard Deviation) presented. Means and SDs for age and duration of exposure are arithmetic means and SDs. All others are geometric means and SDs.
[c] Time-weighted inhalation exposure estimate (i.e. dose).
[d] Renal cortex cadmium concentration; assumes 145 g weight for the total kidney and a 1.5 ratio between cortex and total kidney concentration.

Cadmium exposure histories based on employment records, area monitoring techniques, and personal sampling data were obtained for all 82 exposed workers. The chronological record of each worker's job assignments was obtained from personnel files at the smelter. Cumulative exposure estimates were developed for each member of the cohort from industrial hygiene data provided by Smith (Ex. 4–64). That is, for each worker, the time-weighted inhalation exposure (TWE) was calculated by multiplying the duration of exposure in a given work area (t_i) by the estimated inhalation exposure for that area and year (E_i) and then summing these values to obtain cumulative exposure or

$$TWE = \Sigma (E_i T_i).$$

For the actively employed workers, a significant correlation ($r=0.70$, $p<0.001$) was observed between TWEs and liver cadmium burden. Furthermore, whenever a worker's liver burden exceeded 40 ppm and exposure exceeded 400–500 $\mu g/m^3$-yr, there was evidence of renal abnormalities. The highest correlation was obtained between the kidney cadmium burden data and TWEs for the active workers without evidence of kidney dysfunction ($r=0.83$, $p<0.001$). The percentage of workers with renal abnormalities was found to increase as exposure increased. (See Section VI—Quantitative Risk Assessment.)

iv. *Jarup et al (Ex. 8–661).* Jarup sought to model the relationship between cadmium exposure and tubular proteinuria. The Swedish battery factory where Jarup conducted his investigation was the same as where Kjellstrom conducted his study of cadmium exposure and kidney dysfunction. Jarup collected data from 326 male and 114 female cadmium battery workers with at least three months of employment between 1931 and 1982. The only other criterion for being included in the study was that at least one measurement of urinary β_2-M must had been made for each worker.

The response variable used in this study was β_2-M levels in urine. β_2-M in urine was measured using the

radioimmunoassay (RIA) method, Phadebas, developed by Pharmacia. Since β_2-M levels had been measured since 1972, the β_2-M level for any worker was taken as the average of all β_2-M levels measurements made for that worker. Workers with β_2-M levels exceeding 310 μg/g Cr were judged to have tubular proteinuria.

Jarup considered three distinct measures of exposure in his analysis. First, he considered cadmium in air which had been measured since 1947. Using information on length of employment obtained from company files for each worker, Jarup estimated cumulative cadmium dose by multiplying the length employment in a particular work area by the average air concentration of cadmium for that area and time period and then summing the product of these for each worker.

The second measure of exposure considered by Jarup was cumulative blood cadmium dose. Data on blood cadmium levels together with other laboratory data had been collected at regular intervals since 1967. Cumulative blood cadmium dose was estimated as the average blood cadmium concentration times the times the number of months employed.

The final measure of exposure considered by Jarup was an alternative method for calculating cumulative blood cadmium dose. The study authors hypothesized that because air cadmium concentrations were much higher in the 1940's and 1950's, workers hired before 1967, particularly those hired before 1950, would have had higher blood cadmium concentrations during those periods, and therefore simply multiplying average blood cadmium concentrations by number of months employed might underestimate the true cumulative blood cadmium concentrations. The alternative measure the study authors devised was to use linear regression to model the relationship between year and blood cadmium levels for each worker and then to extend the observed relationship to the years for which there was no data. Forty workers show evidence of tubular proteinuria. The results of Jarup's analyses indicated that a dose-response relationship exists between kidney dysfunction and exposure regardless of the measure of exposure used, but they also suggested that cumulative blood cadmium level may be a more sensitive indicator of cadmium-induced renal dysfunction than cumulative cadmium in air. Table V–3 shows the prevalence of tubular proteinuria among workers grouped according to cumulative airborne cadmium exposure and cumulative cadmium exposures in blood estimated using the alternative method.

TABLE V–3.—CUMULATIVE AIRBORNE CADMIUM EXPOSURES BY PERCENT PREVALENCE OF KIDNEY DYSFUNCTION

Cumulative exposure (CumExp)(μg/m³-years)	Mean Cum Exp	Number people	Percent dysfunction[1]
<359	131	3	1.1
359-<1,710	691	7	9.2
1,710-<4,578	3,460	10	23.3
4,578-<9,458	6,581	10	32.3
9,458-<15,000	12,156	5	31.2
<15,000	21,431	5	50.0

[1] Percent dysfunction=number with dysfunction divided by number in that exposure category times 100.

In his paper, Jarup noted that on the basis of data from other studies of the relationship between cadmium in air and kidney dysfunction, it has been estimated that exposure to an average workroom concentration of 50 μg Cd/m³ for 10 years would result in a prevalence of tubular proteinuria of 10%. The corresponding prevalence found in Jarup's study is only 4%, (95% CI=2%–8%), which is also somewhat less than the prevalence reported by Kjellstrom in an earlier study of the same factory (Ex. 4–47). Jarup suggests several possible explanations for why the prevalence of tubular proteinuria is lower in his study than in the others.

First, the earlier studies were all cross-sectional meaning that only workers employed at a certain point in time were included. This study by Jarup included all workers employed for more than three months at the factory. Computation of the cumulative airborne cadmium concentration took into account the varying exposure conditions over time, and the study included workers with low cumulative exposures. In addition, this study had more information about the prevalence of kidney dysfunction among the retired workers, although data on the retired workers were not evaluated separately.

Second, the other studies were relatively small while the Jarup study is one of the largest. This means that the confidence intervals computed for the prevalence observed in the other studies must be wide. According to Jarup, the consequence of this is that even if the variations may seem great between the various studies, there are probably no significant differences between the dose-response relationships reported in the various studies.

Third, the Jarup study was conducted in a battery factory whereas most other studies were carried out in other industrial environments, such as smelters, where the fraction of respirable dust is probably significantly larger. Jarup suggested that this might affect the results of his study. However, given that there are probably no significant differences between the dose-response relationships reported in the various studies, the effect of particle size distributions may be a relatively unimportant factor in the etiology of kidney dysfunction.

Another factor that may have affected the β_2-M levels among these workers is the method used to collect and handle urine samples. The authors did not report whether the samples were spot or 24 hour samples, or what the urine pH was per β_2-M sample. If urine samples were collected over a 24 hour period with pH less than 6.0, it is more likely that the β_2-M would have been degraded and erroneously low β_2-M levels would have resulted. If spot samples were used and pH was not adjusted, then β_2-M would also have been degraded.

Dr. Gunnar Spang, who works for a medical organization providing occupational health services to a large Swedish NiCd battery manufacturer and who was a co-author of this study, testified at the hearing. He submitted post-hearing comments on the number of cases, per cumulative exposure category, that, in his opinion, were cases associated with cadmium exposures (Exs. 58 and 80). His comments alter the findings somewhat. (See Table V–4.)

TABLE V–4.—CUMULATIVE AIRBORNE CADMIUM EXPOSURES OF PERCENT PREVALENCE OF KIDNEY DYSFUNCTION

Cumulative exposure (CumExp)(μg/m³-yrs)	Mean cum exp	Number people	Percent dysfunction[1]
<359	131	0	0
0359-<1,710	691	2	2.6
1,710-<4,578	3,460	9	20.9
4,578-<9,458	6,581	9	29.0
9,458-<15,000	12,156	5	31.2
>15,000	21,431	5	50.0

[1] Percent dysfunction=number with dysfunction divided by number in that exposure category times 100.

He stated that in the lowest dose group with mean dose =131 μg/m³-yrs, no cases were cadmium-related. Thus, the response rate in this group would be zero, as opposed to 1.1% reported by Jarup et al. For the remaining dose groups, the response rates would be as follows: 2.6% for the group with mean dose=691 μg/m³-yrs; 20.9% for the group with mean dose=3460 μg/m³-yrs; 29% for the group with mean dose=6581;

31.2% for the group with mean dose=12156; and 50% for the group with mean dose=21431. Thus, according to Dr. Spang, a dose-response still exists, but the dose-response curve is less steep than the curve described by Jarup. Also, according to Dr. Spang, for a 45 year exposure of about 77 $\mu g/m^3$, one-fifth of all workers would have tubular proteinuria. However, for workers with about 15 $\mu g/m^3$ exposures, over a 45 year working lifetime, the prevalence of kidney dysfunction would be about 2.6%, according to Dr. Spang, as opposed to 9.2%, indicated by Jarup. Dr. Spang testified that several workers in this plant had kidney stones, but he was unable to determine whether the prevalence was greater than that in the general population (Tr. 7/17/90, p. 217).

In summary, workers with tubular proteinuria had a proportionately higher serial CdB dose than their fellow workers without renal dysfunction but with the same cumulative air cadmium dose. Some workers will be more sensitive than others, i.e., their cadmium uptake will be greater than other workers, and, at lower exposures, will have tubular proteinuria. (See section VI—Quantitative Risk Assessment).

v. *Elinder et al., (Ex. L-140-45).* Elinder conducted a study of 58 male and 2 female cadmium-exposed workers employed at least five years before 1978 at a factory that produced coolers, radiators, and heat exchangers in Sweden. The plant began using cadmium containing solders in 1955, but the plant was demolished and a new plant was constructed in 1973. By 1978, the whole workplace had been seriously contaminated and had to be repainted and renovated to reduce the cadmium exposures at the workplace. Since 1978, no cadmium-containing products have been used in this plant. No exposure data from the plant were available before 1976.

β_2-M in urine was measured using a radioimmunoassay (RIA) method, Phadebas, developed by Pharmacia. The night before the health examination each person was asked to ingest about four grams of sodium bicarbonate (Samarin®). This was done in order to produce a pH exceeding 5.6 in the morning urine sample the next day because β_2-M is degraded in acidic urine.

No control group was included; according to Elinder the normal concentration of cadmium and β_2-M in urine and blood has been well documented. Based on the literature the authors selected 300 $\mu g/g$ Cr, the upper 95—97.5 percentile for the urinary excretion of β_2-M among persons without tubular dysfunction, as the upper limit of normal.

Each individual's exposure to cadmium was assessed by a group of four people (one representative from the company, one from the employees, and two from the local labor inspectorate) who had knowledge of the previous conditions in the plant and of the type of work carried out by each worker during the whole period when cadmium was in use.

Exposure was classified into four categories; high, medium, low, and no cadmium exposure. Before 1955 and after 1978 there was no exposure to cadmium at all. Based on the measurements in 1976, it was assumed that high, medium, and low exposure was about 0.5, 0.15, and 0.05 mg/m^3, respectively. The number of years each worker had been occupied in activities that gave high, medium, low, or no exposure were recorded. A cumulative dose was estimated for each worker expressed in milligrams of per cubic meter-years (mg/m^3-yr).

Elinder categorized renal dysfunction based upon β_2-M levels into "slight proteinuria" (β_2-M>300 $\mu g/g$ Cr) or "pronounced proteinuria" (β_2-M levels>1,000 $\mu g/g$ Cr). He then used these two categories of degree of kidney dysfunction to evaluate the relationship between years of exposure and prevalence of β_2-microglobulinuria. Results from this analysis, presented in Table V-5, indicate that as years of exposure increase, the prevalence of slight and more pronounced proteinuria increases.

TABLE V-5.—PREVALENCE OF β_2-MICROGLOBULIN IN RELATION TO YEARS OF CADMIUM EXPOSURE

Years of exposure	Slight proteinuria [1] No. (percent) [2]	Pronounced proteinuria [3] No. (percent) [4]
4 to 7	1 (6)	0 (0)
8 to 13	6 (46)	3 (23)
14 to 19	6 (46)	5 (38)
>20	11 (65)	6 (35)
All	24 (40)	14 (23)

[1] Number of people in that category; β_2> 300 $\mu g/g$ Cr<1000 $\mu g/g$ Cr.
[2] Percent is the number of cases of slight proteinuria divided by the total number of people with the corresponding number of years of exposure.
[3] Number of people in that category; β_2>1000 $\mu g/g$ Cr.
[4] Percent is the number of cases of more pronounced proteinuria divided by the total number of people with the corresponding number of years of exposure.
Source: Elinder et al., (Ex. L-140-45).

When cadmium in urine and proteinuria were evaluated, a close relationship was found. At a urinary cadmium excretion exceeding 10 $\mu g/g$ Cr the proportion of cases of β_2-m excretion exceeding 300 $\mu g/g$ Cr (slight proteinuria) was 88% and the proportion exceeding 1000 $\mu g/g$ Cr (pronounced proteinuria) was 75%.

Elinder evaluated the relationship between age and years of exposure. The prevalence of β_2-microglobulinuria (β_2-M) was increased in workers aged over 59, suggesting that age was a potential confounder in the assessment of the relationship between dose and response. To examine the role of age in this relationship Elinder fit a multiple regression model relating urinary β_2-M excretion to age and cumulative dose using the model:

$\log(\beta_2\text{-M}) = [a \times \text{age}] + [b \times \text{cumulative dose}] + [c]$. Elinder concluded that dose was related to β_2-M-U, whereas age was not. In further analysis, when workers over age 59 were excluded, the prevalence of β_2-microglobulinuria still increased with the number of years of exposure, with the estimated cumulative dose, and urinary cadmium. Thus, Elinder concluded that age is not an important confounding factor in this study.

Degree of kidney dysfunction was also related to cumulative cadmium exposure and to CdU. Table V-6 shows that for cumulative cadmium exposure, the prevalence of slight and more pronounced proteinuria both increase as exposure increases. Indeed, Table V-6 suggests that there is a 19% risk of developing tubular proteinuria (urinary β_2> 300 M/g Cr) at a cumulative cadmium dose of less than approximately 22 $\mu g/m^3$ over a 45 year working lifetime (1 mg/m^3/45 years=22.2 $\mu g/m^3$.) If exposures are between 22 and 44 $\mu g/m^3$ over a 45 year exposure period, this risk increases to 32%.

TABLE V-6.—PREVALENCE OF β_2-MICROGLOBULIN IN RELATION TO CUMULATIVE CADMIUM EXPOSURE

Cum exposure (mg/m^3-yrs)	Slight proteinuria [1] No. (percent) [2]	More pronounced proteinuria [3] No. (percent) [4]
<1	3 (19)	0 (0)
1 to <2	7 (32)	4 (18)
2 to <3	4 (44)	3 (33)
3 to <5	<5 (62)	4 (50)
≥	5 (100)	3 (60)
All	24 (40)	14 (23)

[1] Number of people in that category; β_2>300 $\mu g/g$ Cr <1000 $\mu g/g$ Cr.
[2] Percent is the number of cases of slight proteinuria divided by the total number of people with the corresponding level of cumulative exposure.
[3] Number of people in that category; β_2>1000 $\mu g/g$ Cr.
[4] Percent is the number of cases of more pronounced proteinuria divided by the total number of

people with the corresponding level of cumulative exposure.

Source: Elinder et al., (Ex. L-140-45).

Finally, Table V-7 shows that for CdU, like age and cumulative cadmium exposure, the prevalence of slight and more pronounced proteinuria both increase as CdU increases. Table V-7 indicates that CdU above 15 μg Cd/g Cr are associated with very high risks of kidney dysfunction (82% for β_2-M levels above 1,000). (For further discussion of this study see Section VI—Quantitative Risk Assessment).

TABLE V-7.—PREVALENCE OF β_2-MICROGLOBULIN IN RELATION TO CADMIUM LEVELS IN URINE

CdU (μg/g Cr)	Slight proteinuria [1] No. (percent) [2]	More pronounced proteinuria [3] No. (percent) [4]
≤2.1	1 (7)	0 (0)
2.1 to ≤5.1	3 (25)	0 (0)
5.1 to ≤10.1	6 (33)	2 (11)
10.1 to ≤15.1	4 (80)	3 (60)
>15.1	10 (91)	9 (82)
All	24 (40)	14 (23)

[1] Number of people in that category; β_2>300 μg/g Cr <1000 μg/g Cr.
[2] Percent is the number of cases of slight proteinuria divided by the total number of people with corresponding levels of CdU.
[3] Number of people in that category; β_2>1000 μg/g Cr.
[4] Percent is the number of cases of more pronounced proteinuria divided by the total number of people with corresponding levels of CdU.

Source: Elinder et al., (Ex. L-140-45).

vi. *Mason et al. (Ex. 8-669-A).* Mason conducted a detailed investigation of renal function among 75 male workers with at least one year of employment as cadmium brazers at a copper-cadmium alloy production facility in the U.K. Seventy-five unexposed workers, matched to the exposed workers on age, sex, and employment status, served as controls. Although not individually matched for smoking history, the proportion of current, former, and non-smokers was similar among the exposed and the controls as was the number of pack-years smoked. Only 11 exposed workers were employed in the production of alloy at the time of the study; for many of the exposed workers, occupational exposure had ceased some years before the study was undertaken.

The medical evaluation for both groups of workers included a questionnaire, a medical examination, blood and urine analyses, and *in vivo* measurements of kidney and liver cadmium levels by prompt-gamma neutron activation. Retinol binding protein (RBP) was measured using the enzyme linked immunosorbent assay (ELISA) and β_2-M was measured with a Phadebas β_2-M microtest kit by Pharmacia.

Measurements of cadmium in air of the factory had been taken between 1951 and 1983. Personal and area sampling data were available from 1964 to 1983. Pre-1964 exposures were estimated after discussion with occupational health physicians, occupational hygienists, representatives from management and the work force, and took into account changes in production and ventilation. Questionnaires and plant data were used to obtain each worker's exposure history. A cumulative exposure index was calculated by summing the products of length of time employed at a particular exposure level multiplied by exposure level.

Significant increases in the urinary excretion of albumin, RBP, β_2-M, N-acetyl-β_D-glucosaminidase (NAG), alkaline phosphatase, gamma-glutamyl transferase, and significant decreases in the renal reabsorption of calcium, urate, and phosphate were found in the exposed group compared with the referent group. Measures of glomerular filtration rate (GFR) creatinine clearance, serum creatinine, and β_2-M indicated a reduction in GFR in the exposed population. Many of these tubular and glomerular function indicators were significantly correlated with both cumulative exposure index and liver cadmium burden.

RBP was the biological marker chosen to measure renal function. RBP was not age-related in the unexposed population. The upper 95th percentile for urinary BP calculated for the unexposed population, 40 μg/mmol Cr or 356 μg/g Cr, was the level used to define workers with tubular proteinuria. The frequency of tubular proteinuria in exposed workers, grouped according to a cumulative exposure index, is presented in Table V-8.

TABLE V-8.—PREVALENCE OF KIDNEY DYSFUNCTION BY CUMULATIVE CADMIUM EXPOSURE

Cumulative exposure [1]	Number normal [2]	Number abnormal [3]	Percent abnormal
<500	96	5	4.9
>500 to <1000	14	0	0.0
>1000 to <1500	3	5	62.5
>1500	4	20	83.3

[1] Cumulative Exposure measured in μg/m³-year.
[2] Normal measured by Retinol Binding Protein (RBP) <40 μg RBP/mmol Cr.
[3] Abnormal measured by Retinol Binding Protein (RBP)>40 μg RBP/mmol Cr.

Mason used a two phase linear regression model to regress a variety of biochemical markers on cumulative cadmium exposure and on liver cadmium in order to identify an inflection point signifying a threshold level above which changes in renal function occur. (The appropriateness of this and other models is discussed further in Section VI—Quantitative Risk Assessment.) Urinary total protein, retinol binding protein, albumin, and β_2-M all suggested a threshold at about the same cumulative exposure level of 1100 μg/m³-yrs whereas changes in the tubular reabsorption of urate and phosphate suggested a higher cumulative exposure threshold.

In 1991, Hartley and Mason 1991 (Ex 150) extended the Mason study to include a follow-up analysis of the effects of cadmium exposure on changes in glomerular filtration rate (GFR). In this paper, recently submitted for publication, six indicators of glomerular function were evaluated. These included three glomerular filtration variables, (β_2-M in serum, creatinine in serum, and creatinine clearance), and three different estimates of creatinine clearance. The exposed population was split into five groups of approximately equal size on the basis of cumulative cadmium exposure: 0–250 μg/m³-yrs, 500–1000 μg/m³-yrs, 1000–3300 μg/m³-yrs and greater than 3300 μg/m³-yrs. The one-sided 95% interval in the referent population was used as the cut-off point for normal or abnormal results with respect to each glomerular filtration variable. For those variables correlated to age, the equation representing the 95% one-tailed prediction boundaries of regression with age was used to indicate normality or abnormality. Thus a 5% frequency of abnormality would be expected in the referent population. The results are presented in Table V-9.

TABLE V-9.—FREQUENCY OF ABNORMALITY FOR GLOMERULAR FILTRATION VARIABLES PERCENT ABNORMALITY BY TYPE OF GFR INDICATOR

Cum. Exp. $\mu g/m^3$-yrs	β_2 S	Cr. S	Cr Cl	Gault	Hull	Mawer
Control	6	5	5	3	3	3
<250	6	6	6	.....	6	.....
250 to 500	.....	.....	.....	.....	.....	.....
500 to 1000	.....	22	22	14	8	14
1000 to 3300	24	24	28	18	12	18
>3300	60	54	32	46	40	46

Dose-response and dose-effect relationships were observed over the range of exposures encountered, with a significant decrease in GFR at cadmium exposures greater than 1000 $\mu g/m^3$-yrs. The results show a trend towards increasing abnormality in the six indicators of GFR used, with exposure to cadmium of greater than 500 $\mu g/m^3$-yrs.

vii. *Thun et al.*, (Ex. 19–43–B). Thun conducted a study of kidney function among workers at a cadmium smelter in Denver, Colorado. The smelter recovers cadmium from "bag house" dust, a waste product of nonferrous smelters. The cadmium from the bag house dust is further refined into cadmium metal or highly purified cadmium oxide and cadmium sulfide. Forty-five male workers participated in the study. Seventeen of these were production workers and two were salaried workers employed at the smelter at the time of the study. Of the remaining 26, 18 were former long-term production workers and 8 were former short-term production workers. Thirty-two male hospital workers of similar age, ethnic and geographic background served as controls.

To estimate each worker's cumulative exposure to airborne cadmium, detailed work histories were linked with industrial hygiene data collected through 1976 and updated company measurements through 1985. The length of time spent working in a particular department was multiplied by the estimated cadmium exposure level in that department. The sum of these products represents the worker's cumulative exposure or dose, adjusted for respirator use as described by Smith (Ex. 4–64). Workers at this smelter were subjects in a number of studies of the health effects of cadmium, and a more detailed description of their exposures may be found in the discussion of the carcinogenicity of cadmium in the Health Effects section of this preamble.

Workers were required to fill out a questionnaire, provide spot urine and blood samples, and take a pulmonary function test. Fewer cadmium workers smoked than did controls (38% vs. 44%, $p=0.6$), and of those who smoked, the workers reported smoking fewer pack-years than the controls (14.6 vs. 22.1, $p=0.29$). Indices of renal tubular function included urinary excretion of β_2-M, retinol binding protein (RBP), calcium, and phosphate. Additional analyses for evidence of tubular injury and glomerular function rate (GFR) were performed. Urinary β_2-M was measured by the radioimmune assay (Pharmacia), and in order to standardize for urine volume, results were corrected to microgram of analyte per gram of creatinine. Level of lead in blood were also measured. Urine pH levels were not reported.

Workers were classified as having abnormal renal function if any of the following conditions were met: β_2-M >486 $\mu g/gr$ cr; serum creatinine ≥ 1.4 mg/dl; RBP >321 $\mu g/g$ Cr; tubular reabsorption of phosphate (TRP) <69.4%; or, tubular reabsorption of calcium (TRC) <97.56%. The limits for TRP and TRC are the lower 95% confidence level on the geometric mean of these markers estimated from the control population. The limits for β_2-M, RBP, and creatinine are the upper 95% confidence level on the geometric mean of these markers estimated from the control population. Thun found that 24 of the 45 study subjects (53%) suffered some form of renal abnormality. In addition, Thun reported that two of 32 controls (6%) were abnormal by this definition (personal communication, 11/91). The results from this study are in Table V–10.

TABLE V–10.—SEVENTY-SEVEN PARTICIPANTS, CADMIUM SMELTER STUDY [1]

	Cadmium Workers	Unexposed	P value
Number	45	32	.....
Age (mean±SD)	54.4±15.5	50.1±13.0	0.2
Percent Hispanic	58%	16%	0.0001
Percent Current Smokers	38%	44%	0.6
Pack-years (mean±SD)	14.6 (19.8)	22.1 (29.4)	0.29
Years Cadmium Work (GM, range)	19 (1–38)	0	.....
Cumulative Exposure (mg/m^3/days) [2]	604 (0–5383)	0	.....
Blood Cadmium, $\mu g/l$ (GM±SD)	7.9±2.0	1.2±2.0	<0.0001
Urine Cadmium, ($\mu g/gr$ Cr) (mean±SD)	9.3±6.9	0.7±0.7	<0.0001
β-2 in Urine, ($\mu g/gr$ Cr) (GM±SD)	470 (4.4)	190 (1.6)	0.0001
RBP in urine, ($\mu g/gr$ Cr) (GM±SD)	266 (7.3)	88 (1.9)	0.0012
Systolic BP, (mm Hg) (GM±SD)	134 (1.14)	120 (1.14)	0.0004
Diastolic BP, (mm Hg) (GM±SD)	80 (1.13)	73 (1.13)	0.002
Blood Lead, ($\mu g/dl$) (GM±SD)	11.9±1.8	8.3±1.4	0.0013

[1] Exs. 8–670 and 19–43–B

[2] Converted to $\mu g/m^3$-years, (Thun, Ex. 83), by multiplying mg/m^3 by 1000 and dividing 365, or (604 times 1000 divided by 365=1655 divided by 45=36.8) 1,655 $\mu g/m^3$-years; or 36.8 $\mu g/m^3$ for 45 years.

Several medical conditions were reported more frequently by the cadmium workers than by the controls including kidney stones (18% vs. 3%, p=.07), prostatic disease (20% vs. 6%, p=.09), diabetes (18% vs. 3%, p=.07), and hypertension (38% vs. 16%, p=.03).

The relationship between cumulative exposure and the prevalence of various renal abnormalities was examined, and a dose-response relationship was observed. The prevalence of abnormalities increased with cumulative exposure to cadmium with multiple renal abnormalities becoming apparent in persons with cumulative exposure ≥ 300 mg/m³-day (or 822 μg/m³-yrs which is equivalent to an exposure of 18 μg/m³ over a 45 year working lifetime). (See Section VI—Quantitative Risk Assessment).

viii. *Summary.* A summary of the major findings from these seven studies follows. For cumulative exposures up to 500 μg/m³-yrs, the prevalence of kidney dysfunction ranged from 4% to 32%; for cumulative exposures above 500 to 1,000 μg/m³-yrs, the prevalence of kidney dysfunction ranged from 9% to 66%; and for cumulative exposures above 1,000 μg/m³-yrs, the prevalence of kidney dysfunction ranged from 21% to 55%.

Taken together, the data from the seven studies would seem to refute the position of a number of commentors regarding what level of airborne cadmium represents a "safe" level. For example, Dr. Kazantzis has stated that exposure to 20 to 30 μg/m³ of cadmium for 8 hours per day for 45 years (900 to 1350 μg/m³-yrs) is the no-observed-effect level for kidney effects (Ex. 19-43A). On behalf of the Cadmium Council, Dr. Spang testified that workers will not have renal dysfunction if their cumulative cadmium exposures are up to 900 μg/m³-years (which is equivalent to 20 μg/m³ for 45 years). Dr. Spang cited Sweden's standard of 20 μg/m³ for respirable cadmium as adequate to prevent kidney dysfunction (Tr. 7/17/90, p. 217). Dr. Bond, who directs the medical surveillance program of two cadmium compound manufacturers in the United States, questioned the results from studies that show dysfunction at relatively low cadmium exposures. He did not agree with the definition of pathology used in these studies. Dr. Bond stated that a 20 μg/m³ PEL would be reasonable and would not result in significant renal disease (Ex. 119).

Despite the opinions of these eminently qualified physicians, other record evidence indicates that the exposure level which they propose as "safe", 20 μg/m³ for 45 years, (900 μg/m³-years) would result in a high prevalence of kidney dysfunction, in excess of 10% (Exs. L-140-50; 4-47; 4-27; L-140-45). OSHA also notes that the Swedish physician Dr. Elinder stated that the proposed OSHA regulations were better than the present regulations in Sweden (Ex. 55). Finally, while the Agency acknowledges Dr. Bond's objection to the definition of pathology used in these studies, OSHA is impressed by the consistency of the definition of pathology used by the various researchers in their studies which have been published in peer-reviewed journals.

Drs. Thun, Elinder, and Friberg reviewed these seven occupational studies together and concluded that the studies could be compared and pooled despite the fact that they varied in size, in criteria used to define kidney dysfunction, and in the amount of available exposure information. Pooling the data from the seven studies allowed the authors to obtain an estimate of the prevalence of dysfunction among workers with low cadmium exposures. In most of the studies, the number of workers with small exposures was too small to obtain a reliable estimate of prevalence, and therefore these workers had to be combined with workers with higher levels of exposure.

Results from the pooled analysis are presented in Table V-11.

TABLE V-11.—OCCUPATIONAL STUDIES RELATING KIDNEY DYSFUNCTION TO CUMULATIVE EXPOSURE TO CADMIUM [1]

Study	N	Prevalence [2] at exposures [3]			
		100 to 199	200 to 299	300 to 399	400 to 499
Ellis, 1835	82	0/3		0/3	2/3
Thun, 1989	45	0/2	0/4	0/2	0/1
Falck, 1983	33		1/3	1/2	0/7
Kjellstrom, 1977	[4] 240				
Jarup, 1908	440	1/110	1/35	1/25	0/20
Elinder, 1985	60			0/2	0/1
Mason, 1988	75	2/10	0/6	0/8	1/2
Pooled Data (%)		2.4%	4.2%	4.8%	8.8%

[1] Source: Thun, M.J., Elinder, C.G., Friberg, L., "Scientific Basis for an Occupational Standard for Cadmium," *Am. J. Ind. Med.*, 20: 629-642, 1991, (Ex L-140-50).
[2] Prevalence = number diagnosed as having kidney dysfunction in a specific exposure category compared the total number of workers in that exposure category.
[3] Exposures = in units of μgCd/m³-years.
[4] Included in Jarup.

The prevalence of kidney dysfunction among workers with cumulative exposures between 100-199 μg/m³-yrs was 2.4%. For workers with exposures between 200-299 μg/m³-yrs, the prevalence was 4.2%. For workers with cumulative exposures between 300-399 μg/m³-yrs, the prevalence was 4.8%. For workers with cumulative exposures between 400-499 μg/m³-yrs, the prevalence was 8.8%.

Thun et al. also plotted the observed prevalence from each of the seven studies by cumulative exposure. The data show a similar pattern between dose and response for each of these studies. The prevalence of kidney dysfunction increased sharply at cumulative exposures above 500 μg/m³-yrs. In all of the studies except Jarup, the prevalence of kidney dysfunction was about 10% when the cumulative exposures reached about 450 μg/m³-yrs.

c. *Other studies.* Not all of the epidemiological studies on the renal effects cadmium that were submitted to the record had large enough cohorts or adequate dose data to assess the relationship between exposure and dysfunction. Nonetheless, these studies are useful for assessing the relationship between a variety of biological markers and kidney dysfunction. Specifically, these studies can be used to assess the efficacy of a variety of biological markers as a determinant of the critical concentration of cadmium which induces kidney dysfunction.

i. *The NIOSH Health Hazard Evaluation of Gates Nickel-Cadmium Battery Plant (Ex. 128).* The National Institute of Occupational Safety and

Health (NIOSH) conducted two medical surveys of workers exposed to nickel and cadmium dusts in a nickel-cadmium battery plant in the U.S. The first survey was done in February 1989 and was completed by 39 male workers in the plate-making and pressed plate areas of the plant where there is potential for exposure to high levels of cadmium. A group of 36 males, selected by the company and thought to have no cadmium exposure, served as controls. The second survey was done in October 1989 and was complete by 91 workers in areas with either low or high exposure to cadmium but minimal exposure to nickel.

Both studies entailed administration of a questionnaire; measurement of height, weight, and blood pressure; and collection of first-voided morning urine samples and fasting serum samples. The questionnaire collected information about age, history of diabetes, hypertension, smoking, non-steroidal anti-inflammation drug use, and previous occupational exposures to cadmium, lead, and solvents. No information was provided on the pH of the urine samples or on how the urine samples were collected and handled.

In the first survey, the biologic makers selected to assess renal function included urinary phosphorous, β_2-M and RBP which were creatinine-standardized to adjust for variations in urine concentrations. Levels were considered abnormally high if they exceeded the arithmetic mean level plus two standard deviations in the unexposed population, standardized for creatinine.

The biologic markers used in the second survey were similar to those used in the first survey except that urinary excretion of β_2-M was not measured. Other indices of renal tubular function used in the second survey included urinary excretion of calcium and glucose. The laboratory reference values for normal limits of β_2-M and total protein were urinary β_2-M<300 μg/liter and total protein <135 mg/l. For RBP the reference values were less clear and covered a wide range of levels, e.g. urinary RBP<30–190 μg/l or 0–406 μg/l.

Exposure data which were provided by the company were noted by NIOSH to raise several questions. One of these was whether exposures, which were reported as 8-hour TWAs, truly represented 8-hour TWAs. The company reported to NIOSH that in order to compensate for their normal 12-hour workshifts, the company modified the OSHA PEL by reducing it by 33 percent. Another problem was that because of a lack of consistent workstation terminology, considerable manual compilation of the computerized data was necessary in order to reconstruct each worker's exposure history. Finally, NIOSH believed that actual work practices may have differed from those reported on the printouts.

No consistent differences in urinary proteins between the cadmium-exposed group and the non-exposed group were observed in either survey. Furthermore, cumulative airborne cadmium levels as calculated from the exposure data provided by the company did not show a significant relationship with any measure of renal function used in this investigation. In both surveys, however, the analysis of cadmium-exposed workers with CdU levels greater than 10 μg/g Cr (23% in the first survey and 28% in the second survey) compared to those with less than 10 μg/g Cr clearly suggested that the group with higher levels of CdU did have modest elevations of the urinary proteins.

In the first survey, 3 of the 39 cadmium-exposed workers (8%) demonstrated evidence of cadmium-induced renal dysfunction. Two of these workers had elevated levels of only albumin in their urine, while the third had elevated levels of β_2-M and RBP as well. In the second survey, 3 of 91 cadmium-exposed workers (3%) had elevated levels of urinary albumin, but none had elevated levels of urinary RBP. In comparison, of the 69 workers in both surveys with no or low exposure, none had evidence of abnormally high levels of urinary proteins.

The possibility of glomerular dysfunction was suggested in the first survey by a slightly higher mean serum creatinine in the exposed group than in the control group. NIOSH noted that when one considers that the non-exposed group was significantly older than the exposed group, the difference in serum creatinine may actually be larger than reported.

The NIOSH authors concluded that cadmium-induced renal dysfunction is evident in this study population. They also found that subclinical effects such as significant increases in mean levels of the urinary tubular enzymes, N-acetyl-β_D-glucosaminidase (NAG; p=.05) and urinary alanine aminopeptidase (AAP; p=.02), are apparent in cadmium-exposed workers with CdU levels above 10 μg/g Cr compared to those below this level.

ii. *Lauwerys et al, (Ex. 8–718).* Lauwerys conducted a study of 11 workers employed in a small factory in Belgium which used or produced cadmium oxide, cadmium metal, cadmium sulfide, and various cadmium salts. Workers were observed for 13 months. Although the factory employed only seven workers on the production side, Lauwerys was able to follow a total of eleven workers because four workers left the plant and four new employees were hired during the study period.

The total airborne concentration of cadmium at the various work locations was very high. The median values ranged from 110 to 2125 $\mu g/m^3$. Reliance on personal protective devices was minimal; the authors noted that only one worker wore a mask during work. In view of the hygiene practice of the workers, the authors considered that ingestion of cadmium may have played a role in the overall exposure.

During the observation period, 150 personal air samples were collected. Each sampling period lasted two to nine hours. The airborne cadmium levels sampled in this factory ranged from 88 to 14,232 $\mu g/m^3$ with overall median, mean, and standard error of 565, 1119, and 125 $\mu g/m^3$, respectively. Omitting the most extreme result (14,232 $\mu g/m^3$), the values ranged from 88 to 6276 $\mu g/m^3$ with overall median, mean, and standard error were 563, 1031, and 90 $\mu g/m^3$, respectively.

Cadmium concentrations in workers' blood and urine were measured. Because of the employee turnover and the high degree of collaboration requested from the workers (repeated blood and urine sampling) it was not possible to survey all the workers during the same length of time. On the other hand, Lauwerys considered the high employee turnover to be an advantage for this type of survey because it allowed the follow-up of newly employed workers.

An evaluation of renal function was performed once for each of the current workers (n=8). To do so, urine was collected over a known period of time (usually 4 to 5 hours). The volume of urine was measured, and 10 ml was immediately transferred into a tube containing 1 ml of 0.4 mole/liter phosphate buffer, with a pH of 7.6. These samples were stored at −20 °C and β_2-M was measured using the radioimmunoassay (RIA), Phadebas from Pharmacia. Aliquots of urine were taken for the determination of creatinine, total proteinuria, amino aciduria, and some enzymatic activities (B-galactosidase, lactate dehydrogenase, alkaline phosphatase, total and tartrate resistant acid phosphatase, and catalase). The remaining volume was then stored at 4°C with 0.1 percent sodium azide as preservative until ultrafiltration for electrophoresis and quantitation of individual proteins (orosomucoid, albumin, transferrin, and IgG). A sample of blood was also taken

for determining the creatinine level and the same enzymatic activities and specific proteins in plasma as in urine. Despite the great scatter of the individual results, Lauwerys stated that for most workers exposed for more than 250 days, the average cadmium in urine levels were similar. The overall mean cadmium level was 161 μg/g Cr with a standard error of 9 μg/g Cr, regardless of type of exposure. All but one of these workers were exposed primarily to cadmium oxide. The one not exposed to cadmium oxide was exposed primarily to cadmium sulfide.

According to Lauwerys, the results of this study indicate that an integrated exposure of 1500 to 3000 $\mu g/m^3$-yrs leads to kidney disturbances and/or renal lesions. Lauwerys also concluded that workers whose exposure is such that CdU never exceed 15 μg/g Cr would not develop kidney lesions.

To evaluate the mechanisms by which cadmium is taken up into the blood and urine in new workers, Lauwerys studied four new workers. One worker was followed for only 30 days. This worker, who wore a respirator, was exposed to cadmium oxide dust and salts (mean cadmium concentrations in air were 1829 $\mu g/m^3 \pm 528$; the median exposure level was 1167 $\mu g/m^3$). This worker exhibited a much lower increase of cadmium concentration in blood and urine than the other three new workers. Lauwerys indicated that this worker was more motivated to follow better hygiene practices (handwashing, no smoking at work) than the other workers and this limited his total exposure.

Results of biological monitoring for the other three workers are presented in Table V–12.

TABLE V–12.—CADMIUN IN BLOOD AND CADMIUM IN URINE LEVELS [1] IN NEW WORKERS EXPOSED IN A PLANT PRODUCING VARIOUS CADMIUM COMPOUNDS BY EXPOSURE LEVEL AND TYPE OF EXPOSURE AND SMOKING HABITS OF WORKER

Worker	Mean air [2]	Median air [2]	Smoker status [3]	Exp. type [4]	CdB-20 [5]	CdB-140 [6]	CdU-20 [7]	CdU-140 [8]
A_1	1329±436	613	S	A	30	120	10.0	17.2
A_2	2043±452	1926	S+	B	20	120	7.5 [9]	20 [10]
A_3	2031±263	1827	NS	B	50	105	25.0	25

[1] from visual review of figures (Ex. 8–718).
[2] μg Cd/m^3.
[3] S=smoked<1 pack/day; S+=smoked>1 pack/day; NS=non-smoker.
[4] Main Type of exposure: A=Cadmium oxide dust and fume; cadmium carbonate powder; cadmium salts; B=cadmium oxide dust;
[5] cadmium in blood levels after approximately 20 days of exposure, in μgCd/liter whole blood.
[6] cadmium in blood levels after approximately 140 days of exposure, in μgCd/liter whole blood.
[7] cadmium in urine levels after approximately 20 days of exposure, in μCd/gram creatinine.
[8] cadmium in urine levels after approximately 140 days of exposure, in μgCd/gram creatinine; average of four samples taken on days 130, 140, 142, and 144;
[9] average of two samples taken on days 10 and 24;
[10] average of samples taken on day 138 and 146 of exposure.

Regarding cadmium in blood levels, Lauwerys concluded that after the start of exposure, the concentration of cadmium in blood increases linearly up to 120 days and then levels off. Kjellstrom (1977, referenced in Ex. 8–718) found a similar evolution of cadmium concentration in blood with time among workers newly exposed to a much lower level of cadmium dust, about 50 $\mu g/m^3$. Kjellstrom reported, however, that the steady state level (about 3 μg/100 ml) was five times lower than that found in the workers examined in Lauwerys study.

Kjellstrom's findings are not surprising given the fact that the cadmium pollution in the Lauwerys plant was significantly higher than that in the cadmium-nickel battery factory investigated by Kjellstrom (1977). One can conclude that when equilibrium is reached, the cadmium level in blood is a good indicator of the average intake during recent months. This was also confirmed by Lauwerys by the finding that in three workers, the blood cadmium levels measured before and after a leave of absence of 4 weeks were not significantly different.

Dr. Lauwerys calculated the linear regressions between the duration of exposure and the cadmium levels in blood for the various phases identified (two for blood). Since cadmium levels in blood of workers exposed for more than 120 days are mainly a reflection of exposure, Dr. Lauwerys expected that no significant correlation between duration of exposure and cadmium levels in blood during phase 2 would be found. The observed relationship between cadmium in blood and exposure in phase 2 was not statistically significant. Thus, levels of cadmium in blood reflect recent exposures, but if exposures have been very high, will not decrease significantly, at least over four weeks.

Regarding cadmium in urine, Lauwerys (Ex. 8–718) concluded that the interpretation of the urine data is certainly less straightforward than that for blood. For one thing, the kidney function of the workers must be taken into consideration since it is known that kidney lesions may be associated with an increased urinary excretion of cadmium.

Dr. Lauwerys calculated the linear regressions between the duration of exposure and the cadmium levels in urine for the various phases identified (four for urine).

Dr. Lauwerys proposed the following hypothesis to explain the evolution of cadmium concentration in urine found during this survey. In workers newly exposed to high levels of cadmium, phases 1 and 2 are concomitant with a rapid and marked increase of cadmium body burden probably associated with an induction of metallothionein. As this binding process becomes progressively saturated, a sharper increase in cadmium concentration in urine occurs (phase 3) which eventually, if high exposure persists, will be mainly a reflection of recent cadmium intake (phase 4) rather than an indicator of body burden. Dr. Lauwerys noted that the beginning of the second phase, during which the cadmium binding sites become progressively saturated, corresponds to a urinary concentration of cadmium of approximately 15 μg/g Cr. This would suggest that as long as this level is not exceeded in male workers exposed to cadmium the saturation of all the body binding sites is not yet reached. If the binding occurring during phase 2 is a true detoxication process, which Dr. Lauwerys indicated remains to be confirmed, one would expect that workers whose exposure is such that cadmium in urine never exceeds 15 μg/g Cr would not develop kidney lesions. This hypothesis is in agreement with Lauwerys' previous clinical observations of signs of kidney damage

in some workers who excreted more than 15 μg Cd/g Cr (Lauwerys et al. 1974). Hence for adult males occupationally exposed to cadmium, Lauwerys proposed a tentative biological threshold of 10 μg Cd/g Cr in urine. The validity of this proposal is confirmed by the correlation between CdU and cadmium in kidney found in 309 Belgian workers whose cadmium in kidney was measured *in vivo* by neutron activation. It was found that a cadmium concentration in renal cortex between 200 and 250 ppm, considered as the critical level, corresponds to a CdU concentration of approximately 10 to 15 μg Cd/g Cr (Roels et al. 1979).

However, Dr. Lauwerys stated that it should be stressed that this biological threshold is proposed only for adult males occupationally exposed to cadmium and does not necessarily apply to other groups of the general population, e.g., women after menopause and children, whose sensitivity to cadmium could be different.

Lauwerys findings agree with those of De Silva (Ex. 8–716) who noted that the urinary cadmium concentrations rise and fall with exposure, probably with a delay of several months.

iii. *Roels et al. (57–K).* Roels studied the effects of cadmium on male workers employed in one of two Belgium zinc-cadmium plants. Two hundred and sixty-four workers (264) were included in the analyses. Of these, 236 were active employees (Group A) and 28 were either retired or had been removed from jobs where they were exposed to cadmium (Group R).

To assess the cadmium pollution at the plants, airborne cadmium concentrations were measured with static air samplers at each of the principal worksites. In one plant, cadmium concentrations ranged from 3 to 67 $\mu g/m^3$, and in the other plant, they ranged from 5.8 to 168 $\mu g/m^3$. When monitoring was conducted at the worker's breathing zone, these levels were much higher.

For each worker, cadmium concentrations in the liver and in the kidney were measured *in vivo* by neutron capture gamma-ray analysis using the transportable measurement system developed at the University of Birmingham, U.K. Cadmium in the blood and cadmium, β_2-M, albumin, total protein, and calcium in the urine were also measured. For each urine sample, an aliquot of 5 ml was immediately transferred into a tube containing a buffer with a pH of 7.6 and stored at −20 °C until β_2-M levels and albumin were measured. β_2-M was measured by radioimmunoassay using the Phadebas microglobulin test developed by Pharmacia.

Workers were considered to have abnormal kidney function if their total urinary proteins exceeded 250 mg/g Cr, if their β_2-M exceeded 200 μg/g Cr, or if their albumin exceeded 12 mg/g Cr. These criteria were derived from a group of 88 unexposed workers whose urinary cadmium levels were below 2 μg/g Cr.

One hundred and forty-nine (149) of the active workers were engaged in jobs not directly related to cadmium production and these workers were found to have normal renal function. The remaining 87 active workers were involved in cadmium production daily, and of these, 15 (17%) had signs of renal dysfunction.

Examination of the cumulative frequency distributions and the correlations between the various biological parameters in different subgroups led the authors to the following conclusions: (a) Calciuria is not much different among the subgroups; (b) CdB mainly reflects recent exposure to cadmium in the absence of cadmium-induced renal damage; (c) CdU follows the body burden of cadmium but increases proportionately much more in workers with renal dysfunction particularly when signs of tubular dysfunction are present; and (d) cadmium in the liver is proportional to duration and intensity of cadmium exposure in workers without as well as with renal dysfunction. The study authors also concluded that renal cortical cadmium does not differ between cadmium workers with and without renal dysfunction, but the observation on which this conclusion is based can be explained by a progressive decrease of cadmium in the kidney cortex after the onset of the renal damage.

The results of this investigation support the concept of a critical concentration of cadmium in the kidney cortex which must be achieved before dysfunction occurs. That concentration was found to range from 160 to 285 ppm in this study. When the critical concentration exceeds 285 ppm, the probability is very high that all persons will show signs of renal dysfunction. This study also demonstrated that in the absence of kidney dysfunction, CdU is correlated with the body burden of cadmium ($r=0.59$), but that CdB is not.

On the basis of the interrelationships among cadmium in the liver, cadmium in the kidney cortex, CdU, and the other biological indicators of renal function, Roels concluded that the probability of developing cadmium-induced renal dysfunction in male cadmium workers appears to be very low when the critical CdU level of 10 μg/g Cr is not regularly exceeded. This CdU level corresponded to an average cadmium body burden of 160 to 170 mg.

iv. *Roels et al. (Ex. 12–38A).* In order to assess the significance of the early renal changes induced by chronic exposure to cadmium, Roels conducted a study of 23 retired workers at two non-ferrous smelters in Belgium. These workers had been removed from jobs entailing exposure to cadmium oxide as dust and fume (Ex. 57–K). They had been removed from exposure either because the level of β_2-M in urine exceeded 300 μg/l ($n=18$) or because the level or RBP in urine exceeded 300 μg/l ($n=17$). In addition, 8 workers had levels of albumin in their urine in excess of 20 mg/l. At the time of removal from cadmium exposure, serum creatinine concentrations were normal in 18 workers (<13 mg/l), marginally elevated in 3 workers (between 13 and 14 mg/l), and significantly elevated in 2 workers (>20 mg/l).

The average length of occupational exposure to cadmium was 25 years for these 23 workers with a range from 6 to 41.7 years. Workers had been removed from exposure for 6 years on average before they had their first follow-up examination. The mean age at first follow-up examination was 58.6 years with a range from 45.5 to 68.1 years. During each of five follow-up surveys conducted annually, workers were questioned about their health status and drug consumption, and a sample of venous blood (20 ml) and urine (100 ml) was collected. The results of the five annual follow-up surveys are included in Table V–13.

TABLE V-13.—CHARACTERISTICS AND BIOLOGICAL PARAMETERS OF 23 MALE SUBJECTS WITH SIGNS OF CADMIUM INDUCED RENAL CHANGES, WHO WERE REMOVED FROM EXPOSURES FOR 6 YEARS: SUMMARY OF FIVE-YEAR FOLLOW UP SURVEYS

Characteristic	First	Second	Third	Fourth	Fifth
CdU[1]	22.2±2.9	16.0±2.2	15.5±1.6	15.6±2.0	18.0±2.9
CdB[2]	14.3	11.8	10.1	9.3	9.7
β_2U[3]	1292	1260	1684	1918	1743
RBPU[4]	1146	801	829	1396	1351
CrU[5]	1.37	1.23	1.52	1.34	1.48

[1] Cadmium in urine, mean ± SEM, μg/liter urine.
[2] Cadmium in blood, μg/liter whole blood.
[3] Beta 2 microglobulin in urine (μgβ_2/g Cr), standardized to grams creatinine given in row 5.
[4] Retinol binding protein in urine (μgRBP/g Cr), standardized to grams creatinine given in row 5.
[5] Creatinine in urine (μg/liter).

This study by Roels confirmed that cadmium-induced proteinuria is irreversible. For the 23 workers, the levels of urinary RBP, β_2-M, and albumin, which were significantly elevated at the time of the first survey following removal from exposure, had not returned to normal levels five years later. In addition, the study found that serum alkaline phosphatase activity significantly increased during the five year follow up period which may reflect an interference of cadmium with bone metabolism, possibly secondary to a reduction in the conversion of 25-hydroxcholecalciferol to 1,25-dihydroxycholecalciferol by the kidney. The most important finding, however, was a significant increase over time in creatinine and β_2-M levels in serum which would indicate a progressive reduction of the glomerular filtration rate (GFR) despite removal from exposure.

Roels estimated that the GFR decreased on average by 31 ml/min/1.73 m^2 in the workers he studied during the five years of follow-up. Based on the work of others, Roels stated that in the age range of 45 to 75, the expected decline over five years should normally not exceed 6.5 ml/min/1.73 m^2. For each of the workers in the study, the reduction in their estimated GFR was, on average, about five times greater than this expected level. Interestingly, it was not more pronounced in workers with impaired renal function at the start of the study than it was in those with subclinical signs of renal damage.

v. *Roels et al. (Ex. 149).* In this study, Roels sought to determine whether an internal dose of cadmium that has not yet induced microproteinuria could affect the filtration reserve capacity of the kidney. Internal dose of cadmium was reflected by cadmium concentration in urine. Microproteinuria was defined as a significantly increased urinary excretion of various plasma proteins: β_2-M>300 μg/g Cr or RBP>300 μg/g Cr, or albumin>15 mg/g Cr, or a combination of these. The subjects in this study were 108 workers at two zinc-cadmium smelters in Belgium with occupational exposed to cadmium. To be included in the study, the exposed workers must have been exposed to cadmium for one year without interruption and must have been excreting more than 2 μg CdU/g Cr. Also, they could not have been exposed to other known nephrotoxins.

One hundred and seven (107) workers with no occupational exposure to cadmium served as controls. To qualify as a control, a worker should never have been occupationally exposed to any nephrotoxins. The level of cadmium in the urine of a control was required to be below 2 μg/g Cr and there could be no sign of microproteinuria. The control workers were closely matched to the exposed workers on age, and care was taken to see that both groups had similar socioeconomic (education, salary) and environmental (place of residence) characteristics.

A detailed occupational and medical questionnaire was given to each study participant. In addition, data on each worker's dietary habits during the week before the study was also collected. In order to be included in the final statistical analyses, participants in the study must have complied scrupulously with the study protocol that required them to refrain from taking analgesics, and their medical history must not have shown any pathological condition that might have influenced renal function.

During the 30 minutes prior to the baseline test, a spot urine sample (100 ml) was collected. An aliquot of 4 ml was immediately transferred to a tube containing 0.4 ml phosphate buffer, pH 7.6, and kept at −20 °C until the analysis of β_2-M, RBP, and albumin were performed. These proteins were measured by automated assays relying on latex particle agglutination.

Because early changes in glomerular function cannot be detected by the measurement of basal GFR, Roels developed a test to assess the filtration reserve capacity of the kidney and to detect any early renal changes induced by cadmium. In order to do this, Roels defined the filtration reserve of the kidney as the difference between baseline GFR and the maximal GFR induced by an adequate stimulus such as an acute oral load of proteins or an infusion of amino acids. The maximal GFR obtained during such stimulation would thus represent the maximum filtration capacity. When Roel's test was applied to his study subjects, the results confirmed the observation in previous studies that the age-related decline of the baseline and maximal GFR is accelerated in male workers with cadmium induced microproteinuria.

Another analysis was performed for workers less than age 50 and over age 50. Microproteinuria was present in 20 cadmium workers, all older than 50. It was found, however, that a renal cadmium burden that has not yet caused microproteinuria does not impair the filtration reserve capacity of the kidney.

In conclusion, this study indicates that the age related decline of the baseline and maximal GFR is exacerbated in the presence of cadmium-induced microproteinuria. The investigation supports Roels' previous estimate of the threshold effect concentration of CdU (10 μg/g Cr), which is intended to prevent the occurrence of microproteinuria in cadmium exposed male workers. Roels noted that this conclusion, however, may not be extrapolated to the general population because there are indications that in an occupationally active male population, the influence of the healthy worker effect may lead to an underestimation of the risk of cadmium for other groups of the general population. Also, sensitive workers may not be adequately protected if CdU levels exceed 10 μg/g Cr.

vi. *Bernard and Lauwerys (Ex. 35).* Bernard and Lauwerys studied 25 male workers who had been removed from jobs with exposure to cadmium when they were found to have elevated levels of β_2-M, RBP, or albumin in their urine.

The serum levels of creatinine and β_2-M in these workers were found to increase significantly with time. Over a five year period, the average level of creatinine in serum increased from 12 mg/l (SE=1.1 mg/l) to 15.5 mg/l (SE=2.2 mg/l), and the average level of β_2-M in serum increased from 1.89 mg/l (SE=0.12 mg/l) to 3 mg/l (SE=0.42 mg/l). The average levels of serum creatinine in two groups of 23 age-matched controls after five years were found to be 11.3 mg/l and 11.2 mg/l, and the average levels of serum β_2-M for these two groups were found to be 1.9 mg/l for both groups. Thus, age could not account for the increase observed in the exposed workers.

The GFR was estimated according to Wibell et al., as referenced by Bernard. All workers showed a decrease in estimated GFR which ranged from 9 to 78 ml/min/1.73 m^2 over the five year observation period. The average decrease of GFR over that period amounted to 31 ml/min/1.73 m^2, a value which is about five times greater than that observed for the normal population. Investigations of cadmium-exposed workers in Belfium and the U.S. have demonstrated that a low or high molecular weight proteinuria is likely to develop in 10 percent of exposed subjects when the concentration of the metal in the renal cortex reaches about 200 ppm. The corresponding critical levels in urine and blood have been estimated at 10 μg/gr Cr and 10 μg/liter whole blood (lwb), respectively (Ex. 57–K). Once it has appeared, according to Drs. Bernard and Lauwerys, cadmium proteinuria is in most cases irreversible. Follow up studies indicate that the progression of renal dysfunction after cessation of exposure is very slow. Bernard and Lauwerys, in their recent five year prospective study, demonstrated that despite this slow evolution, cadmium nephropathy may progress to renal insufficiency.

vii. *Toffoletto et al. (Referenced in 19–43A).* Toffoletto presented a paper on the effects of renal function from occupational exposure to cadmium at a conference on heavy metals in Edinburgh in 1989. Toffoletto studied 91 workers exposed to cadmium between 1981 and 1988 in an Italian factory producing and processing cadmium alloys. Periodic measurements of environmental cadmium concentrations had been made for 13 years, and information was available from a biological monitoring program that had been in operation for 8 years. Only subjects with three or more years of exposure or with three measurements of CdU or CdB were included in the study.

The authors used biological monitoring results from a control population to establish the upper limit of normal for CdB and CdU levels: 2.3 μg/liter whole blood (lwb) and 3.0 μg/liter urine (l urine), respectively. At the time of this study, the biological limit values recommended for CdB and CdU were 10 μg/lwb and 10 μg/l urine, respectively. Elevated β_2-M levels above 260 μg/l were used as an indicator of early tubular damage. For β_2-M analyses, urine samples were adjusted for pH, and β_2-M levels were measured using the Phadebas microtest kit.

Among workers whose CdB and CdU levels were always below 10 μg/lwb or below 10 μg/l urine, 3% and 2.7% respectively, had β_2-M levels above 260 μg/l. Workers with at least one CdB level greater than 10 μg/lwb or one CdU level above 10 μg/l urine (33.3% and 16.7% of workers, respectively) had elevated β_2-M levels. Forty-eight workers had measurements of CdB, CdU, β_2-M, RBP, N-acetyl-β_D-glucosaminidase (NAG), and microalbumin. These workers were evaluated for kidney function. The results are in Table V–14.

TABLE V–14—ASSOCIATION BETWEEN TUBULAR AND GLOMERULAR FUNCTION INDICATORS AND THEIR DISTRIBUTION DIVIDED INTO THREE GROUPS OF LEVELS OF URINE (CDU)

CdU (μg/l)	Total number of people	Number abnormal (percent)
<3	7	4 (57)
3–10	14	8 (57)
>10	27	18 (67)

Four of seven workers with median CdU levels less than 3 μg/l had abnormal levels of NAG, microalbumin, or RBP. Eight of 14 workers with median CdU levels between 3–10 μg/l had abnormal levels of at least one of the four indicators of kidney function (β_2-M, NAG, RBP, or microalbumin). Eighteen out of 27 workers with median CdU levels greater than 10 μg/l had at least one elevated abnormal kidney function test result. In this latter group, four workers had abnormal levels of all four kidney function measurements.

Among ten workers with elevated β_2-M levels, half had CdB levels less than 10 μg/lwb. (See Table V–15.) Their mean CdU level was 11 μg/l (range 2.5–13.8). Their mean cumulative exposure was 460 μg/m^3-yrs (range 260–721). The other five workers had a mean CdU level of 20.8 μg/l (range 12.6–26.2) and mean cumulative exposures of 5982 (1965–8382).

TABLE V–15.—MEAN CADMIUM IN URINE AND BLOOD LEVELS AMONG 10 WORKERS WITH ELEVATED BETA 2 MICROGLOBULIN LEVELS BY CUMULATIVE CADMIUM EXPOSURES

Number of workers	CdU (μg/l)	CdB (μg/l)	Cumulative exposure [1]
5	<10	11.0 (2.5–13.8)	460 (260–721)
5	<10	20.8 (12.6–26.2)	5892 (1965–8382)

[1] μg/m^3-years.

Toffoletto et al. concluded that if CdB and CdU levels are kept constantly below 10 μg/lwb or 10 μg/l urine, the prevalence of kidney dysfunction measured by elevated levels of β_2-M would be below three percent. However, five workers in this study (5.9%) with a mean exposure of 460 μg/m^3-yrs (or 10.2 μg over a 45-year working lifetime) had elevated β_2-M levels above 260 μg/l.

viii. *Buchet et al., (Ex. 8–201).* The renal function of workers occupationally exposed to cadmium (n=148) was compared with that of workers with no occupational exposure to heavy metals (n=88). The exposed and control populations were employed in two cadmium smelters in Belgium. In order to be a control subject, the worker had to fulfill several conditions: all levels of CdU had to be below 2 μg/g Cr; in the judgement of the plant physician, the worker had to have no occupational exposure to cadmium; and the controls belonged to the same socioeconomic class as the exposed workers.

Five-hour urine samples were collected from the workers while at work. Urine was pH adjusted and samples for β_2-M analyses were frozen

at −20 °C. The concentration of β_2-M was measured by radioimmunoassay using the Phadebas β_2-microtest kit developed by Pharmacia Diagnostics.

Descriptive characteristics of the exposed and control groups are included in Table V–16.

TABLE V–16.—DESCRIPTIVE CHARACTERISTICS OF CADMIUM EXPOSED WORKERS AND CONTROLS

Parameter	Controls	Exposed
Number	89	148
Age (years)	38.6	46.5
Duration of Employment (years).	8.4	15.4
Mean Level of Cadmium in Urine (μg/100 creatinine).	0.88	15.76
Mean β_2 in Urine (μg/gr creatinine).	71 (for N=87 workers).	739
Prevalence of Kidney Dysfunction Based on β_2>200 μg/gr Cr (percent).	6.8	[1] 16.2

[1] $p<0.025$

Renal dysfunction was defined by elevated levels of β_2-M above 200 μg/g Cr, among other definitions. The prevalence of renal dysfunction was significantly different between exposed workers and controls. The prevalence of abnormal results was not different between smokers and nonsmokers.

Buchet concluded that excessive exposure to cadmium increased the urinary excretion of both low and high molecular weight proteins and of tubular enzymes. These changes were mainly observed in workers excreting more than 10 μg Cd/g Cr or with CdB levels above 10 μg Cd/lwb. However, among workers whose CdU levels were consistently below 2 μg Cd/g Cr, controls, and among workers whose CdU levels were between 2–9.9 μg Cd/g Cr, the prevalence of kidney dysfunction was six percent. The prevalence of kidney dysfunction among workers whose CdU levels were between 10–19.9 μg Cd/g Cr and ≥20 μg Cd/g Cr was 15 and 40 percent, respectively.

ix. *Summary.* The eight studies reviewed above demonstrate a consistency in the levels of biological parameters associated with renal dysfunction. In all but one study by Laywerys, kidney dysfunction was found in workers whose cadmium in urine exceeded 10 μg Cd/g Cr.

The NIOSH Health Hazard Evaluation found modest elevations in low and high molecular weight proteins in the urine of workers whose CdU levels exceeded 10 μg/g Cr. It demonstrated that subclinical effects such as significant increases in mean levels of urinary tubular enzymes, NAG and alanine aminopeptidase (AAP), are apparent in cadmium-exposed workers with CdU levels above 10 μg/g Cr compared to those below this level.

Lauwerys (Ex. 8–718) concluded from his study that workers whose exposure is such that CdU levels never exceed 15 μg/g Cr would not develop kidney lesions. Roels (Ex. 57–K) concluded that on the basis of the interrelationships among levels of cadmium in liver, kidney cortex, and urine, it can be concluded that the probability of developing cadmium-induced renal dysfunction in male cadmium workers appears to be very low when the critical CdU level of 10 μg/g Cr is not regularly exceeded. This CdU level corresponded to an average cadmium body burden of 160–170 mg. In his 1989 paper, Roels (Ref. in Ex. 149; also Ex. 12–38–A) concluded that his study indicated that the age related decline of the baseline and maximal GFR is exacerbated in the presence of cadmium induced microproteinuria. The investigation supports Roels' previous estimate of the threshold effect concentration of CdU (10 μg/g Cr), which is intended to prevent the occurrence of microproteinuria in cadmium exposed male workers. Roels noted that this conclusion, however, may not be extrapolated to the general population because there are indications that in an occupationally active male population, the influence of the healthy worker effect may lead to an underestimation of the risk of cadmium for other groups of the general population.

Bernard and Lauwerys (Ex. 35) concluded that the results of their study demonstrated that a low or high molecular weight proteinuria is likely to develop in ten percent of exposed subjects when the concentration of the metal in renal cortex reaches about 200 ppm. The corresponding critical levels in urine and blood have been estimated at 10 μg/g Cr and 10 μg/lwb, respectively.

Toffoletto (Ex. 19–43–A) concluded that if CdB and CdU levels are kept constantly below 10 μg/lwb or 10 μg/l urine, the prevalence of kidney dysfunction measured by elevated levels of β_2-M would be below three percent. However, five workers in this study (5.9%) with a mean exposure of 460 μg/m^3-yrs (or 10.2 μg over a 45 year working lifetime) had elevated β_2-M levels above 260 μg/l.

d. *The biological significance of cadmium-induced kidney dysfunction.* Prolonged exposure to cadmium may lead to glomerular proteinuria, glucosuria, aminoaciduria, phosphaturia, and hypercalciuria (Exs. 8–086b: 4–28; 14–18, p. 157). These conditions are indicated by excess urinary amino acids, glucose, phosphate, or calcium, respectively. Each of these elements are essential to life, and under normal conditions their excretion is regulated by the kidney. Once low molecular weight proteinuria has developed, however, these elements may dissipate from the body. Loss of glomerular function may also occur, indicated by a decrease in the glomerular filtration rate and an increase in serum creatinine. Severe cadmium-induced renal damage may develop into chronic renal failure and uremia at which point some form of dialysis or kidney operation will be needed (Ex. 55).

Kidney dysfunction persists for years even after cessation of exposure. Loss of calcium and phosphorus may contribute to the increased risk of kidney stones observed in workers. Even in his early study of cadmium workers, Dr. Friberg noted renal stones as a common finding among cadmium-exposed workers (Ex. 4–29). Dr. Friberg testified that, in his opinion, kidney stones are a serious sequelae to cadmium-induced renal dysfunction. He and others originally thought that the increased prevalence of kidney stones observed in his studies was confined to Sweden, But later, the increased prevalence of kidney stones was observed in England, and in the U.S. Kidney stones, according to Dr. Friberg, is a very serious disease and is also a sign of a more generalized disorder of the mineral metabolism in the kidney (Tr. 6/6/90, p. 106).

Others held a different opinion about the prevalence of kidney stones among cadmium-exposed workers. For example, Dr. Spang stated that kidney stones are common in the general population of Sweden (20% in men and about 5% in women), and although he observed cases of kidney stones among cadmium-exposed workers, he did not know if the prevalence was different from that of the general population (Exs. 80; 81).

Cadmium may also precipitate clinical osteopathy in persons with inadequate dietary calcium intake (Ex. L–140–50). Diets low in vitamin D and calcium may be a contributing factor to sequelae subsequent to cadmium-induced renal dysfunction.

There are at least two hypothesized scenarios by which cadmium-induced tubular proteinuria can cause other adverse health effects (Ex. 8–086). Under the first of these, cadmium-associated tubular dysfunction causes damage to the production of biologically active metabolites such as vitamin D which occurs primarily in the kidney. Under

the second scenario, cadmium may cause atrophy of the gastrointestinal tract thereby reducing its ability to absorb essential elements such as calcium and phosphates. If both scenarios are true, it would lead to loss of essential elements and poor absorption of other minerals to replace those lost.

The gravity of cadmium-induced renal damage is compounded by the fact that there is no medical treatment to prevent or reduce the accumulation of cadmium in the kidney. Dr. Friberg has testified that there is currently no form of chelating agent that could be used without substantial risk (Ex. 29). In contrast to other heavy metals, current chelation therapy does not reduce the body burden of cadmium without producing significant renal damage. When chelated cadmium arrives in the kidneys, the cadmium may still be toxic to renal cells. Thus, large amounts of cadmium may move from the liver or muscle storage sites, overwhelm the kidney's usual attempts to store cadmium in a less toxic form, and accelerate deterioration of renal function.

The kidney cortex contains about three million nephrons. Dr. Goyer testified that:

> * * * a young, healthy adult uses about half of these * * * as * * * their function is lost because of old age or * * * diseases * * * the number of these that are functioning through life continually decreases * * * (Tr. 6/6/90, p. 124).

OSHA believes that the loss of function of the proximal tubules as indicated by tubular proteinuria, elevated levels of β_2-M in the urine, constitutes material impairment of health.

OSHA acknowledges that the significance of the dysfunction as evidenced by elevated levels of β_2-M in the urine is controversial. Part of this controversy arises from the fact that a worker with elevated levels of β_2-M may not experience any symptoms, and although tubular dysfunction can be determined through medical testing, it usually does not manifest itself at first with overt symptoms.

Dr. Goyer testified that the confusion over the interpretation of pathological significance of elevated levels of β_2-M stems from the fact that injury to the tubuli ultimately affects the functioning of the glomerulus. According to Dr. Goyer, the confusion lies in part in the fact that cadmium's earliest effect is primarily in the tubule, while kidney function is usually measured in the glomerulus (Tr. 6/6/90, pp. 126–127).

While most physicians would agree that glomerular effects and loss of GFR must be taken more seriously than a slight elevation in β_2-M in urine, the finding of elevated levels of low molecular weight protein in the urine by itself indicates kidney dysfunction in the tubule. As Dr. Friberg stated in his testimony, each part of the nephron is dependent on every other part of the nephron. It is his expectation that if one part of the nephron suffers damage it is more likely that another part will suffer damage (Tr. 6/6/90, pp. 107–108). Ultimately then, cadmium-related tubular effects will be manifested as an effect on the function of the glomeruli, either subsequently to or in association with the onset of tubular proteinuria.

Because of the functional reserve of the kidney, the adaptive increase in a single nephron's glomerular filtration rate, after total or partial loss of other damaged nephrons, tends to obscure injury until a considerable amount of the functional elements of the kidney, the parenchyma, is irreversibly lost. This implies that under normal conditions, the basal GFR is submaximal. If as has been suggested, glomerular balance is very tightly maintained, reduction of tubular function may have repercussions on the glomerular level (Ex. 149). Early changes in glomerular function are not necessarily detectable by the measurement of basal GFR, but such changes may have a significant impact on health (Ex. 149). In a study by Roels (Ex. 149) it was found that a renal cadmium burden that had not yet caused microproteinuria did not impair the filtration reserve capacity of the kidney, but the age related decline of the baseline and maximal GFR is exacerbated in the presence of cadmium induced microproteinuria.

Not all participants in the rulemaking agreed that elevated levels of β_2-M signified material impairment of health. Mr. Ken Storm, Senior Industrial Hygiene Specialist with Monsanto, stated that elevated levels of β_2-M may reflect a temporary or permanent change in renal function and tubular proteinuria may result from a biochemical lesion of no clinical significance. According to Mr. Storm, tubular proteinuria would be more appropriately viewed as an early indicator of pre-clinical effects and not, in and of itself, as a material impairment of health. Mr. Storm stated that the intent of OSHA to avoid tubular proteinuria is inappropriate because, in his opinion, tubular proteinuria is not a material impairment of health (Ex. 19–14).

Mr. Storm stated furthermore that urinary β_2-M and other biological indicators of early tubular dysfunction, such as n-acetyl-d-glucosaminidase (NAG), are nonspecific indicators of tubular proteinuria. Their presence may indicate past excessive cadmium exposure, exposure to another renal toxin, or loss of renal function due to the normal process of aging or other natural causes (Ex. 19–14).

Studies indicate that age alone cannot account for the excess of β_2-M observed in cadmium-exposed workers. Kowal et al. (Ex. 8–642) evaluated the levels of β_2-M in nonoccupationally exposed populations in the United States and found that the average level in the oldest group studied (107 μg β_2-M/l urine) was only marginally higher than the average level in the groups between age 20 and 70 (69 to 84 μg β_2-M/l urine) (referenced in Ex. 8–668–B). In addition, also, several researchers such as Dr. Elinder evaluated the prevalence of β_2-microglobulinuria by age among occupationally exposed populations and concluded that age was not an important confounding factor (Ex. I–140–45).

The specificity of β_2-M in urine as a marker of cadmium-induced kidney dysfunction is well established. The only other renal toxins or medical conditions which lead to elevated levels of β_2-M are anti-cancer drugs, aminoglycosides (antibacterial antibiotics such as streptomycin), anti-inflammatory compounds, and upper respiratory infections (Dr. Friberg, Tr. 6/6/90, pp. 108–109; Ex. I–140–1). As Michael Thun, M.D., Assistant Vice President for Epidemiology and Statistics at the American Cancer Society testified:

> Low molecular weight proteinuria * * * does occur from other conditions but it's uncommon * * * part of the reason why the (kidney) data are so consistent is that the studies use a rather specific marker of cadmium renal effects * * *. (Tr. 6/7/90, p. 174)

Dr. Bond, medical consultant to SCM Chemicals, testified that:

> * * * no histological abnormalities [are] seen in the proximal tubules * * * when there has been modest increase in urinary B2MG and Cd * * * (people with) * * * mild to moderate increases in urinary B2MG and Cd do not progress to renal failure if there are no other causes present such as infection, diabetes, etc. (Ex. 77)

Dr. Friberg, however, stated:

> It should be emphasized that tubular proteinuria may be accompanied by specific histological changes. Sometimes such changes have been reported before the functional changes. There are abundant data from animal studies showing early histological changes (Ref. by Kjellstrom, 1986, pp. 38–43). Experiments from humans are more limited as only a small number of autopsies or biopsies are available. To the

extent available, histologic changes were seen first of all in the proximal tubules (Ref. by Kjellstrom, 1986, p. 50–53). (Ex. 29).

Morphological changes are those that pertain to the form or structure of the organ. Histological changes are those that pertain to the minute structure, composition, and structure of the tissue of the organ. Twenty-three workers were evaluated for whom autopsy or biopsy data on morphological changes in the kidney were available (referenced in Dr. Friberg's written testimony). Of these, 18 workers had proteinuria. Of the 18 workers with proteinuria, all but three had morphological changes in their kidneys. There were no cases of workers with morphological changes without proteinuria (Ex. 144–3, p. 53). In five of the autopsy reports, the morphological changes in the kidneys were mainly confined to the proximal tubules, whereas the glomeruli were less affected.

These results demonstrate that functional changes in the kidney can occur before the microscopic structure of the kidney is severely damaged. The human data on pathological changes are limited, however, and animal data show that in some studies, morphological changes in the tubules emerge before measurable proteinuria. In the absence of a better test, however, it appears that the use of proteinuria as a screening tool for morphological changes in the kidney will identify all cases of workers with histological or morphological changes in kidney tissue as well as identifying those with only functional changes. These results also show that elevated levels of β_2-M in urine indicate kidney lesions of clinical significance (Ex. 19–14). While a worker with elevated levels of β_2-M in the urine may not manifest any overt symptoms of illness, nonetheless, the tubuli and glomeruli have lesions that compromise the functioning of the kidney as a filtration mechanism. Any other minor kidney trauma may progress rapidly to serious kidney damage.

It is clear from the testimony of world experts that elevated levels of β_2-M should be considered to signify material impairment. Dr. Friberg testified that:

> * * * the beta-2 microglobulin proteinuria * * * should be regarded as an adverse effect * * * predictive of an exacerbation of the age related decline of the glomerular filtration rate * * * the proteinuria in cadmium poisoning is irreversible and is predictive of more severe effects even if the worker is removed from further cadmium exposure * * * It is true that an increased excretion of low molecular weight proteins can be a very early indicator of kidney dysfunction. That's not immediately of the same clinical importance as an overt renal disease. Nevertheless, it is irreversible and the beginning of a process which has a high probability to lead to a progressive disease, a decrease in the glomerular filtration rate which clearly is a serious effect that easily may lead to overt disease. When discussing the kidney damage from cadmium, it is important that we make it clear that we are talking about serious, but often insidious effects on vital organs. The kidney has a considerable reserve capacity but once this is consumed symptoms may appear in swift succession and the condition of the patient then deteriorates rapidly, and the infection or other, in itself trivial disorder, could be a triggering mechanism. It is our responsibility to prevent this situation even among a small proportion of workers. (Tr. 6/6/90, pp. 73, 82, 86).

According to the American Conference of Governmental Industrial Hygienists (ACGIH):

> Persons excreting 290 μg/L B_2-microglobulin are not disabled; indeed they will not experience any symptoms. However, the lesion (from tubular proteinuria) is irreversible and represents a permanent loss of functional reserve. An infection or other condition which compromises renal function, but which would not normally lead to serious illness, could overwhelm the remaining kidney capacity. (Ex. 8–644)

Dr. Kazantzis did not agree with these positions. He testified that in his opinion, tubular proteinuria alone is not accompanied by any specific histological change, that its pathological significance is unclear, and that renal stone formation has been rare in cadmium workers in recent years (Ex. 19–43A). Dr. Kazantzis stated, however, that in a:

> * * * small proportion of long-term heavily exposed cadmium workers, tubular proteinuria has been followed by renal glycosuria, abnormal aminoaciduria, phosphaturia, and hypercalcuria. (Exs. 80; 81)

Dr. Kazantzis continued that progressive decline in renal function is a slow process in workers with cadmium-induced nephropathy and that this decline is unlikely to progress to an increased mortality from chronic renal disease. In support of his opinion, he cited his study (Ex. 8–603) in which approximately 7000 cadmium-exposed workers with more than one year of cadmium exposure between 1942 and 1970 were followed up to 1979 (Ex. 8–684). He found an SMR of 65 for all deaths coded as nephritis and nephrosis; the five year update showed an SMR of 85. One worker classified as being in the "ever high" exposure subgroup died from nephritis and nephrosis.

Dr. Elinder indicated, however, that most workers in Dr. Kazantzis' study had such low cadmium exposures that cadmium-associated illnesses would not be induced (Ex. 4–25). By combining 199 workers with high exposures into a group with over 6000 workers with low exposures into one group, the power of the study to find an effect was reduced Increased mortality from chronic nephritis and nephrosis has been observed in Swedish battery workers (Exs. 4–68 and 8–740). The difference between expected and observed deaths in the Kazantzis study may well be due to local differences in recording certain types of information on death certificates.

Three other epidemiological studies of cadmium exposed workers have shown increased mortality from kidney diseases, genito-urinary tract diseases, or kidney cancer. Thun observed an elevated SMR for genito-urinary cancer (SMR=135, Obs=6) in his total cohort (Ex. 4–67); Dr. Elinder (Ex. 4–25) reported an elevated SMR for genito-urinary diseases in his total cohort (SMR=300, Obs=3.0); and Holden et al. (Ex. 4–39) observed an elevated SMR for genito-urinary cancer in his total cohort (SMR=122, Obs=4.0). Because the number of excess cases in each study is too small to make these findings statistically meaningful, the relationship between cadmium exposure and risk of death from kidney dysfunction is not clear. These three mortality studies, however, provide consistent evidence of excesses of kidney illnesses among cadmium-exposed workers. This suggests the possibility that, at least in some cases, cadmium-induced kidney dysfunction may be associated with excess death.

Death from nephritis, nephrosis or end-stage renal disease is rare. Accurate death rates from kidney disease are difficult to ascertain, in part because such illnesses are uncommon and in part, because they are dramatically underreported by at least 50% [personal communication 4/30/92, National Institute of Diabetic, Digestive and Kidney Diseases]. Dr. Thun indicated that impaired renal function is frequently underreported on death certificates even when the disease is sufficiently severe to require chronic hemodialysis (Modan referenced in Thun; Ex. 4–68). Under-reporting results because deaths from these diseases are coded as deaths due to complications arising from the treatment of these diseases or from sequelae to these diseases such as heart attack, stroke or diabetes.

Treatments for severe kidney diseases such as dialysis or a kidney transplant are available for those who can afford them. As Dr. Friberg indicated, several of his own patients had cadmium-induced uremia and died. If they had

had the opportunity for dialysis or renal transplant, they could have been saved (Ex. 29). Such treatments, however, are grave, especially considering that early forms of kidney dysfunctions can be detected and more serious diseases can be prevented.

An additional part of the controversy over the significance of tubular proteinuria is the question of whether it is a reversible effect. In response to this question, Dr. Goyer, citing a study in Japan, stated that half of the people with β_2-M levels in the range of 500 to 1,000 $\mu g/g$, followed for five years, do not show signs that their disease is reversible. Dr. Goyer testified that indeed, "The disease progressively gets worse * * * [Tr. 6/6/90, p. 136]." Dr. Friberg testified that:

> The continuous release of cadmium from the liver, also after end of the exposure, means that the accumulation of cadmium will take place in the kidneys for a long time after end of exposure. This was shown in animal experiments as early as 1957 by Gunn and Gould * * *. Similarly, there is much data showing that the proteinuria in chronic cadmium intoxication is irreversible * * * two studies from Belgium * * * show beyond doubt that several years after removal of the worker there is either an increase of low molecular weight proteins in the urine or no change at all. There is also an indication that all the subjects with normal levels of beta-2 microglobulin in urine one year before removal can get pathological values * * * a few years later. (Tr. 6/6/90, pp. 74–75)

The main studies referred to by Dr. Friberg were five-year updates on workers who had been medically removed from occupational exposures due to cadmium nephrotoxicity (reviewed by Bernard and Lauwerys, Ex. 35, Roels, Ex. 12–57K). Among male workers who had been removed from cadmium exposure because of elevated urinary excretion of β_2-M, RBP, or albumin, the evidence was that kidney dysfunction increased significantly over the five year period. Once it has appeared, Drs. Bernard and Lauwerys concluded, cadmium-induced proteinuria is in most cases irreversible. Bernard and Lauwerys demonstrated that proteinuria slowly progresses. Despite their finding that this evolution was slow, the authors concluded that the onset of proteinuria should be considered to be an adverse health effect, since such cadmium nephropathy may progress to renal insufficiency.

Dr. Bond stated that the clinical significance of slight increases in urinary β_2-M (for example, 350 $\mu g/l$) is uncertain, but that a repeated finding of β_2-M levels twice that of normal would more likely reflect a permanent effect, based on his experience and the literature. (Tr. 7/18/90, p. 169) Dr. Bond also agreed that cadmium-induced proteinuria must be prevented or minimized in order to prevent material impairment of health (Tr. 7/18/90, pp. 150–258, 175–176). About 20% of the cadmium workers that Dr. Bond has medically evaluated have elevated β_2-M levels. Dr. Bond removed two of these workers from cadmium exposure in 1986 when their β_2-M levels in the urine were 3000 to 5000 $\mu g/l$. Annual testing after removal indicated that urinary β_2-M and cadmium levels did not decline appreciably. Dr. Bond stated that in his opinion, these two workers are not sick based on results from tests of their level of serum creatinine and alpha phosphatase which measure kidney function (Tr. 7/18/90, pp. 189–191). Dr. Bond did indicate, however, that he was "concerned" about the welfare of these two individuals because he did not know if they were likely to develop any further problems. (Tr. 7/18/90, p. 229)

According to Jarup et al (Ex. 8–661) during the ten-year period of follow-up in his study, none of the cases of elevated β_2-microglobulinuria (greater than 310 μg β_2- M/g Cr) discovered in the high dose groups were reversible. The authors concluded that it was unlikely that any of these cases of tubular proteinuria would disappear after such a long follow-up time and that it was quite possible that more cases of tubular proteinuria would develop with a longer follow-up.

It is clear from the record of the rulemaking that despite some controversy, there is general agreement that renal tubular and glomerular lesions represent permanent loss of kidney functional reserve and that the lesions are irreversible. A worker who does not experience overt symptoms of illness may succumb to other illnesses more rapidly. An infection or other condition which would not normally lead to serious illness but which compromises kidney function could overwhelm the remaining kidney capacity (Ex. 8–644). A worker who has only slightly elevated levels of β_2-M in urine may later develop proteinuria, even after cessation of exposures, or the worker may develop more severe forms of renal dysfunction. Such dysfunction is of great concern to OSHA. Renal compromise, described above, meets the definition of material impairment as intended in the OSH Act and as defined in this final standard (sec. 6(b)(5)).

e. *The renal effect of cadmium pigments and other less soluble forms of cadmium—A review of the literature and comments.* OSHA received substantial comment on the renal toxicity of insoluble cadmium compounds, particularly cadmium pigments (Exs. 19–42–A; 19–14). "Solubility" is the process by which one substance is dissolved in another and is separated into its components by chemical action. Some cadmium compounds like cadmium oxide and cadmium sulfide, are relatively less soluble than others such as cadmium chloride and cadmium sulfate. It has been hypothesized that less soluble compounds may be less bioavailable than more soluble compounds and therefore less toxic. "Bioavailability" of cadmium compounds refers to the degree to which cadmium becomes available to the target tissue after exposure.

Several commentors and hearing participants were of the opinion that insoluble cadmium compounds are less toxic to the kidney (Exs. 19–42–A; 19–41; 14–14). For example, according to the Society of Plastics Industries (SPI), a trade organization of more than 2000 members representing all segments of the plastics industry, the health effects associated with cadmium have been observed when exposure has been to compounds that are not typically used in the coloration of plastics (Ex. 19–41). SPI also stated that a variety of animal studies indicate that cadmium sulfide and other similar cadmium-based pigments are significantly less bioavailable than other cadmium compounds. They cited the Agency for Toxic Substances and Disease Registry's (ATSDR) Toxicological Profile for Cadmium (1989) to support their position:

> The toxicity of cadmium depends on the chemical and physical forms of the element. In general, soluble compounds * * * are better absorbed and hence more toxic than highly insoluble forms * * *. Studies described here are focused mainly on cadmium oxide or cadmium chloride, and the results cannot be applied equally to all other cadmium compounds (ATSDR, as quoted in SPI Ex. 19–41, p. 6).

In a written submission to the record, Richard Bidstrup, Counsel for SCM Chemicals, Inc., also supported such a position (19–42A). He argued that cadmium pigments are less soluble and less bioavailable, and thus less toxic to the kidney. He noted that toxicity to the kidney from cadmium pigments is one to three orders of magnitude less than for other forms of cadmium and that:

> * * * these results are consistent with the mechanistic and solubility data indicating that cadmium ions—the toxic agent of concern—are much less bioavailable from cadmium pigments than from other forms of cadmium. (19–42A)

Mr. Bidstrup, on behalf of SCM, and other commentors (Ex. 19–42–A), cited

separate studies performed by Miksche, Feitz, and Greenberg as sufficient evidence of lower renal toxicity of pigments. These studies are reviewed in more detail below.

i. *Miksche (Ex. 12–10–E).* In this study published in the Proceedings of the Third International Cadmium Conference, Miami, 1981, by the Cadmium Association, Cadmium Council, and Ilzro, Inc., the effect of cadmium exposure on health was evaluated in a group of 36 workers involved in cadmium pigment production and 21 workers involved in acrylonitrile-butadiene styrene (ABS) plastics production. The location of the facilities was not indicated.

Concentrations of CdB and CdU, and β_2-M levels in urine were available from periodic medical surveillance examinations conducted since 1980. The β_2-M in urine was measured using the Phadebas radioimmunological method developed by Pharmacia. Measurement was either completed on the day of urine sampling or the samples were frozen immediately and kept at—20° C until the analysis was performed; sample pH levels were not presented.

The 36 workers in the cadmium pigment production plant had an average of 11.75 years of employment (range of 1 to 32 years). The average air concentrations reported were for 1977, 1979, and 1980 as 50 $\mu g/m^3$, 30 $\mu g/m^3$, and 30 $\mu g/m^3$, respectively. Among the 21 plastics production workers engaged in the application of cadmium pigments, the average length of employment was 11.3 years (range of 4 to 15 years). No exposure levels were reported for this latter group of workers. Miksche indicated that an age-matched control group of workers without occupational exposure to cadmium was used for comparisons with the group of pigment applicators. The results from this study are in Table V–17.

TABLE V–17.—CADMIUM CONCENTRATIONS IN BLOOD AND URINE AND BETA 2 MICROGLOBULIN CONCENTRATIONS IN URINE OF WORKERS IN PIGMENT PRODUCTION OR APPLICATION

Group	Number	CdB [1]	CdU [2]	β_2-M U [3]
Pigment production	36	10.3±2.4 (2–36)	8.78±2.18 (0.5–38)	77.35±22.36 (17.6–304)
Pigment application	21	1.345±0.29 (0.4–3.0)	1.54±0.29 (0.4–3.1)	
Control for pigment applicators			1.26±0.26 (0.2–3.0)	

[1] Mean cadmium in blood level [(Mean±2SEM, or standard error of the mean) and range], µg/liter whole blood.
[2] Mean cadmium in urine level [(Mean±2SEM, or standard error of the mean) and range], µg/gram creatinine.
[3] Mean Beta 2 microglobulin in urine, µg/gram creatinine, [(Mean±2SEM, or standard error of the mean) and range].

Miksche reported no indications of elevated levels of β_2-M among the exposed workers. Mean levels of CdB and CdU among the pigment production workers were above 10 µg/lwb and 5 µg/g Cr respectively which are the levels judged normal by other researchers (e.g. Ex. 29). Miksche reported finding no correlation between β_2-M levels in urine and concentration of cadmium in air. Little exposure data were provided, however, to evaluate this conclusion. The only exposure data reported were the average air concentrations for three years while the study covered 32 years of time during which some of the production workers were potentially exposed. In addition, information on the intermittency of the exposures at these facilities or on the degree of respirator usage was not provided.

ii. *Fietz et al, (Ex. 12–10–F).* The study by Fietz, published in the Proceedings of the Fourth International Cadmium Conference, Munich, 1983, by the Cadmium Association, Cadmium Council and Ilzro, included 67 workers engaged in the production of cadmium pigments and 32 workers engaged in the further processing of those pigments. The location of the plants was not provided. Data for the study were provided by the company(ies) from occupational health screening reports and company exposure monitoring data. Among the information on biological parameters included in the medical evaluations were levels of CdB, CdU, urine creatinine and β_2-M in urine. β_2-M in urine was measured using a Phadebas test. Normal or "tolerable levels" for these biological markers were selected based upon principles laid down in BG Principle G 32 (referenced in Fietz). These levels were: CdU < 17 µg/g Cr, CdB < 15 µg/lwb (BAT); and β_2-M < 300 µg/l urine. According to the authors, smoking data were not analyzed since there were no differences observed between smokers and non-smokers.

Sampling for airborne exposures included both personal and area samples. Air measurements were maximum short-term exposures for a duration of 30 minutes to two hours. Critical workplaces were measured more frequently than noncritical workplaces.

Workers in the study were placed into five different categories based on the type of jobs performed within a specified area. Groups I through III were involved in pigment manufacturing [e.g. raw material mixing, combustion, washing, drying and finishing]. Groups IV and V were involved in pigment use and/or processing (e.g. paint formulation and pigment mixing). The authors indicated that exposure to cadmium pigments comprised about half of the working time for each worker. Two subgroups of workers were also identified: Group A included those who, on average, had worked more than ten years, and Group B included workers who, on average, had worked four years.

The average exposures per year were provided, for the time period from 1978 to 1982. Exposures to cadmium for groups I–III ranged from 14 to 201 $\mu g/m^3$, with the levels decreasing over time. Some workers in groups I and III had higher exposures, ranging from 175–1336 $\mu g/m^3$, but the authors stated that respirators were required for these workers.

For group IV, the exposure level was estimated to be 20 $\mu g/m^3$ in 1981 and 39 $\mu g/m^3$ in 1982. For Group V, only the exposure levels for 1982 were given, ranging from 0.5 to 10 $\mu g/m^3$. These values were much lower than those found in pigment production/manufacturing.

The β_2-M excretion among workers in pigment production is indicated in Table V–18. The levels of CdB and CdU among workers in pigment production are indicated in Table V–19.

TABLE V-18.—β_2-MICROGLOBULIN EXCRETION OF WORKERS IN PIGMENT PRODUCTION AVERAGE LEVELS OF β_2-M IN URINE (μg/GRAM CREATININE)

Groups	1979	1980	1981	1982	Mean
I-A	99.3	46.9	29.5	78.3	64.0
I-B	26.0	43.9	30.9	51.1	39.4
II-A	103.1	146.6	38.24	220.8	128.3
II-B	51.2	31.0	23.4	50.3	37.8
III-A	727.0	457.0	67.15	47.8	279.8
III-B	63.6	79.5	38.2	33.6	50.6

TABLE V-19.—LEVELS OF CADMIUM IN BLOOD AND URINE AMONG WORKERS IN PIGMENT PRODUCTION AVERAGE LEVELS OF CADMIUM IN BLOOD (μg/LITER WHOLE BLOOD) and CADMIUM IN URINE (g/GRAM CREATININE)

Group	Cadmium in blood					Cadmium in urine				
Year	1978	1979	1980	1981	1982	1978	1979	1980	1981	1982
IA	20	15	11	7	7	6.0	9.2	10.9	9.1	8.4
IB	12	8	9	7	9	4.6	5.4	7.1	6.4	6.3
IIA	19	19	13	14	16	16.2	15.2	14.1	10.0	12.7
IIB	8	7	6	5	6	4.3	3.2	3.1	3.1	3.1
IIIA	16	13	10	9	8	7.6	10.0	12.2	6.9	8.5
IIIB	11	9	6	6	8	4.4	4.1	5.3	4.8	4.5

CdU and β_2-M levels were higher in the production workers, Groups I–III, than for pigment users with lower exposures (Groups IV–V). According to Fietz, workers in Groups IV and V had levels of CdB, CdU and β_2-M in urine that corresponded to the levels of unexposed normal groups, but these levels were not given.

Each worker in Group A received greater exposure which was evident from their higher CdB, CdU and β_2-M levels. The CdU levels of workers in Group B were considered to be tolerable levels, based on the criteria stated above. On the basis of these limits, seven production workers had to be removed to a cadmium free workplace as a precaution against further damage.

The authors concluded that the study showed that the use of technical measures such as exhaust ventilation, sealing of machines, enclosure of sources of dusts and consistent use of respirators can reduce the cadmium air levels and the harmful effects from cadmium. The results from the study, however, are limited for evaluating whether the low levels of cadmium and β_2-M in the urine observed in the pigment users were the result of the lower absorbability of cadmium pigments or lower cadmium air concentrations.

iii. *Greenberg et al. (Ex. 12–10–G).* The Greenberg study was a follow-up study of 38 workers exposed to both lead and cadmium during the manufacturing of pigments and vitreous enamels. The follow-up was performed in two phases, one in Pittsburgh and one in Cleveland. The results of this study were published in the Archives of Environmental Health, in 1986.

In the Pittsburgh phase of the study, all workers at the plant were contacted through their union representatives, and over a seven month period, a total of 44 workers (40%) volunteered for admission to the Clinical Research Unit of the University of Pittsburgh School of Medicine. During a three day in-patient stay, detailed work and exposure histories were obtained, a physical examination was performed, and detailed laboratory studies were undertaken. Subjects were considered smokers if they had ever regularly smoked.

The second phase of the study was performed at the Cleveland work site during a single session two to nine months after the Pittsburgh hospitalization. Workers who participated in the Pittsburt phase of the study were evaluated for tibia lead content by x-ray fluorescence and for liver and kidney cadmium content by neutron activation.

In order to evaluate renal function, urine was collected for determination of 24 hour creatinine, β_2-M, and cadmium excretion. The normal value for β_2-M was set at ≤ 370 μg/24 hour sample. CdU concentrations greater than 5 μg/l and CdB levels greater than 7 μg/lwb were considered to be abnormal (Tsuchiya, referenced in Greenberg). Total urinary protein levels were considered to be abnormal if the levels exceeded 150 mg/24 hour. Maximal urine concentrating ability after an 18 hour water deprivation was determined to establish abnormal urinary osmolality (>800 mOsm/kg).

As part of the renal function tests performed for these workers, minimum urine pH was determined. This test was performed using the oral administration of ammonium chloride (Wrong and Davies, referenced in the paper). Normal pH, as stated in the paper, was less than 5.4. Urine pH was not reported for the urine samples used in the determination of β_2-M levels, but the normal level achieved during renal function testing, pH<5.4 in 30 of 31 workers tested, is a level at which β_2-M in urine will degrade. It is unclear whether the ammonium chloride test interfered with the accuracy of urinary β_2-M determinations.

As part of the preliminary screening, environmental exposures to cadmium and lead were determined by measurement of airborne concentrations of the two metals in personal and area air samples. For the 38 workers who provided such data, the average length of employment reported was 20.7 years (11 to 37 years). Cadmium air levels were reported as "single measurements" with a range of 0 to 384 μg/m^3. The mean airborne level of cadmium in maintenance departments was reported as 5 μg/m^3. The mean airborne level of cadmium in "cadmium departments" was reported as 229 μg/m^3. The authors did not state whether these values were time weighted averages (TWA). The authors, however, did state that 31 percent of the values among all workers measured exceeded the NIOSH recommended level of 40 μg/m^3, which is a TWA.

Detailed work history information, reported by the workers during the

medical examinations in the hospital, was scored for exposure to cadmium or lead independently according to a protocol established by Greenberg. If a worker was never warned that his/her CdU or CdB levels were elevated as determined by plant safety officials or if a worker never worked in an exposure area, the worker was classified as having no exposure. Workers were classified as having light exposures if they had no elevated levels of CdU or CdB or they worked briefly or transiently in exposure areas. Workers were classified as having moderate exposures if their CdU or CdB levels were normal or moderately elevated, if more than half of their work time was spent in exposure areas, or if they were a smelter operator. Workers were classified as having heavy exposures if their levels of CdU or CdB were known to have been high, they had been removed from their job site because of elevated levels, and/or they were exposed to intense or prolonged exposure. For some workers, this information was unavailable and these workers were classified as having unknown exposure levels. Workers who were unable to recall warnings about levels of cadmium in blood or urine were classified as having been moderately exposed.

Owing to the long duration of employment and the plant policy of switching workers from one area to another, most workers had mixed exposure to both lead and cadmium processing areas. As a rule, subjects were unable to recall details of warnings about toxic blood urine lead or cadmium levels. Thus the bulk of subjects were classified as having moderate exposure to both metals.

The authors reported that normal kidney cadmium burdens were considered to be levels up to 8.6 mg for non-smokers and 12 mg for smokers. Normal liver concentrations of cadmium were up to 7.0 μg/g and 9.5 μg/g for these two groups, respectively. The authors considered that the critical value for renal cadmium content was 30 mg. Workers were classified according to smoking status since cigarette smoking constitutes a significant exposure to cadmium. The mean value of kidney burden for nonsmokers (7.4±4.4 mg) was significantly lower ($P<.02$) than the value of 12.3±7.2 mg for smokers. Four of 18 (22%) nonsmokers and 8 of 20 (40%) smokers had kidney burden values above normal. No subject had a kidney burden above the critical concentration of 30 mg.

The mean liver cadmium value in nonsmokers was 4.5±2.6 μg/g and was significantly lower than the 7.90±4.9 μg/g value of their co-workers who smoked ($p<.02$). Four of 18 nonsmokers (22%) and 5 of 20 smokers (25%) had liver cadmium levels above normal. No worker had a value for liver cadmium above 40 μg/g, the value at which it has previously been shown that renal cadmium levels are associated with renal damage.

Urinary cadmium concentrations averaged 3.4±3.7 μg/l and ranged from undetectable to 16 g/l. Three of 38 workers (8%) had elevated cadmium in urine concentrations. CdU excretions ranged from undetectable to 24.5 μg/24 hr (mean=6.43±7.7 μg/24 hr). CdB levels ranged from below the 1 μg/lwb detection limit to 9 μg/lwb. If the undetectable values were taken to be 1 μg/lwb, the mean value was 3±2 μg/lwb. Three of 37 subjects (8%) had values above the upper limit of normal for CdB (7 μg/lwb). Three workers had elevated levels of β_2-M. Three workers had abnormal levels of total protein in urine.

The results of the qualitative dose-response among smokers are presented in Table V–20. It was not possible to perform a similar analysis in the nonsmokers because virtually all these workers gave a history of moderate occupational exposure.

TABLE V–20.—CADMIUM IN URINE LEVELS AMONG SMOKING WORKERS WITH INDUSTRIAL EXPOSURE TO CADMIUM PIGMENTS (GREENBERG, 1986)

Cadmium levels	Exposure history		
	High N=5	Moderate N=9	Low N=4
Liver (μg/g)	11.0±6.1	7.1±4.7	6.0±4.2
Kidney (mg)	17.2±9.4	13.3±6.0	6.4±2.5
Urine (μg/24hr)	[1]11.2±8.7	[1]6.6±4.1	1.2±1.7

[1] Significantly different when compared to low exposure group.

Few significant renal abnormalities were observed in this cohort of exposed workers. The prevalence of increased β_2-M or protein excretion was low; only six workers had an increase of one or the other and only two of these workers had excessive cadmium body burdens. When measured body burdens of cadmium were accounted for, however, it was not surprising that the evidence of renal dysfunction attributable to cadmium was low. The highest kidney cadmium burden in any of the subjects in the study was approximately 20 mg, a value below the 31—42 mg value that has been shown in previous studies to be the critical level for renal toxicity. A dose-response model used by these authors previously, according to Greenberg et al., would have predicted that less than five percent of the population in the present study should have abnormal urinary β_2-M or protein excretion. The authors stated that the relatively low renal burdens seem, therefore, to reflect low exposure conditions.

iv. *De Silva, (Ex. 8–716).* De Silva and Donnan conducted a study of past and present workers at a small cadmium-pigment manufacturing plant in Australia. Cadmium-in-air tests were conducted in July 1977. Personal samplers were worn for at least three shifts by each of the men working on the three main processes: Furnace work, crushing, and general duties and cleaning. The results indicated that all TWA exposures were greater than 1 mg/m^3, with about 50 percent of the dust in the respirable range. There was little difference in the exposures experienced by men carrying out different duties. The furnace operated almost continuously whereas exposure during other processes, general duties, milling, crushing, and cleaning, were intermittent. The furnace operation was usually carried out by the same two men whose CdB concentrations confirmed their heavy exposure (54 μg Cd/lwb and 24 μg/lwb).

The three most heavily exposed workers, the two furnace operators and a raw blend operator, experienced respiratory damage and symptoms of kidney dysfunction after only seven years of employment. The estimated weekly average total cadmium dust exposure of these workers was approximately 1.5 mg/m^3 for the furnace operators and approximately 2 mg/m^3 for the raw blend operator. For workers engaged in other duties, dusty work occupied about half their time, and their estimated weekly average total cadmium dust exposure was approximately 0.7 mg/m^3.

The levels of cadmium in blood and urine (CdB and CdU) were measured in the workers. Excessive absorption of cadmium was found in five of nine current workers. All five had CdU levels at or above 10 μg/l, and two, with CdU levels in excess of 25 μg/l, had proteinuria. Three older men, two past employees and the factory manager who had not been engaged in production work for at least ten years, were found to have elevated levels of CdU although exposure had ceased many years earlier. In all three of these cases, proteinuria was present.

Three current workers and the three older men had been employed in production at the plant for at least 7

years. Each of these men experienced chronic cadmium poisoning and showed signs of renal tubular damage. Two of the current employees, one of whom had severe symptomatic emphysema, were excreting more than 40 μg/day of cadmium, had protein in their urine, and had impaired ability to acidify and concentrate urine. The other current employee was excreting 22 μg/day of cadmium in urine, and although he was not passing proteins, there was evidence of damage to his kidney tubules. His respiratory function tests showed moderately severe emphysema. The plant manager who had not been exposed for over ten years was passing cadmium at the rate of 14 μg/day. He had proteinuria and decreased ability to acidify and concentrate urine. Another of the older employees had been examined for cadmium poisoning, and the third older employee had a mild defect in concentration and acidification of urine and a moderate obstruction of his airways.

None of the men with exposures for less than seven years showed symptoms when the initial study was conducted, although one worker did have a mild airway obstruction. When renal function tests were conducted on these workers some two and one-half years later, however, symptoms began to appear. One worker had a decreased ability to concentrate urine, although no proteinuria was detected, while another worker showed normal renal function but intermittent proteinuria. Exposures roughly equivalent to 78 μg/m³ over a 45 year working lifetime [at 700 μg/m³ for three to five years, or 3,500 μg/m³-yrs for a maximum cumulative exposure) resulted in signs of cadmium poisoning not associated with clinical symptoms.

The results of this study indicate that kidney damage may occur even when concentrations of cadmium in urine are low (i.e. 15 μg/l) in workers with current exposure to cadmium. The authors suggest that if CdU levels exceed 15 μg/day, (the approximate equivalent of 15 μg/l), they should be regarded as unacceptably high, and should be kept below 15 μg/day to avoid the possibility of renal damage. In the case of the three people with past exposure to cadmium, cadmium in urine remained below 15 μg/day, according to the authors, but this did not indicate freedom from kidney damage. The authors concluded the respirable fraction of insoluble cadmium dust should not be regarded as merely nuisance dust.

v. *Wibowo et al., (Ex. 8–729).* In 1982, Wibowo conducted a study of "second degree" users of cadmium compounds in the Netherlands. Thirty-four pairs of workers, one exposed and one control, were matched according to age, smoking habits, ethnic origin and factory. Study subjects were employed in one of five factories: A glass bottle production plant using cadmium pigments for label decoration; a plastic production plant using cadmium stabilizers; a cadmium plating department of an aero-engine factory; a wall-paper decoration plant using cadmium stabilizers and pigments; and a television tube production factory using cadmium sulfide for its flourescence property. Cadmium exposure in each of the factories was characterized as low, but no exposure data were presented.

Workers were evaluated for renal effects. Venous blood and spot urine samples were collected to measure CdB, hemoglobin, hematocrit, CdU, β_2-M in urine, and creatinine in urine. Measurements of β_2-M were performed according to the radioimmunoassay method with the Phadebas β_2-microtest kit (Pharmacia Diagnostics) and were standardized to the creatinine content of the urine. To prevent degradation of β_2-M, the pH was brought to above 5.5 by adding 0.5 M NaOH. For external control, the laboratory participated in an international comparison program for CdB.

Results of the analysis lead the authors to conclude that in "second degree" cadmium users, low cadmium exposures are reflected in CdU levels but not in CdB levels. This in turn would indicate an increased body burden due to long term, low level "second degree" occupational exposure to cadmium. An observation of statistically significantly elevated CdB and CdU levels among exposed workers in the aero-engine factory relative to controls supported this position. The authors concluded that even

> * * * At the very low levels of exposure the body burden increases with the duration of cadmium exposure and indirectly with smoking habits. (Ex. 8–729)

vi. *Verschoor et al., (Ex. 19–42–8).* In 1987 Verschoor conducted a study of renal function in 27 workers with second degree cadmium exposures. The workers were employed in one of two plants that were in the Netherlands; nineteen worked in a plant where cadmium is incorporated into the production of plastics (plant A), and eight worked in a plant where cadmium was used in the welding of radiators (plant B). Eight workers at a grain elevator located in the same geographic area as the plastics production plant who had no occupational exposure to cadmium served as controls. These eight were of similar age and smoking habits as the exposed workers.

One subject from plant B was known to have clinical renal dysfunction and was excluded from the analysis. (This dysfunction had existed for more than ten years and had not been caused by cadmium exposure.) The analyses, therefore, were carried out on 26 exposed workers and 8 referents.

Spot urine samples and venous blood samples were collected using standard procedures to protect against contamination. Cadmium-free disposable syringes and polythene tubes and boxes were used for the sample collection. CdB and CdU levels were measured for biological monitoring. β_2-M and creatinine in serum, blood urea nitrogen (BUN), and IgG and albumin in urine were measured to evaluate glomerular function. RBP and β_2-M in urine and the lysosomal enzyme NAG in urine were measured as indicators of change in tubular function, and total urinary protein was measured as an overall renal parameter. Only urine samples with pH greater than 5.5 were used for the determination of β_2-M levels. Urinary density was chosen by Verschoor to adjust for the differences in the urinary creatinine concentrations between the exposed groups. All the urinary parameters were adjusted for a urinary density of 1,020 because this was the mean value of the urinary density of the group with level of CdU below 5 μg/g Cr.

Cadmium concentrations were not measured in either plant. Instead, CdU levels were used to estimate relative cadmium exposures. Workers with higher levels of CdU were considered to have been exposed to higher levels of airborne cadmium than workers with lower levels of CdU. The cadmium-exposed workers were thus divided into groups according to their CdU levels: The no increased exposure group whose CdU levels were less than 3 μg/g creatinine (30 nmol/l); the low occupational exposure group whose CdU levels were between 3 and 5 μg/g creatinine (30 to 50 nmol/l); and the higher occupational exposure group whose CdU levels were greater than 5 μg/g creatinine (50 nmol/l).

Most of the urinary parameters were found to be within the normal range. No significant differences were observed between the exposed workers and the controls for creatinine in serum, BUN, total urinary protein, or albumin in urine.

The levels of CdU and CdB among all exposed workers were elevated over the levels CdU and CdB in the referent population. For workers in plant A, the

geometric mean of CdB levels was 1.26, 5.78, and 0.2 ug/lwb for workers in Plant A, Plant B, and the control group, respectively. The geometric mean of CdU levels was 2.3, 11.1, and 0.68 ug/gr Cr for workers in Plant A, Plant B, and the control group, respectively.

Only workers in the higher occupational exposure group (i.e. the group whose CdU levels exceeded 5 μg/g Cr) had excess levels of those biological markers which indicate change in tubular function. For this group of workers, all of whom were employed in plant B, the levels of urinary β_2-M, RBP, and NAG were statistically significantly elevated over the levels of these parameters in the control group ($p < .05$).

vii. *Kawada et al. (Exs. 8–732).* In 1986 Kawada studied 29 workers who were exposed to cadmium pigments either in pigment manufacturing (CdS pigments or cadmium selenide pigments) or in synthetic resin preparation. The purpose of the study was to evaluate the relationship between β_2-M in urine and NAG activity, in workers with low levels of CdU. Thirty-five non-exposed workers were also evaluated; these were new workers on a rotation system and non-exposed workers.

Area samples found that the highest exposures ranged from 3 to 350 μg/m³. The mean respirable dust concentrations for the most highly exposed workers ranged from 0.18 to 3.0 μg/m³. Urine samples were collected stored at 4—6°C; pH levels were not specified. Levels of β_2-M in urine were analyzed using the enzyme immunoassay kit (Fujirebio Inc., Tokyo).

Cadmium, NAG activity, β_2-M, and creatinine in levels in urine were measured twice in the exposed workers, once in April and again in September. The geometric mean of CdU was found to be 0.7 μg/g Cr in April (range of 0.2 to 9.5 μg/g Cr) and 1.2 μg/g Cr in September (range of 0.5 to 7.0 μg/g Cr). The correlation coefficient between CdU and NAG was 0.261 in April (n=61) and 0.389 in September (n=50). The correlation coefficient between CdU and β_2-M was 0.241 in April (n=63) and 0.115 in September (n=50). Kawada concluded that NAG is a more sensitive indicator of cadmium absorption than β_2-M even at CdU levels of less than 10 μg/g Cr.

viii. *Kazantzis et al. (Ex. 8–102).* In 1962, Kazantzis conducted a study of 12 of the 13 men who produced cadmium pigments for use in paint, plastics and glass in a small British factory. While both cadmium oxide and the cadmium pigments (cadmium sulphide, cadmium zinc sulphide and cadmium seleno-sulphide) were produced in this factory, it was during the production of pigments workers experienced the greatest cadmium exposure due to the repeated handling of the material. The authors observed that

> • • • For similar quantities handled, the ratio of exposure for pigments is something like two and a half times as great as for oxides. (Ex. 8–102)

No exposure data were available. Instead, workers were grouped based on length of employment at the plant, combined with the type of work the men performed. These data were gathered through in-depth interviews and surveys with the employees. The authors found that three men had been in the factory for 2 years or less, four had 12 to 14 years of exposure, and five men had 25 to 31 years of exposure.

Venous blood samples were taken and analyzed for urea, carbon dioxide capacity, chloride, sodium, potassium, inorganic phosphate, alkaline phosphatase, cholesterol, calcium and uric acid. Random 24-hour urine samples were also collected to measure urinary protein, cadmium, calcium, amino acids, inorganic phosphate and sugar. Freshly passed specimens showed that pH of the urine of all 12 workers was somewhat acidic, falling between 4.85 and 6.55. Chest X-rays taken and comprehensive respiratory function tests were performed.

All five of the workers who had been exposed to cadmium compounds for more than 25 years showed consistent clinical proteinuria. In addition, three workers with fewer years of exposure showed renal tubular disorders and greater than normal protein in the urine. CdU exceeded 30 μg/day in 10 of the 12 workers studied. Several of the workers with clinical proteinuria showed definite respiratory impairment.

In addition to the 12 men studied by Kazantzis, there was one more with over 25 years of exposure who died before the study began, presumably from chronic cadmium poisoning. A great deal of health information for this worker was abstracted posthumously from his medical records and autopsy report. Specimens of lung, liver and kidney were analyzed for cadmium content. The cadmium concentration in the kidney was 55 μg/g wet weight and in the liver was 88 μg/g wet weight. In the lung, the cadmium concentration, 500 μg/g wet weight, was extremely high.

This study is the oldest reviewed by OSHA, and the biological parameters monitored for kidney dysfunction are less specific than those currently accepted as the most reliable indices for cadmium-related health effects. Nonetheless, the evidence suggests appreciable abnormal clearance of amino acids, calcium, glucose, phosphate, urate, water, and faulty acidification of the urine. The study authors concluded that:

> The findings establish that chronic cadmium poisoning can arise in the pigment industry, and suggest that cadmium proteinuria is clinically significant and should be regarded as an early manifestation of renal tubular damage. (Ex. 8–102)

ix. *Summary.* Epidemiological studies of workers in pigment-production and pigment-using facilities show that cadmium is absorbed into the body and that cadmium pigments should not be regarded separately from other cadmium compounds. Results from the studies submitted by industry do not support the position that cadmium pigments pose less hazard to workers than other cadmium compounds.

SCM cited the study by Miksche (Ex. 12–10–E) as evidence that cadmium pigments are not as toxic to the kidney as other forms of cadmium (Ex. 19–42A). Data from the study, however, indicate that the cadmium production workers were absorbing cadmium from pigments, as evidenced by the fact that the mean CdB and CdU levels of these workers were 10.3 μg/1wb and 8.78 μg/g Cr, respectively. The β_2-M levels in these pigment production workers were normal. Among pigment applicators, no abnormal levels of CdU, CdB, or β_2-M were found, but no exposure data were provided. This makes it impossible to evaluate cadmium exposures among the production workers.

The Cadmium Council (Ex. 19–43) questioned OSHA's argument that the low body burdens reported by Miksche might be due to "low exposure" when, according to the Council, workers in the cohort were exposed for up to 32 years and when, according to the Council, airborne cadmium levels were found to be 50 μg/m³ in 1977 and higher than that before 1977. In response, OSHA notes that 32 years represents the maximum length of exposure for a worker in the Miksche cohort and that the mean lengths of exposure for the two separate plants were 11.75 years and 11.3 years. The Agency also notes that no exposure data are available at all for the application plant, and the exposure level of 50 μg/m³ represents the average exposure for only one year at the production plant. Exposure levels at the production plant for the other two other years for which exposure data are available were lower than 50 μg/m³.

The study by Fietz (Ex. 12–10–f) was also cited by industry as evidence that cadmium pigments are far less toxic to the kidney than other forms of the metal.

Again, the Cadmium Council rejected the argument made by OSHA that the low levels of urinary analytes observed in this study were due to low levels of exposure (Ex. 19–43). The Council stated that in 1978 these workers were being exposed to 147 to 201 $\mu g/m^3$ of cadmium, and they still had "generally low" cadmium body levels. OSHA notes, however, that cadmium pigment production workers did show evidence of overexposure to cadmium even when levels of CdU as high as 17 $\mu g/g$ Cr and CdB as high as 15 $\mu g/lwb$ [BAT] were considered "safe". Furthermore, the exposure data are insufficient to evaluate the exposures for Groups IV and V, and it is clear from the data that exposures in the pigment-user facility were much lower than in the production facility.

The statements by the Cadmium Council regarding high exposures (147 to 201 $\mu g/m^3$) in the Fietz cohort being associated with low body burdens in 1978 are misleading. The authors reported that in 1978, average cadmium exposures ($\mu g/m^3$) in 1978 for Groups I, II, and II were 147, 194, and 201, respectively but that production of cadmium pigments comprised about half of the working time. This would result in exposures of 73.5, 97, and 100 $\mu g/m^3$. In Group IA, IIA, and IIIA, that is among the workers who had worked for an average of ten or more years, the levels of CdU in 1978 were 6 $\mu g/g$ Cr, 16 $\mu g/g$ Cr, and 8 $\mu g/g$ Cr, respectively. In Group IA, IIA, and IIIA, the levels of CdB in 1978 were 20 $\mu g/lwb$, 19 $\mu g/lwb$, and 16 $\mu g/lwb$, respectively. Levels of β_2–M in urine for these groups were not available for 1978, however, in 1979, for workers in Groups IA, IIA, and IIIA, the levels of β_2-M were 99 $\mu g/g$ Cr, 103 $\mu g/g$ Cr, and 727 $\mu g/g$ Cr, respectively. Thus, if workers experience cadmium or cadmium-pigment exposures similar to those in Group III and if workers have more than ten years of employment in a plant with exposures similar to those in this study workplace, some (7/67=10.4% or more) will have renal dysfunction as indicated by β_2–M levels greater than 300 $\mu g/g$ Cr.

According to comments submitted to OSHA during the rulemaking, levels of CdU above 15 $\mu g/g$ Cr and levels of CdB above 10 $\mu g/lwb$ are levels that indicate cadmium has been absorbed and systemically distributed throughout the body via the bloodstream; overexposure to cadmium has occurred; and excessive cadmium body burden is present. Based on this definition it is evident that cadmium exposures in pigment production plants can result in uptake of cadmium by the body. If exposure levels are kept close to those observed in this study for 1962 when exposures ranged from 0.5 to 10 $\mu g/m^3$, few workers will be at risk of kidney dysfunction, regardless of the type of cadmium compound used.

The Cadmium Council and SCM cited Greenberg's study (Ex. 12–10G) as evidence that among cadmium pigment workers,

> * * * the prevalence of increased β_2–microglobulin or protein excretion was low. (Exs. 19–43 and 12–10–G)

SCM commented that this finding was significant given that the average length of employment for these workers was 20.7 years, and 31% of recent exposure measurements exceeded 40 $\mu g/m^3$ (11 of 35 recent samples). The study authors themselves, however, concluded that the relatively low renal burdens reflected low exposures. Furthermore, according to the definition of "normal" test results established by the authors, three of 38 (8%) workers had elevated CdU concentrations; three of 37 (8%) subjects had values above the upper limit of normal for CdB; three workers had elevated levels of β_2–M; and, three workers had abnormal levels of total protein in urine. Finally, the finding of dose-response relationships between liver cadmium burdens and exposure, kidney cadmium burdens and exposure, and levels of cadmium in urine and exposure indicate that cadmium absorption occurs in pigment production facilities.

SCM referenced the study by Wibowo (Ex. 8–729) and the study by Verschoor (Ex. 19–42–8) to assert that:

> * * * There is no human evidence indicating that cadmium pigments have caused significant renal effects (Ex. 19–42–8).

Careful review of these studies, however, indicate that the downstream, or secondary users of cadmium pigments in these studies either had low exposures or the compounds used were insoluble. Nonetheless, low level exposures to insoluble cadmium pigments are absorbed into the bloodstream and result in levels of CdB and CdU that are elevated over background. The Verschoor study in particular suggests that even when second degree usage of cadmium pigments, such as in the plastics plant, are low, small amounts of cadmium are absorbed and systemically distributed to the kidneys. The low levels of CdB and CdU among the plastics workers in Plant A can not be attributed solely to lower absorption of insoluble compounds since no exposure data are available; the low levels of CdB and CdU may be due to lower exposure levels.

De Silva (Ex. 8–716) concluded from his study that the insoluble respirable cadmium compounds are less able to enter the blood stream than the soluble compounds. According to De Silva, this is supported by the case reported by Kazantzis et al, 1963, (referenced in De Silva) which resulted in necropsy and showed an unexpectedly high concentration of cadmium in the lung, compared with other published figures from cases of chronic cadmium poisoning due to soluble cadmium. While less cadmium enters the blood, however, De Silva concluded that more is retained in the lung. Respirable insoluble compounds probably contribute significantly to the lung damage, and, therefore, according to De Silva, there is no reason for differentiating between soluble and insoluble respirable cadmium, due to their effects on the lung.

The lower biological indices of absorption obtained after exposure to insoluble compounds of cadmium may be due to a reduced ability of the respirable fraction to enter the blood stream rather than to the reduced solubility of the non-respirable fraction in the gut. It could perhaps be concluded that non-respirable insoluble compounds may be slightly less hazardous than soluble compounds, but to regard them as merely nuisance dust is not only risky, according to De Silva, but also liable to misinterpretation and to encourage carelessness in their use.

Dr. Friberg was questioned about the relative toxicity of cadmium compounds, in particular cadmium pigments. In his testimony, Dr. Friberg discussed the findings of the study by De Silva as follows:

> * * * It's a small study but still I think it is, to some extent, impressive. (Workers) were exposed to insoluble cadmium at a pigment manufacturing plant * * * all * * * had signs of the tubular dysfunction * * * in the abstract * * * (the authors)
>
> * * * suggested that urinary cadmium concentration should be kept below * * * 15 micrograms per day, but this was in 1981, to avoid the possibility of renal damage and that the insoluble respirable fraction of cadmium dust should not be regarded as merely a nuisance dust. There was a lot of information of blood levels * * * after a couple of months exposure values of cadmium in blood per liter * * * (were) * * * something like * * * 18, 6, 9, 14, 24, 7, 17, 22, 10, 21, and 10 * * * very high levels. But as they mentioned somewhere, there could, of course, be some form of an exposure also to a soluble dust * * * (Tr. 6/6/90, pp. 90–91)

Thus, relatively insoluble cadmium pigments are taken up into the blood and may damage; there is medical evidence from studies of workers exposed to cadmium sulfide and cadmium pigments, although limited, that all cadmium compounds have been associated with renal effects at comparable exposure levels, regardless of the chemical compound.

f. *Evidence in animals.* Experimental animal studies, some of which are reviewed below, support the finding that cadmium induces proteinuria in humans. Studies also support the concept of a threshold or critical concentration of cadmium in a target organ and the finding that increased concentrations of β_2-M in the urine constitute biological markers of cadmium-induced tubular proteinuria (Exs. 30; 8–86).

Friberg induced proteinuria in rabbits by exposing them to 8 mg/m^3 of cadmium oxide dust by inhalation for 5 hours/day for 8 months (Ex. 4–29). In the same study, rabbits injected with 0.65 mg/kg cadmium sulfate developed proteinuria after two months of exposure. A number of other experimental studies in which animals were exposed either orally or through injection have also resulted in cadmium-induced proteinuria (Exs. 8–086b; 8–402).

Some studies have induced glomerular proteinuria in experimental animals while others have induced mixed-type proteinuria. For example, Bernard (Ex. 4–20) injected rats with 1 mg/m^3 of cadmium chloride for 5 days/week for 2 months. The induced proteinuria was characterized by increased excretion not only of low molecular weight proteins but also of high molecular weight proteins indicative of glomerular dysfunction. In a similar study (Ex. 4–49), rats injected with cadmium showed mixed-type proteinuria, and after prolonged oral exposure, rats developed glomerular proteinuria.

i. *The renal effects of cadmium pigments and other less soluble forms of cadmium in animals.* OSHA received comment from SCM, SPI, and the Dry Color Manufacturers Association (DCMA), a trade association representing small, medium, and large pigment manufacturers in the U.S. and Canada, that studies by Hazleton Laboratories, Glaser, and Rusch demonstrate that absorption of cadmium and the potential for renal effects from pigment is much lower than that from other cadmium compounds (Exs. 19–42–A; 19–41; 120). For example, Richard Bidstrup, Counsel for SCM Chemicals, Inc., stated that these studies "demonstrate that absorption of cadmium and potential for renal effects from pigment is from 10 to 1,000 times less than that from other cadmium compounds (Ex. 19–42–A)." In addition, he referred to other studies with longer exposure times that have reached the same conclusion (i.e., Heinrich et al., 1986; Princi and Geever, 1950; and Oberdorster, undated; all in Ex. 19–42A).

According to the DCMA, in-vitro data also support its position that the cadmium in pigments is less bio-available than the cadmium in other compounds because cadmium pigments are relatively insoluble in the dilute acids (i.e., a pH of about 4) often found in biological systems (Ex. 120). DCMA states that, in contrast to the sulfide, cadmium oxide is highly soluble in dilute acids, which explains, in DCMA's view, the equivalent lung toxicity of cadmium oxide and other water-soluble cadmium compounds. In contrast, the solubility of cadmium pigments at a pH of 4 was much lower. Therefore, the oxide is "thousands of times" more soluble in the dilute acid environment of the lung than cadmium sulfide, and the oxide is therefore much more bioavailable than the sulfide (Ex. 120). DCMA reported that work by Stopford shows a good correlation between weak-acid extraction and serum extraction. In addition, a positive relationship has been demonstrated between the amount of acid-extractable cadmium in pigments and the "resulting body burdens after ingestion" (Ex. 120, p. 10).

OSHA has reviewed the main animal studies submitted by industry representatives in support of their assumption that cadmium pigments are less toxic to the kidney. The Agency review is presented here.

Hazelton Laboratories conducted a short term rat feeding study to determine whether or not there was a positive correlation between cadmium solubility and cadmium absorption through the gastrointestinal tract (Ex. 12–10–B). In this study, extraction tests were conducted with distilled water and with acid to determine the solubility of 12 different cadmium pigments. These same pigments were then fed to rats for one week at levels of 10,000 ppm and 50,000 ppm in the diet to evaluate the level of absorption of cadmium from the pigment. For purposes of comparison, rats were also fed a highly soluble cadmium compound, $CdCl_2$, at a concentration of 10 and 50 ppm in the diet. The proportion of cadmium absorbed was determined by measuring the amount of cadmium found in the urine, kidneys and liver and dividing by the amount of cadmium found in the feces and GI tract contents. The degree of solubility of the pigments was much lower than the degree of solubility of $CdCl_2$. $CdCl_2$ was 61% soluble whereas the pigments were from 0.06% to 1.36% soluble. Correspondingly, the proportion of cadmium absorbed from the pigments was also much lower than for $CdCl_2$: 0.65% of the $CdCl_2$ was absorbed compared to .0004% to .0060% of the cadmium pigments.

From these data the authors concluded that there was a positive correlation between solubility and absorption; the greater the solubility the greater the amount absorbed by the body. OSHA notes, however, that this feeding study lasted only one week. While the percent of cadmium absorbed from the pigments after one week's exposure is relatively low compared to $CdCl_2$, the total percentage absorbed after chronic exposure to cadmium pigments (e.g. 18 months) is not known and may be more substantial.

In the study by Princi and Geever (Ex. 8–459), 30 dogs were divided into three groups: ten dogs served as controls; ten dogs were exposed to cadmium oxide; and ten dogs were exposed to cadmium sulfide. Exposure lasted six hours per day for five days per week. Concentrations of cadmium in air ranged from 3 to 7 mg/m^3. Ninety-eight percent of the particles were less than 3 microns in diameter. The average length of exposure for cadmium sulfide was 895 hours, or about 30 weeks (895 hours divided by 30 hours per week is approximately 30 weeks); the longest exposure was 1,417 hours (approximately 47 weeks). The average length of exposure for cadmium oxide was 1,102 hours (approximately 37 weeks); the longest cadmium oxide exposure was 1,319 (approximately 44 weeks). Four dogs exposed to cadmium oxide eventually died of bronchopneumonia. The authors noted that because of these deaths, exposure times varied. Several dogs had to be killed because of severe injuries received from fighting among themselves. Despite these limitations, the authors reported that a sufficient number of dogs survived the entire experiment to produce significant results. No information was provided on the survival times for any of the animals in this study.

The authors concluded that most of the cadmium dust inhaled was stored in the lungs, liver and kidneys. Lesser amounts were stored in bones and teeth. The authors further concluded that cadmium sulfide (CdS) and cadmium oxide (CdO) differ greatly in solubility and absorbability, and must therefore differ greatly in the amounts required to produce intoxication.

For the ten dogs exposed to CdO, the average level of cadmium in blood was 67 μg/lwb, and the average level of cadmium in urine was 130 μg/l. For the ten dogs exposed to CdS, the average level of cadmium in blood was 50 μg/lwb, and the average level of cadmium in urine was 50 μg/l. Clearly, a portion of the CdS dose was systemically absorbed into the body, however, a portion of the CdS may have decomposed into more soluble ionic forms, e.g., $CdSO_4$ (Exs. L–140–27–B, L–140–44), increasing the cadmium's solubility. OSHA notes, however, that at exposure levels as high as 3 to 7 mg/m³, the percent dissolution of CdS to more soluble forms is probably low (see, for example, L–140–27–B). The average level of cadmium in the lungs for the ten dogs exposed to CdO was 2.64 mg/100 gm (range from 1.16 to 4.7 mg/100 gm). For the ten dogs exposed to CdS this level was 3.63 mg/100 gm (range from 1.23 to 6.02 mg/100 gm). The authors concluded that more CdO was absorbed from the lungs, but OSHA notes that more CdS remained in the lung.

The study by Rusch (Ex. 12–10–D) was an acute inhalation study involving the exposure of male and female Sprague-Dawley rats to dusts of cadmium carbonate ($CdCO_3$), cadmium yellow pigment, cadmium red pigment and to cadmium fume at concentrations of 100 mg/m³ for two hours. The animals were then followed for 30 days in order to determine whether there were differences in uptake and distribution of compounds with different solubilities. The "cadmium red" was a finely divided red powder in hexagonal crystal form containing 69.9% cadmium, 16.4% selenium, and 13.2% sulfur (sulfide). Particle size analysis by sedimentation indicated that 99% of the particles were less than 5 micrometers in diameter. Cadmium yellow was a finely divided powder in a hexagonal crystal form produced by high temperature calcination. It contained 77.4% cadmium, 21.7% sulfur (sulfide), 0.28% zinc, and 0.27% selenium. Ninety-six percent of the particles were less than 5 micrometers in diameter. The cadmium carbonate was a reagent grade white amorphous powder which was finely divided by milling. The cadmium fume material was derived from a 10% aqueous solution of cadmium acetate dihydrate. The aerosol was produced by passing the solution through several heating processes and absorption containers prior to administration to the test animals.

No mortality was observed among rats exposed to either cadmium pigment after 30 days follow-up, but 3 out of 52 rats (6%) died from exposure to $CdCO_3$ and 25 out of 52 rats (48%) died from exposure to cadmium fume. In the pigment-exposed groups, greater amounts of cadmium were eliminated by the feces at faster rates than for the $CdCO_3$-exposed rats. The rats exposed to $CdCO_3$ also showed higher kidney cadmium levels. The authors stated that $CdCO_3$ followed predicted patterns of uptake, distribution and retention, whereas the pigments showed only minimal uptake and tissue deposition. Therefore, it appeared that inhalation exposures to soluble compounds resulted in more rapid uptake and higher body burdens than did exposure to less soluble cadmium compounds. OSHA notes that in this study, the exposure level was extremely high, lasted only 2 hours, and follow-up was for only 30 days. This makes it difficult to extrapolate the results to occupational settings where exposures may occur over long periods of time and at low doses or where exposures may occur repeatedly at high levels.

In the study by Glaser et al., (Ex. 12–10–C), male Wistar rats were exposed continuously for 30 days to aerosols of cadmium chloride and cadmium oxide at 0.1 mg/m³ and aerosols of cadmium sulfide (CdS) at 1 mg/m³. CdS was administered at a higher dose because of its lower solubility.

No clinical signs of intoxication were observed among any of the exposed groups. Mean CdU in the CdS group showed a slight but statistically significant increase ($p<0.05$) over the controls at the end of the exposure period. Mean CdU was also slightly statistically significantly elevated for the CdO group ($p<0.05$) at the end of the observation period.

Glaser found that cadmium was retained in the lung, liver and kidneys for all three compounds tested. Lesser amounts of CdCl2 were retained in the lungs of exposed rats compared to the amount of CdO and CdS retained. After one month's exposure approximately 25 μg of cadmium were retained in the whole lung of $CdCl_2$ exposed rats whereas approximately 50 μg and 140 μg of cadmium were retained in the lung for CdO and CdS exposed rats, respectively. The authors note that a 10 times greater exposure in the form of CdS did not result in a 10 times greater amount of cadmium in the whole lung. Therefore they suggested that there must be a difference in toxicokinetics (i.e. deposition, dissolution, clearance or toxicity) for CdS. OSHA notes, however, that photodecomposition of CdS may have occurred thereby altering the compounds administered to the lung to include more soluble forms of cadmium, (e.g., $CdSO_4$), and affecting the amount that would be retained in the lung.

Glaser also observed that for the $CdCl_2$ and CdO exposed rats, more of the cadmium was distributed to the cytosol fractions of the lung than for the CdS exposed rats, indicating that more of the CdS was retained in the extracellular fractions and was not absorbed into the cell. For a site-of-contact carcinogen, which some evidence suggests cadmium may be, it is entirely possible that the more insoluble the compound, the greater the carcinogenic potential. In fact, there was evidence of a cytotoxic effect to the alveolar macrophages from exposure to CdS equal to that observed from exposure to CdO.

Each of the cytotoxic effects observed in the rats exposed to CdS and CdO were greater than the effects observed in the rats exposed to $CdCl_2$. In addition, the lung metallothionein-cadmium content for rats exposed to CdS and CdO were similar to one another but greater than the metallothionein-cadmium content in $CdCl_2$ exposed rats. Metallothionein is produced in response to cadmium ions and, according to the authors, is an indication of cadmium's bioavailability. In the liver and kidney, cadmium burdens were significantly higher for the CdO exposed rats and for the CdS exposed rats than for the $CdCl_2$ exposed rats. After one month's exposure, approximately 15 μg of cadmium had accumulated in the liver and kidney of $CdCl_2$ exposed rats compared to 70 μg and 60 μg of cadmium which had accumulated in the livers of CdO and CdS exposed rats, respectively. The authors stated that it was unexpected that cadmium accumulation in the liver and kidney would be lower for $CdCl_2$ exposed rats than for CdO and CdS exposed rats because of $CdCl_2$'s higher solubility; they had thought that cadmium accumulation was correlated to the solubility of the compound. Some of the elevated liver burdens noted by Glaser for CdS exposed rats may be due to photodecomposition of the CdS (Exs. L–140–44; L–140–27–B), but this would not explain the high liver burdens for the CdO exposed rats.

The results of this study suggest that absorption and bioavailability may not be simply equated to the compound's solubility. For example, Glaser found that the body burdens of cadmium in the kidney and liver for CdO and CdS exposed rats were similar despite the fact that ten times more CdS was administered. This would imply that the lower solubility of CdS may be

responsible for the lower accumulation of cadmium. It has been suggested that such a result could be due to photodecomposition, but if photodecomposition did occur and a substantial amount of CdS degenerated into more soluble forms, it would be difficult to explain why 10 times more CdS resulted in a liver burden equivalent to that of the CdO exposed rats (Exs. L–140–44; Ex. L–140–27–B). The body burdens of cadmium in the kidney and liver are higher for CdO and CdS exposed rats than $CdCl_2$ exposed rats despite the fact the $CdCl_2$ is more soluble than CdO, CdS. $CdCl_2$ may be more soluble than cadmium compounds into which CdS may have photodecomposed. Thus factors other than solubility influence the systemic absorption and bioavailability of cadmium pigments. These factors could be further influenced by long term exposure (i.e. greater than one month).

According to DCMA, a later study by Glaser et al., 1990, (Ex. 8–694–B) shows that ionic cadmium released by photodecomposition accounts for the apparent increase in availability seen in this study. Gunter Oberdörster, Ph.D., Professor of Toxicology at the Environmental Health Sciences Center at the University of Rochester and formerly of the Fraunhofer Institute for Toxicology and Aerosol Research in West Germany, analyzed the data from this study, however, and concluded that they showed only a 2- to 3-fold reduction in the availability of cadmium from pigments (Ex. 120, p. 20).

OSHA concludes that the Hazleton Laboratory, Glaser, Princi, and Rusch studies do not provide adequate evidence to show that cadmium pigments are not as toxic as other forms of cadmium. (See for example Ex. 12–10.) These studies used short exposure periods that might not be relevant to long-term, low-level occupational exposures or obtained conflicting results that do not indicate a simple relationship between solubility and bioavailability. OSHA has also reviewed the studies by Heinrich and Oberdörster, and has addressed the main comments from these two experts in its discussion of the carcinogenicity of cadmium pigments.

DCMA submitted comments on the mechanisms by which cadmium pigments could be less toxic to the kidney and less bioavailable than other cadmium compounds (Ex. 120). DCMA stated that the chemistry of pigment compounds is substantially different from that of other compounds. Because the cadmium ion is "soft", based on its low charge-to-mass ratio, and the sulfide ion is also soft, sulfide ions stabilize the cadmium ions in pigment compounds. DCMA argued that any pigment-derived cadmium ions that were dissolved in biological fluids would already be complexed by water molecules or chlorides, both of which are hard ligands. According to DCMA, this concept of hard/soft ions would also suggest that the sulfide is less soluble than other chemical forms of the metal (Ex. 120, p. 11). However, soft-acid/soft-base theory refers to stronger bonding associated when large, easily polarized anions coordinate to large, easily polarized cations. This theory is used to explain the enhanced stability compared to ions that are mismatched in size, and does not pertain to chemistry of sulfide (Ex. 152). Since the human body can muster formidable chemistry in defense against foreign material, CdS may be solubilized in the body by a number of mechanisms (Ex. 152). For example, as Dr. Friberg stated, and as mentioned previously:

> * * * It seems to be quite clear that you cannot talk about insoluble dust * * * once this dust comes down to the lungs and is taken up by the macrophages then the solubility could be quite different from the solubility *in vitro* * * * (Tr. 6/6/90, pp. 102–103).

Other commentors agreed with Dr. Friberg. Once an insoluble cadmium pigment enters the lungs, some is absorbed into the body and some is retained in the lungs (Ex. L–140–50). The portion of cadmium that is systemically absorbed is retained for up to 30 years depending upon the part of the body in which the cadmium is stored. Even low atmospheric levels of cadmium accumulate in the body (Ex. L–140–50). Ellen Silbergeld, Ph.D., Adjunct Professor of Toxicology and Pharmacology and Experimental Therapeutics at the University of Maryland Medical School and Adjunct Professor of Health Policy at the Johns Hopkins School of Hygiene and Public Health, testified at the hearing regarding the bioavailability of different cadmium compounds. Dr. Silbergeld testified that solubility in aqueous media is only one aspect "of the physical, chemical, and potential biological behavior of a compound for purposes of estimating toxicity" (Tr. 6/7/90; pp. 228–235). Other factors that must be considered are particle size, portal of entry, chronicity of exposure, and other types of cellular response, which may be "much more important than this particular measure of aqueous solubility" (Tr. 6/7/90, pp. 228–235). Dr. Silbergeld testified further that many studies that have attempted to "exonerate" other metal-containing pigments such as lead pigments have shown that when exposure is chronic and the outcome is chronic (as opposed to acute), the molecular compound of the metal is "relatively unimportant." Dr. Silbergeld stated that "those differences in solubility would be unlikely to confer a difference in terms of tissue dose beyond the range of one or two" (Tr. 6/7/90, p. 229). Dr. Silbergeld continued that when the compound is encountered chronically from the external environment and remains within the body compartments for a long period of time, one factor such as solubility does not make much difference in overall toxicity" (Tr. 6/7/90, p. 229).

Dr. Silbergeld described the process of phagocytosis or endocytosis as a process where intracellular organelles come to the defense of the invaded cell which leads in turn to a "very great increase in the local concentrations of the compound at the site of inclusion, and which results in the cell's secretion of acids that change the chemical by encouraging dissociation of the metal from the salt or incorporation of the metal from the salt or incorporation of the metal onto a carrier protein, etc. Also, the cell may react in a way that produces oxidative stress" (Tr. 6/7/90, pp. 228–235).

Another argument made by DCMA was that metallothionein, a protein that contains 33 percent sulfur organized in seven clusters, "coordinates" metals such as cadmium in a very tight structure. Thus, metallothionein, once bound, may actually protect against cadmium's carcinogenic effects [DCMA cites Testimony at 3–56, 3–58] (Ex. 120, p. 11). DCMA then argued that, because the cadmium in pigments is also "tightly held between layers of sulfur atoms in a hexagonal * * * packing array, * * * the sulfur in pigments can be anticipated to protect organisms against the toxic effects of cadmium ions in the pigments" (Ex. 120, p. 12).

Based on its review of the *in-vivo* and *in-vitro* studies, DCMA concluded that cadmium pigments are not metabolized by similar mechanisms or at similar rates as other cadmium compounds. Thus, according to DCMA, "OSHA cannot assume that cadmium pigments have toxicity equal to [that of] other cadmium compounds" (Ex. 120, p. 12). This hypothesis was countered by analogies drawn between cadmium with other compounds such as lead, nickel, and asbestos (e.g. M. Costa, Tr. 6/7/90, pp. 56–58). Dr. Silbergeld suggests that endocytotic incorporation of insoluble materials may lead to higher concentrations within the cell which could, in turn, heighten the potential

toxicity of "soluble" [sic, insoluble] compounds (Ex. 120, p. 13). DCMA dismissed this idea because studies have shown that most cadmium sulfide was in the extracellular compartments of the lung (Glaser 1986, cited in Ex. 120) and that most of the cadmium from pigments is retained in the lavagable portion of the lung and is not bound to the cells (Oberdörster, cited in Ex. 120). Further, DCMA noted that Oberdörster's work shows that cadmium sulfide is cleared from the lung by the same mechanism used to clear nuisance dust. DCMA believes that these studies, which show that cadmium pigment is retained and cleared outside the lung cells obviate OSHA's position that "the endocytotic assimilation of cadmium pigments is a plausible mechanism for assuming an equal potency for adverse effects from these compounds" (Ex. 120, p. 14).

After reviewing these comments, the Agency believes there are insufficient data to conclude that one hypothesis is more acceptable than another. Furthermore, experimental data appear to show cytotoxic differences even between amorphous and crystalline cadmium sulfide compounds, for example, in the incidence of transformations in Syrian hamster embryo cells (Ex. 92). Crystalline CdS compounds, which perhaps are more similar to the hexagonal crystalline cadmium red pigments used in the Rusch *et al.* study (Ex. 12–10–D) than amorphous compounds, displayed greater cell-transforming activities at both cytotoxic and non-cytotoxic levels than did the amorphous compound. Qualitative assessment indicated considerably less uptake of amorphous CdS than of crystalline CdS although this phenomenon was difficult to observe quantitatively with light microscopy (Ex. 92). OSHA recognizes that in occupational settings, all CdS will not necessarily be in its hexagonal crystalline form. Furthermore, all pigments will be mixtures of more and less soluble forms of cadmium.

Among the studies which have examined cadmium pigments there is some evidence to suggest that cadmium pigments are less soluble than other cadmium compounds such as cadmium chloride. It is possible that due to their relative insolubility the pigments are also less available to the body tissues. The evidence is equivocal, however, with respect to the observable toxic effects. The short term animal tests seem to show fewer adverse effects (e.g. lower mortality and cadmium body burdens) among animals exposed to cadmium pigments. The animals, however, were exposed for only short periods of time. Yet, even in these short term exposure studies there is evidence of accumulation of cadmium in the lung, liver and kidney. There is also positive evidence of tumor formation in rats exposed to a cadmium pigment compound. In epidemiological studies of pigment users, low urinary cadmium and beta-2-microglobulin levels were observed among cadmium pigment workers but, in most cases, the level of exposure was poorly reported or not given, raising the possibility that the lack of effect seen among these pigment exposed workers was simply a result of low exposure (e.g. Ex. 8–729). Among workers employed in the manufacture of cadmium pigments, renal effects were noted, and in one study, it was concluded that "insoluble cadmium" pigments and dusts should not be regarded merely as nuisance dusts because such dusts can cause kidney damage (Ex. 8–716). Although there is some evidence to suggest that cadmium pigments are less soluble than other cadmium compounds, there is not sufficient data to show that this reduced solubility correlates with a reduced toxicity, especially after long term exposure. One study even suggests an increased bioavailibility with a less soluble cadmium compound. After long term exposure to cadmium pigments, cadmium may in fact be retained or may accumulate in body tissues and result in adverse health effects in a manner similar to the adverse effects which have been observed after long term exposure to other cadmium compounds.

OSHA concludes that there is insufficient evidence to quantify a difference in renal potency, and there is a lack of agreement between commentors on the presence of renal effects among pigment workers. Given the limitations of these data and the severity of the type of health effects that can result from rather small errors in estimates of risk, OSHA should not regulate cadmium pigments, or CdS pigments, differently from other cadmium compounds. OSHA acknowledges that several commentors hold the opinion that CdS is less bioavailable, but the opinions vary on the degree of difference in bioavailability, i.e., 2–3 fold reductions in some studies; reductions of 10 to 15 in other studies; a reduction of thousands times less in another study. The data are inadequate to develop public policy decisions that would allow some workers to be exposed to higher amounts of cadmium than other workers, based upon type of compound alone. Opinions differ on the type of cadmium compound in use in the workplace. In the absence of data that indicate only relatively insoluble forms of cadmium sulfide will be present, OSHA cannot separate one cadmium compound from others for regulatory purposes. OSHA must err on the side of worker-health and believes that mixtures of relatively more and less soluble forms will be present at one time or another in the workplace.

3. Pulmonary Effects

Reduced pulmonary function and chronic lung disease indicative of emphysema have been observed in workers with prolonged exposure to cadmium fume and dust. In a study by Friberg (Ex. 4–29), workers at an alkaline accumulator factory exposed to cadmium dust at estimated concentrations of 3 to 15 mg/m^3 for 9 to 34 years experienced impaired olfactory sensation, shortness of breath, and impaired lung function with associated poor physical working capacity. Rabbits exposed to cadmium dust from that factory exhibited chronic inflammatory changes in the nasal mucosa and signs of emphysema in the lung (Ex. 4–29).

Subsequent studies have confirmed the findings of these initial clinical and experimental studies. Bonnell (Ex. 4–22) and Kazantzis (Ex. 4–42) studied workers exposed to cadmium fume at copper-cadmium alloy factories for 5 to 15 years. The average concentration of cadmium over an 8-hour period was reported not to have exceeded 270 μg/m^3. The workers exhibited shortness of breath and impairment of pulmonary function, which were suggested to have been the result of emphysema. Similarly, a study of workers exposed to cadmium dust at concentrations below 200 μg/m^3 for greater than 20 years showed significantly lower pulmonary function compared to within plant non-exposed controls (Ex. 4–50). Smith (Ex. 4–63) examined workers who were exposed to airborne cadmium at 0.2 mg/m^3 or greater for 6 years or more at a cadmium producing plant. Workers were found to have decreased pulmonary function and mild to moderate interstitial fibrosis. Findings in this study suggested that the lung damage was due to prolonged exposure rather than repeated acute exposures. No worker's medical records showed evidence of acute illnesses which would have occurred if cadmium air levels were 5 mg/m^3. Furthermore, a dose-response relationship between reduced pulmonary function and months of cadmium exposure was observed (i.e. pulmonary function decreased as the months of exposure increased). It should be noted that in many of these studies

proteinuria was observed in a number of the workers who experienced adverse respiratory effects indicating that both chronic systemic effects and damage at site of contact result from inhalation of cadmium dusts and fumes.

4. Skeletal Effects

Workers with progressive forms of proteinuria have exhibited skeletal system effects associated with improper bone mineralization such as osteoporosis and osteomalacia. It is possible that cadmium-induced disturbances in the kidney are associated with these adverse effects (Ex. 8–086b, pp. 111–158). For example, the active metabolite of vitamin D, 1,25-dihydrocalciferol (1,25 DHCC) forms in the kidney and stimulates intestinal absorption of calcium which is required for normal bone mineralization. As cadmium accumulates in the renal cortex it may inhibit the metabolism of vitamin D to its active metabolite. Additionally, cadmium-induced renal damage may decrease the tubular reabsorption of calcium, and thus increase the urinary excretion of this essential element from the body. Recent studies of patients with cadmium-induced bone defects have also shown reduced concentrations of vitamin D metabolites in their blood (Ex. 8–189).

Bone mineralization may also be inhibited when there is interference with collagen metabolism. Cadmium may inhibit the formation of collagen fibers by interfering with the copper-dependent enzymes responsible for the cross linking of collagen molecules into fibrils. These fibrils form collagen fibers which in turn provide the fiber structure necessary for proper mineralization of bone. Improper bone mineralization results in a decreased density and softening of bone, conditions associated with osteoporosis and osteomalacia.

In humans, adverse bone effects have been observed after long-term exposure to cadmium. In a follow-up study of workers exposed to cadmium dust for 28 to 45 years, several workers showed hypercalciuria (an excess of calcium in the urine) with one case advancing to osteomalacia (Ex. 8–9). A case study by Friberg of a battery plate worker exposed to cadmium for 36 years documents the development of renal tubular dysfunction and severe osteomalacia (Ex. 8–170). Friberg notes, however, that relative to the number of workers with reported severe renal tubular damage the reported number of cases of adverse bone effects is low (Ex. 8–086b, p. 140).

One reason adverse bone effects occur infrequently may be that the bone has a reserve of calcium to maintain an adequate level in the body and thus it may take a long period of time for cadmium to induce bone disease. A second reason is that dietary deficiencies, in addition to cadmium exposure, may be necessary to induce bone effects. For example, in cadmium-polluted areas of Japan, cases of Itai-Itai disease, (a condition characterized by osteomalacia and renal tubular dysfunction), have been causally related to cadmium exposure from contaminated rice. However, among the cases there was also a dietary deficiency of calcium and vitamin-D, suggesting that the inadequate consumption of essential food elements and vitamins may have been a contributing factor to the disease (Ex. 8–086b, p. 151–153).

In animals exposed to cadmium either by injection or ingestion, disturbances in calcium metabolism with osteoporotic and osteomalacic conditions have been observed. For example, chicks exposed to cadmium in their feed for 3 weeks showed a decrease in calcium absorption from the intestine suggesting a possible effect on the formation of 1,25–DHCC (Ex. 8–3). Calcium absorption was observed to decrease as levels of cadmium in the feed increased.

Osteomalacia was induced in rats fed dietary concentrations of 10, 50 or 100 ppm cadmium for 19 months (Ex. 8–112). Osteoporotic changes increased as cadmium doses increased. The rats fed cadmium developed osteoporotic changes in bone before the onset of kidney damage indicating that cadmium may possibly have a direct effect on bone rather than an indirect effect through renal damage (Ex. 8–55). Friberg, however, presents a review of experimental studies in which the preponderance of data seem to suggest that chronic exposure to cadmium induces osteoporosis and osteomalacia subsequent to, and perhaps associated with, renal tubular damage (Ex. 8–086b, p. 115–139).

5. Reproductive and Developmental Effects

a. *Reproductive effects in male animals.* A number of studies have demonstrated testicular necrosis after systemic administration of cadmium salts in animals such as rats, rabbits, monkeys, guinea pigs, golden hamsters and calves. (Ref. in Exs. 8–420; 8–107; 8–337; 8–338; 8–86B). Parizek and Zahor have also reported regressive changes of the seminiferous epithelium in rats within 4 to 6 hours after subcutaneous injection of cadmium chloride or lactate. These changes progress to total necrosis within 24 to 48 hours (Ref. in Ex. 8–420). Morphological changes in the spermatozoa of the ductus deferens and proximal parts of the epididymis occur, but changes in the spermatozoa in distal parts of the epididymis are sometimes also observed. White observed that cadmium is extremely toxic for sperm cells *in vitro* (Ref. in Ex. 8–86). Schmid et al. have shown that the normal sperm motility is inhibited at cadmium concentrations exceeding 1.6 μM (=180 μg/l) (Ref. in Ex. 8–86B). It has been suggested by Chiquoine that cadmium-induced testicular necrosis is common in species possessing scrotal testes and absent from those possessing abdominal testes (Ref. in Ex. 8–86B).

The vascular bed and the blood flow of the testicles are affected very rapidly following injection of cadmium. Cadmium increases permeability of the testicular capillary blood system. Francavilla et al. showed that capillary damage leads to massive vascular escape of fluids and blood substances into the interstitium which subsequently results in edema and circulatory stasis (Ref. in Ex. 8–86B). Organ-specific carbonic anhydrase was suggested by Hodgen et al. to be the primary target of cadmium toxicity in the testicles (Ref. in Ex. 8–86B).

Piscator and Axelsson did not observe any pathological changes in the testicles of rabbits exposed to subcutaneous injections of cadmium (0.25 mg Cd/kg, 5 days/wk) for as many as 24 weeks and then followed for 30 weeks before sacrifice (Ref. in Ex. 8–95). It is suggested that the cadmium accumulated from long-term exposure is mainly bound to metallothionein and that this protein has a protective effect. Zenick et al. did not see any effect of cadmium exposure on testis weight, sperm count, number of abnormal sperm and testis morphology in male Long Evans hooded rats exposed to 0, 17.2, 34.4 and 68.8 mg Cd/l in drinking water over a period of 70 days (Ref. in Ex. 8–86B). Also, reproductive outcome was completely normal in these rats.

Krasovskii et al., however, showed that with chronic dosing, adverse effects on spermatogenesis occurred at lower doses than with acute dosing (Ref. in Ex. 8–86B). They found significant reductions in sperm number and motility and a significant increase in desquamation of spermatogenic epithelium in rats given 0.005 or 0.0005 mg Cd/kg orally for six months. There were no adverse effects at 0.00005 mg/kg. Dwivedi et al. demonstrated a depression of spermatogenesis, increased production of abnormal sperm and atrophy of the seminal vesicles with daily doses of 0.001 m mol/kg (0.2 mg/kg) given intraperitoneally for one

month which was similar to that produced by a intraperitoneal dose of 0.01 m mol/kg (2 mg/kg) (Ref. in Ex. 8–86B). They also noted marked inhibition of choline acetyl transferase activity in the spermatozoa, a change known to be associated with impaired sperm function and sterility. Senczuk and Zielinska-Psuja noted damage to the spermatogenic tubules and interstitial tissue hypertrophy following administration of 8 or 88 mg cadmium chloride/kg in the diet for 12–15 months (Ref. in Ex. 8–88B). These changes, however, were not seen at 3 or 6 months on the diet.

Batteraby et al. demonstrated that administration of cadmium chloride (5 and 50 ppm) in drinking water for up to 40 weeks did not alter the ultrastructural appearance of the prostate gland in rats of varying ages (Ref. in Ex. 8–86B). The testosterone concentration also did not differ significantly from controls. Low levels of cadmium (< 5 ppm) were accumulated by the ventral lobe of the prostate, although the metal was not detectable subcellularly.

Changes in blood androgen and gonadotropin levels have been shown to parallel the extent of histological damage to the interstitial tissue of the testes by several investigators such as Favino et al., Saksena et al., Lau et al., and Dutt et al. (Ref. in Exs. 8–86B; 8–206). The human chorionic gonadotropin (HCG)-induced serum testosterone concentration was reduced to less than five percent of that in control rats even at comparably low doses (0.18, 0.34 and 0.83 mg Cd/kg) resulting in decrease in the weight of the testes, seminal vesicles and epididymis of rats. Changes in secondary sex organs following cadmium injection are thought to be due to these hormones, but Timms et al. have evidence from rat studies suggesting cadmium may itself have a direct effect on the prostate gland (Ref. in Ex. 8–86B).

b. *Reproductive effects in female animals.* Kar et al. demonstrated that the ovaries of prepubertal rats undergo morphological changes after injection (route unspecified) of 10 mg $CdCl_2$ (6 mg Cd/kg) (Ref. in Ex. 8–86B). One week after the administration, recovery was complete. Massive ovarian hemorrhage was induced by injection (route unspecified) of cadmium chloride or acetate (2.3–6 mg/kg) by Parizek et al. (Ref. in Ex. 8–246). Similar results were also reported by Watanabe et al. (Ref. in Ex. 8–370).

Parizek noted that, in contrast to the good survival of nongravid rats and those injected after giving birth, administration of cadmium salts (0.02 mmole/kg; during the last four days of pregnancy) to gravid rats resulted in high mortality (76% for first pregnancies, slightly less for second pregnancies) within one to four days after injection (Ref. in Ex. 8–86B). The first sign of illness in some of the injected gravid rats was the appearance, within six hours of injection, of blood in the urine. Occasionally, when rats were observed at the time of death, violent convulsions were seen. Generalized visceral venous congestion, intense pulmonary congestion, hemorrhagic edema and sometimes massive pleural effusion were seen at autopsy in rats dying within 24 hours after injection. At this stage the kidneys were swollen and hyperemic, with focal or diffuse hemorrhages predominantly situated in the renal medulla.

Copius Peereboom-Stegeman et al. reported that cadmium exposure seems to increase the thickness of the basal lamina in the blood vessels in a dose-related manner in the uterus of female rats subcutaneously injected with 0.36 and 0.18 $CdCl_2$/kg for 8 to 60 weeks. But these are also indications of an increased thickness of the basal lamina with age. Possibly, cadmium exposure was accelerating the age-related changes in these blood vessels (Ref. in Ex. 8–86B).

Exposure of female rats to cadmium sulfate (3 g/day for 4 months) prolonged the estrous cycle in a study by Tsvetkova (Ex. 156). In four months, average length of diestrous phase in the experimental females was 6.2 ± 0.02 days, and in the control 1.2 ± 0.02 days. Der et al. have also shown altered estrous cycles in rats given 250 μg/day of cadmium chloride by intramuscular injection for 54 days (Ref. in Ex. 8–86B). After 25 days, regular cycles ceased and the animals went into persistent diestrus. The dose of 250 μg/day caused other signs of toxicity *viz.* lower weight gain, coarse hair coat, sluggish movements and significant reductions in uterine, ovarian and pituitary weight, but no histological changes in the uterus or ovary. Injection of 50 μg/day produced few toxic signs and had no effect on estrus cycles or reproductive organ weights.

c. *Reproductive effects in humans.* There is only limited data on reproductive effects in humans, there is some evidence in animals. There is no evidence of cadmium-induced testicular necrosis in humans, most likely because extremely high doses would be required to induce such an effect. Friberg suggests that if the absorbed oral dose required to produce a testicular effect is proportional to the doses administered in the injection studies, a dose of 70 mg to a 70 kg man would be required to elicit the same response as the 1 mg/kg dose studied in animals (Ex. 8–86b, p. 185). The lack of data on testicular function following cadmium exposure in humans makes it difficult to draw any conclusions on possible acute testicular effects in man.

OSHA reviewed two reports which addressed the effect of cadmium on the male reproductive system in humans. Exposure data were insufficient in these reports to adequately evaluate dose-response effects.

Smith et al. (1930; Ex. 155) reported five cases of fatalities as a result of chronic cadmium poisoning. The workers were exposed repeatedly to brief, intermittent, but high concentrations of cadmium fume in the manufacture of a copper-cadmium alloy. In the process, a 50 percent cadmium master alloy was first prepared and small quantities added to crucibles of molten copper which were stirred manually. Large amounts of cadmium fume were released. Histopathological examination at necropsy revealed that all five cases had emphysema but little evidence of bronchitis and kidneys with little damage except for slight hyaline arteriosclerosis. In four cases the testes were also examined and all exhibited normal tubules with many mitoses. In all, however, there was very infrequent maturation to spermatids or spermatozoa. The authors stated that the plentiful mitotic activity in the spermatocytes suggests that the depression of maturation to spermatids and spermatozoa is an effect of terminal illness rather than of chronic cadmium toxcity.

The androgen function of men occupationally exposed to cadmium during the manufacture of alkaline storage batteries has been studied by Favino et al. (1968, as cited in Friberg et al., 1986/Ex. 8–86B). Ten cadmium-exposed workers and ten controls matched for age and body weight were examined. The cadmium-exposed subjects worked in one of two processes in the plant. In the first area some chemical and physical processes were carried out to prepare the material for the negative electrode of the storage battery: from a sulphonitric mixture cadmium was precipitated as $Cd(OH)^4$ by NaOH at 70° C, filtered under pressure and dried at about 140° C. Then a fine cadmium powder was prepared which was mixed with kerosene and water. In the second area the technical processes were carried out to supply the elements of the storage battery and to complete the manufacture of the battery by connecting the negative with the

positive electrode, which is a mixture where nickel is the active component. Some cadmium-exposed subjects were working at the time of the study and some had left the plant several years before. Of those currently employed at the plant, those in the first area had, at the time of the study, been continuously working in that area for about two to five years or more without interruption. Those in the second area had been continuously exposed to cadmium until some years before the study initiation and then were employed in other areas of the plant. The control workers had other jobs in the same plant. The majority worked in lead storage battery manufacture.

Androgenic function was assessed by the measurement of basal urinary excretion of 17 ketosteroids, androsterone, etiocholanolone, testosterone, and epitestosterone. There was no significant difference between the exposed and control groups in the mean level of these hormones. Epitestosterone was higher in the exposed versus control groups, but this difference was not significant. None of the workers had proteinuria. The presence or absence of symptoms such as impotence as well as the number of children was reported in cadmium-exposed but not control workers. One cadmium-exposed worker claimed impotence and inability to have children after starting to work with cadmium. This worker had low urinary levels of the 17 ketosteroids, androsterone, etiocholanolone, and testosterone. This worker also had urinary cadmium levels above the normal range. Another worker who also claimed impotence had normal urinary hormone levels. The authors concluded that more information was needed about the first affected worker before it could be determined whether cadmium was toxic to his genital function. OSHA is of the opinion that the above mentioned studies provide no evidence of any adverse effect of cadmium on human testicular function.

d. *Developmental effects.* There are few studies of the developmental effects of cadmium in humans. Tsvetkova (1970; Ex. 156) studied 106 female workers exposed to various cadmium compounds in alkaline storage battery, chemical reagent and zinc casting plants. The exposed workers were from 18 to 48 years of age. They had worked from 2 to 16 years. Workers in the alkaline battery factory were exposed to cadmium oxide in concentrations of 0.1 to 25 mg/m^3. Those in the chemical plant were exposed to a number of soluble cadmium salts in concentrations of 0.16 to 35 mg/m^3. Workers in the zinc casting factory were exposed to cadmium sulfate, cadmium sulfide and metallic cadmium in concentrations of 0.02 to 25 mg/m^3. A control group of workers not exposed to cadmium was also examined, but no further description of this group was provided.

The authors reported that they were unable to show changes in the menstrual cycle of women in contact with the indicated cadmium compounds. It was reported, however, that there were isolated changes in the menstrual cycle which were a function of endocrinal-gynecological illnesses said to develop from working with cadmium compounds. Further details of these illnesses were not provided.

The course and time of pregnancy of the cadmium exposed workers were reported to correlate with physiological norms. The average neonatal weight for either boys or girls born to cadmium-exposed workers employed in either the battery or zinc casting plants was significantly lower ($p < .01$ for each group) than that of the controls. For boys born to control, battery, and zinc casting plant workers, average weights were 3.719 kg±0.120 (11 newborns), 3.217 kg±0.036 (13 newborns), and 3.388 kg ±0.028 (17 newborns), respectively. The average weight of girls born to control, battery, and zinc casting plant workers were 3.544 kg±0.82 (9 newborns), 2.918 kg±0.032 (14 newborns), and 3.106 kg±0.031 (10 newborns), respectively. Neonatal weights of children born to workers in the chemical plant were lower but not significantly than those of controls. Thirteen children (8 boys and 5 girls) were examined. Additionally, 4 out of 27 children of the zinc factory workers were reported to have clear signs of rickets, one had retarded eruption of teeth and two had dental disease. The children of controls were not similarly affected.

It is OSHA's opinion that the limited amount of information on methodology, including selection of controls, provided in this study does not allow one to interpret the findings.

Exposure of animals during pregnancy to cadmium, at doses in the order of mg/kg, gives rise to fetal death as well as severe malformations. Teratogenic effects of cadmium and death of the embryo occur as a consequence of cadmium given in early pregnancy, whereas fetal death is the dominating effect when cadmium is administered shortly before delivery.

Lauwerys et al. and Roels et al. have shown correlations of maternal, placental, and fetal blood levels of cadmium indicating that cadmium accumulates in the placenta (Ref. in Ex. 8–668). Parizek et al. have reported that cadmium salts, given in small amounts to pregnant rats, evoked rapidly progressive changes in the placenta, resulting in destruction of the pars fetalis (Ref. in Ex. 8–555). The cadmium administration appeared to cause hemorrhagic changes and necrosis in the placenta which could lead to embryonic death and uterine hemorrhage as shown by Parizek and Chiquoine (Ref. in Exs. 8–555; 8–86B). The studies by Ferm et al. and Dencker indicated that the transfer of cadmium across the placenta to the fetus varies during gestation. (Ref. in Ex. 8–668) During early organogenesis, in mice and hamster, cadmium reaches the embryo. Berlin and Ullberg observed that after closure of the vitelline duct, cadmium uptake (after parenteral administration) was diminished and remained low throughout the remainder of gestation in mice (Ref. in Ex. 8–668). Similar results were also seen in rats by several investigators such as Sonawane et al., Ahokas and Dilts, and Levin and Miller (Ref. in Ex. 8–86B; 8–88; 8–86B). After a single oral dose of cadmium to rats on day 17 of gestation, little cadmium was detected in the fetus in a study by Ahokas and Dilts (Ref. in Ex. 8–88).

Tsvetkova observed lower fetal weight when pregnant rats were exposed to cadmium sulfate (3 mg/m^3) by inhalation but there was no evidence of increased fetal mortality (Ex. 156). In a study by Prigge, exposure of pregnant rats to cadmium chloride aerosols at three dose levels (0.2, 0.4 and 0.6 mg Cd/m^3 continuously for 21 days) also resulted in reduction of weight gain in all three groups of exposed pregnant rats. Fetal weights were also significantly reduced in animals exposed to the highest levels. Fetal alkaline phosphatase activity was also elevated in the most highly exposed group. A marked dose dependent decrease in the activity of alkaline phosphatase was observed in exposed pregnant as compared to exposed nonpregnant animals. Hemoglobin levels and hematocrits were increased in both pregnant and non pregnant animals. However, no changes in fetal erythropoiesis were seen (Ex. 154).

Cadmium administered parenterally during organogenesis caused fetal malformation which varied with the time of administration and strain of animals as shown by Chang et al. and Ferm and Hanlon et al. (Ref. in Ex. 8–668). For example, in the hamster, intravenous administration of 2 mg/kg cadmium sulfate on day 8 of gestation induced a high percentage of fetal

deaths and facial deformities in survivors. Exencephaly and skeletal defects were also observed by Ferm and Carpenter (Ref. in Ex. 8–668).

A dose dependent increase in teratogenic effects was also seen by Ishizu et al. after subcutaneous administration of cadmium chloride (0.33, 0.63, 2.5 or 5.0 mg/kg) to pregnant mice on day 7 of gestation (Ex. 8–195). At the dose of 5.00 mg/kg, exencephaly, lack of tail, rachischisis and vaginal atresia were noted. When the fetuses were treated and stained with alizarin, skeletal malformations in the skull region, vertebral parts and ribs were observed. When external malformations were combined, the total malformation appearing rate exceeded 80 percent. When dosage of cadmium was reduced to 2.5 mg/kg, 0.63 mg/kg or 0.33 mg/kg, both external and skeletal malformations were reduced significantly, malformation appearing rate was less than one percent with 0.63 mg/kg and zero with 0.33 mg/kg. The concentrations of cadmium in the liver, kidney and placenta of mice exposed to cadmium were 800, 450 and 10 times higher than the control mice. There was no measurable amount of cadmium in the fetuses of cadmium chloride injected mice. In authors opinion, administered cadmium stayed mostly in the placenta at least in the late pregnancy and was not transferred to the fetuses (Ex. 8–195).

A dose-dependent rise in the fetal death rate, decrease in fetal weight, and increase in the rate of anomalies, which included micrognathia, cleft palate, clubfoot and small lungs were noticed in rats after daily subcutaneous injection of 4, 6, 8 or 12 mg cadmium chloride (2.6 to 7.7 mg Cd)/kg given for 4 consecutive days beginning on day 13 and extending to the 16th day of gestation were reported by Chernoff (Ex. 8–155).

A high incidence (as many as 80%) of the fetuses with hydrocephalus were seen by Samarawickrama and Webb when pregnant rats were given a single intravenous injection of 1.25 Cd/kg between days 9 and 15 of gestation. Other defects observed were anophthalmia, microphthalmia, gastroschisis and umbilical hernia. It is mentioned in the report that 1.1 mg Cd/kg produced no malformations, while 1.35 mg Cd/kg killed all embryos (Ex. 8–157).

In a study by Schroeder and Mitchener, oral administration of cadmium (10 ppm in doubly deionized water) to breeding mice resulted in a loss of strain in two generations (Ex. 153). Sharp angulation of the distal third of the tail, a congenital abnormality, was seen in 16 percent of the F_1 and F_2A generations. Of the offspring that lived beyond weaning 13 percent were runts and 30 percent died. Inability to breed in F_2B generation by some pairs was also noted.

In contrast, no growth, reproduction, or frequency of malformations were noted by Wills et al., after four descendant generations of rats were exposed to very low cadmium concentrations in the diet; 0.07, 0.10 and 0.125 Cd/kg (Ref. in Ex. 8–66B). However, exposure levels were so low, in fact close to the natural background levels, that toxic effects were hardly to be expected.

A lower placental and fetal weight was also seen by Tsvetkova after exposure of female rats to cadmium sulfate (3 g/day for 4 months by inhalation) (Ex. 156). The cadmium content in the liver of the experimental group embryos was 17.64 ± 40.02 μg/g, and the control group 7.99 ± 0.04 μg/g. The progeny of the experimental rats exposed to cadmium were less viable than the controls.

Ferm and Layton suggested that teratogenic effects of cadmium in the hamster or mouse could be prevented by pretreatment with small amounts of cadmium, indicating a protective mechanism involving induction of metallothionein (Ref. in Ex. 8–668). Several investigators such as Lucis et al., Arizono et al., and Hanlon et al. have shown that cadmium administered to pregnant animals binds to a metallothionein-like protein in the placenta (Ref. in Ex. 8–668).

Samarawickrama and Webb demonstrated a reduced zinc uptake in the rat fetus after cadmium treatment on day 9 to 15 of gestation, suggesting that the inhibition of DNA synthesis, by inhibiting zinc-dependent thymidine kinase activity, as the mechanisms of damage in the fetus. Dose was found to be critical; 1.1 mg/Cd/kg was not teratogenic in rats, while 1.25 mg Cd/kg caused high incidence of terata and 1.35 mg Cd/kg killed all fetuses (Ex. 8–157).

e. *Conclusions.* In conclusion, based on the studies presented above, OSHA believes that there is strong evidence that acute systemic administration of cadmium leads to testicular necrosis in various species. Regressive change in seminiferous epithelium, morphological changes in spermatozoa and inhibition of sperm motility after acute exposure are well substantiated. OSHA is of the opinion that acute administration of cadmium leads to morphological changes in ovaries and ovarian hemorrhage in female rats. However effects of cadmium on the reproductive organs after long-term exposure to low levels of cadmium are usually mild or absent. The lack of toxic effects seems to be associated with protective effects of metallotheionein that binds cadmium. Nevertheless, OSHA assumes that adverse effects on spermatogenesis occur after chronic dosing with cadmium at levels as low as 0.0005 mg/kg. Significant reduction in sperm number and motility and significant increase in desquamation of spermatogenic epithelium have been shown in rats given 0.0005 mg Cd/kg orally for six months. Chronic administration of cadmium leads to an increase in the thickness of the basal lamina in the blood vessels in a dose-related manner in the uterus of female rats. Based on Parizek study, OSHA believes that pregnant rats are more sensitive to the adverse effect of cadmium than the nonpregnant female rats. OSHA also concludes that there is sufficient evidence to indicate that chronic administration of cadmium can prolong the estrous cycle in rats. OSHA regards cadmium to be teratogenic and fetotoxic during early pregnancy as well as fetotoxic when administered shortly before delivery in rats.

6. Other Effects

Other adverse effects have been reported in experimental animals chronically exposed to cadmium. There are scattered reports of chronic effects on the gastrointestinal tract, peripheral nervous system and endocrine organs. More commonly documented effects in animals include anemia, changes in liver morphology, immunosuppression, and hypertension. For example, various experimental animals fed or injected with cadmium have commonly exhibited anemia, possibly due to cadmium's influence on the absorption and distribution of such metals as zinc and iron (Ex. 8–086–B, p. 167). Similarly, rats chronically exposed to cadmium oxide dust by inhalation developed anemia (Ex. 4–29). Animals exposed to cadmium by various routes of administration have shown morphological changes in the liver as well as disturbances in hepatic enzyme concentrations (Ex. 8–086–B, p. 161). Chronic oral exposure of mice to cadmium through drinking water decreased antibody synthesis (Ex. 8–24) and induced immunosuppression (Ex. 8–35).

There is conflicting evidence with respect to cadmium induced hypertension. Several studies have shown an increase in blood pressure after exposure to cadmium. Hypertension has been induced in rats orally exposed from 3 to 24 months to 0.1 to 10 mg cadmium/liter drinking water (Ex. 8–14). In this study, levels as low as 0.1 mg/l for 3 months increased

systolic blood pressure. The renal cortical level was 5 to 30 μg cadmium/g wet weight, which is below the critical concentration at which proteinuria is commonly detected. There are also studies, under similar experimental conditions, which have shown no hypertensive effects (Ex. 8–086b, pp. 170–173). It has been suggested that dietary differences may have caused the different responses, because rats on rye-based diets exhibited increased blood pressure whereas rats on other non-rye-based diets did not.

7. Conclusions about Non-Carcinogenic Effects

There is an abundance of data clearly indicating that exposures to cadmium in the industrial environment can cause serious toxic effects in human beings. Not only are there many experimental studies showing the acute and chronic effects of cadmium exposure, but there is also a great amount of human evidence among cadmium-exposed workers indicating adverse effects from chronic exposure to cadmium.

In humans, one of the earliest observable adverse effects from chronic exposure to cadmium is tubular proteinuria, the presence of an excess amount of low-molecular weight proteins in the urine (Exs. 12–07, 4–27, 4–28). This condition indicates impairment or loss of kidney function. Because of the body's ability to accumulate and store cadmium over long periods of time this condition may develop even after a reduction in or cessation of external cadmium exposure. Upon prolonged exposure tubular proteinuria may progress to more severe forms of renal dysfunction such as glycosuria, aminoaciduria, phosphaturia, and glomerular proteinuria or chronic nephrotoxicity. There is no specific treatment for chronic cadmium poisoning or for restoring kidney function. Persons with cadmium induced renal disease are at increased risk for developing kidney failure if additional renal insults occur such as exposure to other nephrotoxins including medications, infections of the renal-urinary system, obstruction of the urinary system, or reduced volume of blood flow to the kidneys due to reduced blood volume or vascular disease. In cases of cadmium-induced kidney damage, rigid control of diet, water intake and electrolyte balance in addition to medical treatment is required. Since other environmental sources of cadmium such as water, food, and ambient air may contribute to the total body burden, it is necessary to minimize all exposure to cadmium to prevent additional adverse health effects.

As noted in the lead standard (43 FR 52952), diseases resulting from exposures to heavy metals proceed in five stages: (1) Normal, (2) physiological change of uncertain significance, (3) pathophysiological change, (4) overt symptoms (morbidity), and (5) mortality. Within this process there are no sharp distinctions, but rather there is a continuum of effects. Categories overlap due to the variation in individual susceptibilities and exposures in the working population. Although step 2 is of uncertain significance, by step 3 (pathophysiologic changes) significant adverse health effects have occurred. Tubular proteinuria is considered by OSHA to represent pathophysiologic changes of consequence, and such changes represent material impairment, given OSHA's current understanding of the progressive stages of cadmium effects.

Other adverse health effects of concern to OSHA include reproductive effects, liver and spleen effects, and, noncarcinogenic lung effects, such as bronchitis. OSHA is of the opinion that the animal and human data are remarkably consistent. Human studies show high acute cadmium toxicity in the form of renal, liver, and pulmonary effects, and the animal studies show similar effects. There is renal damage and lung disease (bronchitis) in chronically exposed humans and in chronically exposed animals. There is also good correlation between ITAI-ITAI disease in humans and demineralization of the bone in animals, and liver damage is seen both in humans and animals.

C. Mutagenicity

A wide range of tests have been conducted to determine the mutagenic effects of cadmium. The mutagenicity of cadmium has been tested in bacteria, plants, insects, and mammalian cells, including human cells, *in vitro* and *in vivo*. Comprehensive reviews of these various investigations have been provided by Friberg (Ex. 8–086b, p. 223), Degraeve (Ex. 4–24), and EPA (Ex. 4–04). Both positive and negative results have been reported from these studies. This has lead to a somewhat confusing picture as to the mutagenicity of cadmium. The following section will give an overview of the more pertinent studies covered in the above reviews.

Cadmium has been shown to modify the metabolism of both RNA and DNA. Evidence has been obtained both *in vitro* and *in vivo* in microorganisms, plants, and mammalian cells showing enhancement and inhibition of RNA synthesis, degradation of DNA repair, inhibition of DNA synthesis, and inhibition of thymidine incorporation into DNA.

Gene mutation studies on microorganisms, yeasts, and mammalian cells have given mixed results on cadmium's mutagenic effects. For example, positive and negative mutagenic responses were observed in histidine reverse mutation assays using the bacteria *Salmonella typhimurium*. Some of these studies were considered inconclusive because several protocols were used in the assays. For example, different strains of *S. typhimurium* were tested using different dose regimens (e.g. single doses and doses with other chemicals). Conflicting and inconclusive results were also observed in gene mutation studies using yeast. For example, in a test for the induction of petite mutations, p-mutants were induced at the high and low doses but not at the middle dose. In a similar yeast assay, no p-mutants were induced at all, however; the dose was so toxic that only one percent of the yeast cells survived. Gene mutation assays using mammalian cell cultures of mouse lymphoma and chinese hamster cells have shown increased mutation frequencies with cadmium treatment.

Conflicting results were also reported in mutagenicity tests on fruit flies. Negative results were observed in sex-linked recessive lethal mutation tests, but positive results were observed in dominant lethal mutation tests. However, among the negative results it was noted that in one case too few chromosomes were tested while in another case the number of chromosomes tested was not reported. Thus, the scope of the tests may have been too small to detect a positive response.

In higher order plants, the mutagenicity tests have been mostly positive. Aberrations such as chromosomal lesions and breaks were induced in several different species of plants.

In mammalian cells, *in vitro* studies on human lymphocytes, have shown increased incidences of structural chromosomal aberrations after treatment with cadmium. Among the observed aberrations were chromatid breaks, symmetrical and asymmetrical translocations, and deletions. *In vitro* tests on other mammalian cells in culture, such as Chinese hamster cells, displayed no increase in structural chromosomal aberrations with cadmium treatment but did show an increase in numerical chromosomal aberrations (e.g. hyperploidy and diploidy).

Numerical aberrations were also observed *in vivo* in the oocytes of mice and hamsters treated with cadmium. In these studies no structural chromosomal aberrations were noted. Numerical aberrations were also observed in the blastocytes of cadmium treated mice, indicating that aberrations induced in the oocytes may be transferred to the embryo. Other *in vivo* tests on mice have shown negative responses. For example, in micronucleus assays, the frequency of micronuclei in experimental groups did not increase compared to control groups. Also, in dominant lethal assays no increase in mutants was observed in mice injected with cadmium chloride compared to controls. Heritable translocation assays revealed no observable translocations in the spermatocytes of the F_1 progeny of mice injected with cadmium chloride.

As in other test systems, *in vivo* studies on humans have produced conflicting results. For example, lymphocytes from the blood samples of some patients suffering from Itai-Itai disease showed a high rate of chromosomal aberrations such as chromatid breaks and translocations; however, a similar examination of other Itai-Itai patients showed no aberrations. Similarly, positive and negative results were observed *in vivo* among cadmium exposed workers in two different smelter plants. It was noted that for the positive effects these workers may also have been exposed to other metals such as lead and zinc which might have induced or contributed to the observed aberrations.

Thus, although a number of positive mutagenic responses have been observed, there are also a number of conflicting negative responses. It is difficult to make comparisons or to make conclusions about these conflicting results since the studies investigated different endpoints, and often used different protocols. Thus, until more conclusive mutagenicity studies are conducted and reported, cadmium may be considered to be a potential mutagenic agent.

D. Carcinogenic Health Effects

Cadmium has been shown to induce cancers in laboratory animals and is associated with lung and prostate cancer in man. Cancer is the second most common cause of death in the U.S. today. Lung cancer claims the largest share of cancer deaths among males and the second largest share of cancer deaths among females. The National Center for Health Statistics reports that in 1980, the lung cancer death rate was 68.8 per 100,000 for males and 24.4 per 100,000 for females.

Mortality and incidence are related by the case fatality rate, the proportion of incident cancer cases that terminate as cancer deaths. When a cancer is well defined and the mortality rate is similar to incidence, as with lung cancer, the case fatality rate is close to 100 percent. Few cases of lung cancer are curable, despite advances in medical and surgical oncology. Survival rates for lung cancer patients are poor with about 10% surviving five years or more after diagnosis (Ex. 8–62). OSHA considers lung cancer to represent the gravest material impairment of health because it is almost certainly fatal.

For prostate cancer, the case fatality rate is lower. Prostate cancer does not always lead to death. Males may have prostate cancer for some time without any clinical manifestation of the disease. Some of these tumors lack the capacity for rapid growth, while others invade surrounding tissue and metastasize to distant organs and cause death. In 1980, 22,881 men died of prostate cancer; the prostate cancer death rate was 20.8 per 100,000 men. Early diagnosis and treatment have reduced the mortality rates associated with prostate cancer. Nevertheless, because workers who work with cadmium are found to be at higher risk (Ex. 8–683) of prostate cancer, OSHA has evaluated the relevant epidemiological studies of prostate cancer among cadmium exposed workers. Prostate cancer also represents the gravest material impairment of health.

1. Evidence in Animals

Cadmium has been shown to be a carcinogen in animals when administered by inhalation. The strongest evidence of carcinogenicity comes from a rat bioassay by Takenaka et al (Ex. 4–67). In this well conducted study, cadmium was found to induce lung carcinomas in exposed Wistar rats. Incidence in the exposed groups was statistically significantly elevated over the incidence in controls, and a statistically significant dose-response was observed.

Takenaka exposed three groups of male rats continuously for 18 months to cadmium chloride aerosols with nominal cadmium concentrations of 12.5, 25, and 50 $\mu g/m^3$. An additional group of 41 rats served as controls. The animals received water ad libitum during the experiment but were fed only 8 hours per day to minimize food contamination. The rats were observed for 13 months after the last exposure, at which time all surviving rats were sacrificed. There was no statistically significant difference in mean survival times among the four groups of rats, although the mean survival time for the high dose group was slightly shorter than the mean survival time for the other groups.

A histopathological examination was given to all rats surviving the exposure phase of the study unless their bodies were too autolyzed to allow such an exam. Cadmium concentrations were measured in the lungs, liver, and kidneys of a subgroup of each exposure group. Concentrations in the lung were nearly as high as in the liver. In all organs concentrations were observed to increase with dose except that only the low dose rats were found to have a slightly higher concentration in the lung than was found in the middle dose rats.

The incidence of lung carcinomas was 0/38 (0%) in the controls, 6/39 (15.4%) in the low dose group, 20/38 (52.6%) in the middle dose group, and 25/35 (71.4%) in the high dose group. The majority of carcinomas were adenocarcinomas; however, epidermoid carcinomas, mucoepidermoid carcinomas, and combined epidermoid carcinomas and adenocarcinomas were observed. The incidence of each of these tumors is presented in Table V–21.

TABLE V–21.—INCIDENCE OF LUNG CARCINOMAS IN MALE WISTAR RATS EXPOSED TO CADMIUM CHLORIDE AEROSOLS [a]

Tumor type 50 $\mu g/m^3$	Controls (percent)	12.5 $\mu g/m^3$ (percent)	25 $\mu g/m^3$ (percent)
Adenocarcinoma 15/38 (39%)	14/35 (40)	0/38 (0)	4/39 (10)
Epidermoid 7/35 (20%) Carcinoma	0/38 (0)	2/39 (5)	4/38 (11)
Mucoepidermoid 0/38 (0%) Carcinoma	3/35 (9)	0/38 (0)	0/39 (0)
Combined 1/35 (3%) Epidermoid Carcinoma and Adenocarcinoma	0/38 (0)	0/39 (0)	1/38 (3)
Total 25/35 (71%) Carcinomas	0/38 (0)	6/39 (15)	20/38 (53)

[a] From Takenaka *et al.* (Ex. 4–67).

The Takenaka study appears to have been the first animal study to conclusively document a lung cancer response from inhaled cadmium. Takenaka noted that a number of prior experimental study results had only raised the possibility of lung cancer being induced by cadmium inhalation. Other studies, however, have shown the induction of lung cancer and other cancers as a result of either inhalation or subcutaneous injection of several different cadmium compounds. The Risk Assessment Guidelines published by the Office of Science and Technology (OSTP) call for taking account of negative as well as positive studies in assessing the weight of evidence.

Since 1980, OSHA has not published guidelines nor a standard concerning how it will assign weight of evidence in the qualitative evaluation of carcinogenicity in experimental animals. Other Agencies have published guidelines, however, including OSTP and EPA. In EPA's guidelines, five conditions are identified that, if present, may lead to a relatively high degree of confidence in the results of animal bioassays:

(1) Biologically independent tumors were found at a large number of sites;

(2) Independent experiments have demonstrated carcinogenic responses in both genders and in multiple species or strains of animals;

(3) There is a clear-cut and statistically significant dose-response relationship;

(4) There is a dose-related shortening of time-to-tumor occurrence; and

(5) There is a dose related increase in the proportion of tumors that are malignant.

Of these five conditions, four appear to exist for cadmium. OSHA requests comments concerning the degree of confidence that should be placed on the experimental study results related to cadmium in light of these five criteria.

The Takenaka study grew out of a pilot study by Heering et al (Ex. 4–04). In that study, 10 rats were exposed for 18 months to cadmium chloride aerosols with a nominal cadmium concentration of 20 $\mu g/m^3$. The animals were sacrificed when exposure ended and four adenomas and one adenocarcinoma were observed.

Results from a study of intratracheal instillations of cadmium oxide are more equivocal. In a study of male Fisher–44 rats, Sanders and Mahaffey found no evidence of cadmium-induced lung carcinomas, but they did observe an increased incidence of mammary fibroadenomas (Ex. 4–61). In that study, three groups of rats were given intratracheal instillations of 25 μg cadmium oxide. Forty-eight rats received one treatment at 70 days of age; 46 rats received two treatments at 70 and 100 days of age for a total dose of 50 μg cadmium oxide; and 50 rats received three treatments at 70, 100, and 130 days for a total dose of 75 μg cadmium oxide. Forty-six rats serving as controls received one intratracheal instillation of 0.9% sodium chloride solution.

The observed incidence of mammary fibroadenomas was 3/45 (7%) in the controls, 7/44 (16%) in the low dose group, 5/41 (12%) in the middle dose group, and 11/48 (23%) in the high dose group. Using the Fisher Exact Test, only the high dose group had a statistically significantly elevated incidence over incidence in the controls ($p=.027$). Two (5%) adenocarcinomas of the lung were observed in the middle dose group. The average number of tumors per tumor bearing rat were 1.4, 1.5, 1.6, and 1.8 for the control, low dose, middle dose, and high dose groups respectively. The authors reported that this difference was significant ($p=.044$) in a chi-square test for independence between number of tumors and treatment groups. Slightly more rats in the control group were found to have no tumors (16%) than treated rats (5 to 7%).

Additional evidence of the carcinogenicity of inhaled cadmium is provided by the results from a long term bioassay by Oldiges et al (Exs. 12–10i, 12–10h, and 12–35). In this study, groups of 20 male and female Wistar rats were exposed to cadmium chloride concentrations at 30 $\mu g/m^3$ or 90 $\mu g/m^3$, cadmium oxide dust at concentrations of 30 $\mu g/m^3$ or 90 $\mu g/m^3$, cadmium oxide fumes at concentrations of 10 $\mu g/m^3$ or 30 $\mu g/m^3$, cadmium sulfate at a concentration of 90 $\mu g/m^3$, cadmium sulfide at concentrations of 90 $\mu g/m^3$, 270 $\mu g/m^3$, 810 $\mu g/m^3$, or 2430 $\mu g/m^3$, or a combination of cadmium oxide and zinc oxide dust at concentrations of 30 and 300 $\mu g/m^3$ respectively or 90 and 900 $\mu g/m^3$ respectively. Twenty male rats and 20 female rats served as controls.

Most groups of animals were exposed for 22 hours per day for 7 days per week. For each of these groups, exposure continued for 18 months or until 25% of that group had died. Other groups of animals were exposed to their cadmium compound for 40 hours per week for 6 months. This shorter exposure protocol was chosen to determine whether a brief exposure period would induce primary lung tumors. Animal groups were followed through month 31 of the study or until 75% of a group had died. At many of the exposure concentrations, doses proved to be too toxic and many animals did not survive the 31 months of study.

Preliminary results from this study are presented in Table V–22. The primary tumors observed in these rats were bronchio-alveolar adenomas, adenocarcinomas, and squamous cell tumors.

TABLE V–22.—INCIDENCE OF PRIMARY LUNG TUMORS IN MALE AND FEMALE WISTAR RATS EXPOSED TO FOUR CADMIUM COMPOUNDS

Exposure [a]	Dose ($\mu g/m^3$)	Sex	Months of exposure [a]	Months of study [b]	Lung tumor incidence
Controls		M		31	0/20
		F		31	0/20
Cadmium Chloride	30	M	18	30	15/20
Cadmium Chloride	30	F	18	31	13/18
Cadmium Chloride	90	M	6	30	11/20
Cadmium Chloride	90	F	6	29	3/18
Cadmium Sulfate	90	M	14	31	11/20
Cadmium Sulfate	90	F	18	29	18/20
Cadmium Sulfide	90	M	18	30	17/20
Cadmium Sulfide	90	F	18	31	15/20
Cadmium	270	M	16	30	14/19

TABLE V-22.—INCIDENCE OF PRIMARY LUNG TUMORS IN MALE AND FEMALE WISTAR RATS EXPOSED TO FOUR CADMIUM COMPOUNDS—Continued

Exposure [c]	Dose (μg/m³)	Sex	Months of exposure [a]	Months of study [b]	Lung tumor incidence
Sulfide	270	F	16	30	16/19
Cadmium	810	M	7	30	11/20
Sulfide	810	F	10	29	13/20
Cadmium	2430	M	4	30	7/16
Sulfide	2430	F	3	31	6/19
Cadmium	[d] 270	M	6	27	3/20
Sulfide	[d] 270	F	6	29	3/20
Cadmium	30	M	18	31	15/20
Oxide Dust	30	F	18	31	15/20
Cadmium	90	M	7	31	9/17
Oxide Dust	90	F	11	31	11/18
Cadmium	[d] 90	M	6	31	4/20
Oxide Dust	[d] 90	F	6	31	3/20
Cadmium	[e] 30	M	18	29	13/18
Oxide Dust	[e] 30	F	18	29	12/20
Cadmium	10	M	18	31	0/19
Oxide Fume	10	F	18	31	0/19
Cadmium	30	M	18	31	3/19
Oxide Fume	30	F	18	31	4/17
Cadmium Oxide and Zinc Oxide Dust	[f] 30/300	M	18	31	0/20
		F	18	31	0/20
Cadmium Oxide and Zinc Oxide Dust	[f] 90/900	M	18	31	8/20
		F	18	31	7/20

[a] Study protocol called for 6 or 18 months of exposure, but exposure was terminated when 25% of an animal group died.
[b] Months of study includes months of exposure. All animals in a group were sacrificed when mortality in that group exceeded 75%.
[c] Incidence is number of animals with at least one primary tumor divided by the number of animals at risk. Primary lung tumors are bronchio-alveolar adenomas, adenocarcinomas, and squamous cell tumors.
[d] Exposure was for 40 hours per week.
[e] Rats were fed a zinc-reduced diet.
[f] Dose was 30 μg/m³ of cadmium and 300 μg/m³ of zinc or 90 μg/m³ of cadmium and 900 μg/m³ of zinc.

The extremely high mortality rates seem to make this study unsuitable for quantitatively assessing the risk associated with each of the cadmium compounds studied or for assessing their relative carcinogenic potency. The study results indicate, however, that while zinc oxide dust may mitigate the carcinogenic potential of lower doses of cadmium oxide, each of the cadmium compounds alone is carcinogenic in animals exposed to these levels through inhalation.

In an inhalation study by Heinrich (Ex. 12–42), male and female Syrian golden hamsters and female mice were exposed to cadmium chloride, cadmium sulphate, cadmium oxide, or cadmium sulfide using exposure concentrations between 10 and 270 μg/m³ for 19 hours per day, five days per week, for 50–70 weeks. An abstract of the study has reported that no cadmium-related significant increase in lung tumor rate was observed in either species. However, complete experimental data were not included.

There have been numerous studies involving the subcutaneous or intramuscular injection of cadmium into both rats and mice. The U.S. Environmental Protection Agency's "Updated Mutagenicity and Carcinogenicity Assessment of Cadmium" presents a summary of many of these studies (Ex. 4–4, p. 62–64).

A short summary of several of these studies is provided in the following section. Several studies have failed to demonstrate a carcinogenic effect from cadmium. In a series of studies, rats and mice were given 5 ppm cadmium acetate or oxalate in drinking water throughout their lives (Exs. 8–308; 8–121; 8–196). Compared to controls, there were no significant differences in the incidence of tumors in animals treated with cadmium, although mortality was increased in rats and male mice. In a study of prostatic changes due to cadmium, Levy et al. (Ex. 8–194) treated rats by subcutaneous injection of cadmium sulphate into the flank once weekly for two years in doses of 0.2, 0.1, and 0.05 mg. A low incidence of sarcomata at the injection site was seen in the treated groups. Levy stated that this finding was not unexpected, having been previously reported by Haddow et al. in 1964, Kazantzis, in 1963, and Health et al., in 1962 (Ex. 8–117). No neoplastic changes were seen in the prostate gland, and there was no treatment-related increase in the incidence of neoplasms at other sites.

In two further studies of the effect of cadmium on the prostate gland by Levy et al. (Ex. 8–034; 8–117), mice and rats were treated with cadmium sulphate by gastric instillation. Dosing regimens were 0.35, 0.18, and 0.087 mg/kg body weight once weekly for two years for rats, and 1.75, 0.88, and 0.44 mg/kg body weight once weekly for 18 months for mice. Concurrent dosing regimens of mice and rat controls were run using gastric instillation of equivalent amounts of distilled water. In both studies, no neoplastic lesions of the prostate or urinary tract were seen. Tumors seen in other organs could not be related to cadmium treatment.

Loser (Ex. 8–643) treated rats with cadmium chloride in the diet for two years at doses of 1, 3, 10, and 50 ppm. Fifty male and fifty female rats were used for each level; 100 rats of each sex served as concurrent controls. Cadmium treatment was not associated with an increased incidence of total numbers of tumors or any specific type of neoplasia.

Other studies (Exs. 4–55; 4–57; 8–253) show that the injection of cadmium metal or certain salts of cadmium produce sarcomas at the site of injection as well as interstitial and Leydig cell tumors of the testes in experimental animals. The simultaneous administration of zinc and cadmium has been found to reduce the incidence of cadmium-induced testicular tumors (Ex. 8–253). For a discussion of these studies, please see Elinder (Ex. 8–086B p. 206).

OSHA has not relied upon the injection and peroral studies for assessing carcinogenic risk, nor upon the preliminary data on inhalation. The

reasons for this are set forth below in the Significance of Risk section of the preamble.

OSHA relied, in part, upon the review by the International Agency for Research on Cancer [(IARC) Ex. 8–656] using IARC's criteria for categorizing animal data. IARC states that $CdCl_2$, CdO, $CdSO_4$, and CdS produced local sarcomas in rats following injection. $CdCl_2$ and $CdSO_4$ produced testicular tumors in mice and rats after subcutaneous administration. IARC concluded that the animal data are "sufficient", that is, a causal relationship has been established between exposures to cadmium and an increased incidence of malignant neoplasms or a combination of benign and malignant neoplasms in two or more species or in two or more independent studies in one species. IARC classifies cadmium as a probable human carcinogen because it is biologically plausible and prudent to regard agents for which there is "sufficient" animal evidence of carcinogenicity as if they presented a carcinogenic risk to humans. OSHA received several comments on the study by Takenaka et al., and on the study by Oldiges et al., which have been addressed in the section on quantitative risk assessment. However, OSHA received substantial comments on the issue of photodecomposition in the study by Oldiges et al., which was subsequently re-published by Glaser et al. with essentially the same data, based upon the same experiments. These comments are addressed below.

2. The Carcinogenicity of Cadmium Pigments

DCMA has submitted comments that there is no evidence that cadmium pigments, per se, are carcinogenic and that even if they were to be considered carcinogenic, they are less potent as carcinogens. These arguments are based upon the opinion that the carcinogenicity of cadmium sulfide (CdS) pigment as administered in the chronic rat inhalation study by Oldiges et al. was the result of CdS undergoing photodecomposition to cadmium sulfate ($CdSO_4$), the latter compound being responsible for the cancers observed in the experimental animals. Secondly, DCMA argued that even if cadmium pigments were determined to be carcinogenic, they are less potent as carcinogens than the more soluble forms of cadmium such as $CdCl_2$ and $CdSO_4$ because they are less soluble and hence less bioavailable in human tissue. DCMA points out that there are applications where cadmium pigments are the only source of exposure to cadmium and that in these situations cadmium pigments should be given a different permissible exposure limit from other cadmium compounds (Ex. 144–20).

DCMA requested that OSHA reopen the record in the cadmium rulemaking on the issue of the toxicity and carcinogenicity of cadmium pigments in order to give the DCMA the opportunity to cross examine OSHA's witnesses on this issue (Ex. 144–20). OSHA reopened the record to receive the results of new studies and comments on these studies and to allow interested parties to comment on opinions of Dr. Oberdörster and Dr. Heinrich, who were requested by OSHA to address the issue of cadmium pigment carcinogenicity.

[Dr. Oberdörster is currently Professor of Toxicology at the University of Rochester and formerly of the Fraunhofer Institute of Toxicology and Aerosol Research in Germany, where the carcinogenicity studies of cadmium compounds and some of the CdS photodecomposition studies were conducted. Dr. Heinrich is a toxicologist with the Fraunhofer Institute of Toxicology and Aerosol Research in Hannover, Germany.] OSHA denied a request to commence a new set of hearings on the issue of cadmium pigment carcinogenicity. OSHA has considered all comments received during the period the record was reopened. OSHA has also considered all comments that were received prior to the reopening of the record.

For background information, a substance is defined as a cadmium pigment, if (1) the contained cadmium is chemically bound to either sulfur (CdS) or selenium (CdSSe) (Sic), and (2) it is used as a colorant, and (3) it contains less than 0.1 percent acid extractable cadmium, as determined by the EN–71 extraction method (DCMA Ex. 120). "Solubility" is the process by which one substance is dissolved in another. Some cadmium compounds, like cadmium oxide (CdO) and cadmium sulfide (CdS), are almost insoluble in water, whereas cadmium chloride ($CdCl_2$) is highly soluble in water. CdO, on the other hand, while insoluble in water is highly soluble in the lung (Ex. 142). In addition to the medium in which a substance can be dissolved, solubility also depends upon the form of the material that is being dissolved. For example, finely divided particles because of their larger surface area/mass ratio are more soluble than larger particles (Ex. 152). More soluble compounds may be more bioavailable and thus more toxic than less soluble compounds, but bioactivity may also be related to mechanical and surface properties (e.g., fibers, SiO_2). "Bioavailability" of cadmium compounds refers to the degree to which cadmium becomes available to the target tissues after exposure.

As presented in OSHA's proposal, data from the Takenaka et al. and Oldiges et al. studies suggested that all of the cadmium compounds administered by inhalation demonstrated a similar qualitative and quantitative carcinogenic response. However, during the OSHA hearing, the issue was raised that the cancer response resulting from inhalation exposure of CdS to Wistar rats in the Oldiges et al. (1989) study may have been the result of photodecomposition of the CdS to cadmium sulfate, the latter compound causing the lung cancer (Ex. 8–694–D). [Note: Virtually the same study was published in 1989 by Oldiges et al. (Ex. 8–694) and in 1990 by Glaser et al. (Ex. 8–694–B). In this section of the preamble, the chronic rat inhalation study for carcinogenicity of four cadmium compounds will be referred to as the Oldiges et al. study (Ex. 8–694–D).]

Based upon preliminary results in his laboratory, Mr. Leonard Ulicny of SCM Chemicals suggested that the particles of CdS pigment in the aqueous suspension used in the Oldiges et al. study may have been solubilized under the influence of light (photodecomposition). Thus, OSHA reopened the docket to receive comments on the issue of the photodecomposition of CdS in the Oldiges et al. study and the role it may have played in the carcinogenic response observed in the study. If complete solubilization only of cadmium pigments and formation of ionic $Cd++$ is responsible for the carcinogenicity of these compounds, the results of the Oldiges et al. study for CdS need to be reconsidered in terms of the carcinogenic response observed in the animals. If, on the other hand, an intrinsic toxic particulate effect contributes also to the carcinogenic effect of cadmium pigments such as CdS, then *in vivo* solubility may not be a good indicator of the carcinogenic potency.

Data from several studies related to insolubility, stability and ionization of CdS were submitted into the record. The data indicate that under proper conditions of light and aqueous suspension of CdS, CdS decomposes and forms cadmium sulfate ($CdSO_4$), and the percent of CdS ionized under such conditions depends upon the concentration of CdS in the aqueous suspension and the intensity of light present.

Mr. Ulicny first raised the issue that CdS particles in suspension may be solubilized under the influence of light (photo-decomposition) based on preliminary results in his laboratory. He performed a solubility study of CdS in aqueous suspension under lighting conditions of 1000 lux for about a week. Gagliardi and Ulicny (1990) presented detailed results of their in vitro experiments (Ex. 144–1) and questioned the validity of the carcinogenic response observed in rats exposed to CdS in the study by Oldiges et al. since a significant fraction of CdS could have been solubilized to soluble $CdSO_4$. They referred to photodecomposition or photo-oxidation of CdS as having occurred under similar conditions in the Oldiges et al. study. However, no evidence was provided at the time of cadmium hearings that such photodecomposition could occur under the relatively low lighting conditions that were present during the Oldiges et al. inhalation study (approximately 50 Lux for 12 hours/day only).

Photodecomposition of CdS was further studied by Glaser et al. in 1991 (Ex. L–140–14). They replicated the aerosol generation procedure employed in the long-term rat inhalation study by Oldiges et al. (1989), the only exception being that the type of CdS used by Glaser et al. was slightly different from that used in the Oldiges et al. cancer study (Ex. 8–694–D). The rat inhalation study had been performed with CdS type E which consisted of 77.1% Cd, 22.0%, S, 0.024% and 0.64% $BaSO_4$, whereas in the solubility study CdS type E1 was used, consisting of 76.5% Cd, 22.2% S, 0.14% Zn, and 0.8% $BaSO_4$. Solubility according to DIN53770 was slightly different, being 0.07% for type E and 0.04% for type E1, and also the specific surface area was 11.8 m^2/g for type E and 8.7 m^2/g for type E1. Type E and E1 had been manufactured by the same process and the same producer, Bayer AG, F.R. Germany, yet they were taken from different batches. Dr. Oberdörster stated that the very small physicochemical differences between the two types should be irrelevant as far as biological effects are concerned (Ex. 141).

In the solubility study by Glaser et al., the CdS aerosol was generated from two different concentrations of the suspension, i.e., 0.38 mg/ml Cd and 1.25 mg/ml. These concentrations of CdS suspension were used to generate aerosol concentrations of 90 and 270 μg per m^3 in the long-term rat inhalation study. The aerosols were generated by nozzle atomizers with attached cyclones to eliminate larger sized particles. The volume that was used daily to generate the aerosol was added each day and amounted to about 300 ml per day. This was adjusted with respect to total cadmium to maintain constancy of the overall cadmium concentration. The light intensity inside the CdS suspension reservoir was measured to be about 50 Lux and the aerosol was generated into the inhalation chambers after being electrically discharged by an ^{85}Kr source before entering the chambers in order to simulate as closely as possible the conditions of the long-term cancer study. The solubility experiment lasted for 64 days; samples of the suspension were taken on days 2, 4, 8, 16, 32 and 64 for measurement of Cd^{++} ions by voltametry and SO_4^{--} by ion chromatography. Aerosol samples were collected on filters taken from the inhalation chambers on day 15 and 30 and were analyzed separately for Cd^{++} and total cadmium. CdS particles were separated from Cd^{++} ions by centrifugation (1400 g for 30 min) and subsequent three fold filtration of the supernatant.

The results showed that under these lighting conditions (50 Lux) a significant solubilization rate of CdS particles in the aqueous suspension occurred. During the 64-day study period, 0.24 mg Cd^{++} per ml was found in the lower concentration of the suspension (0.38 mg/ml), equivalent to 63% being solubilized. In contrast, CdS suspension in the higher concentration (1.25 mg Cd per ml) showed a solubilization of only 11% of total Cd. There was a steady increase of soluble Cd throughout this period which had not quite reached equilibrium at the end of the study period of 64 days. Concurrently with the increase of Cd^{++}, an increase in sulphate could be measured which appeared to reach an equilibrium for the lower concentration (0.38 mg/ml) after about 40 days in the study.

Examination of the filter samples from the collected aerosols showed similarly that the lower Cd concentration (generated from 0.38 mg Cd/ml suspension) had a higher percentage of soluble Cd content (50.6% of total cadmium) compared to the higher concentration (generated from 1.25 mg Cd/ml suspension) which showed only a soluble Cd fraction of about 15% (Ex. L–140–14). According to Dr. Oberdörster, the aerosols are more relevant to actual exposure than CdS concentrations in the suspension because it is the aerosol to which the test animals are actually exposed (Ex. 141). These results indicate that the low lighting conditions present during the chronic rat inhalation study could have resulted in about 50% of the lower concentration of 90 μg CdS/m^3 and about 15% of the higher concentration of 270 μg CdS/m^3 being converted into a soluble form of cadmium. (Ex. L–140–14).

Konig et al. also evaluated the potential for photodecomposition of pigment CdS using the same aerosol generating equipment and protocol as was employed in the long term carcinogenicity study by Oldiges et al. (Exs. L–140–3 and L–140–27–B). The CdS aerosol concentration was kept at approximately 90 $\mu g/m^3$. In about four weeks after starting the experiment, the concentration of cadmium ions in the suspension and in the aerosol reached a plateau at 43.5% and 35.8%, respectively.

These results indicate a slightly lower percentage of photodecomposition as compared to the Glaser photodecomposition study (L–140–14).

Konig et al. (Ex. (L–140–27–B) have also shown that CdS suspended in physiological saline (0.9%) solution at concentrations of 3.33 and 0.83 g Cd/l as applied in the intratracheal instillation studies with rats by Pott et al. (1987) led to solubilization of CdS (Ex. 8–757). The solubilized fraction of Cd within 24 hours was about 3% for the lower Cd concentration (0.83 mg Cd/ml) and about 1% for the higher Cd concentration (3.33 mg Cd/ml). The samples had been illuminated with 800 Lux from fluorescent lamps for 24 hours to approximate the conditions in the study by Pott et al. (1987). The lowest concentration of CdS suspension of 0.16 mg Cd/ml in these same experiments with saline gave the highest solubilization of about 13% within 24 hours.

As a result of the above findings, several questions related to the carcinogenicity of CdS are raised: Can the photodecomposition of CdS to $CdSO_4$ be solely responsible for the carcinogenic effect in rats observed in the Oldiges et al. study? Is inhaled CdS a pulmonary carcinogen? And, if so, how does its carcinogenic potency compare to that of other Cd compounds?

Ulicny and Gagliardi (Ex. 141–1) concluded that the Glaser et al. photodecomposition study demonstrated that inadvertent co-exposure to ionic cadmium ($CdSO_4$) was sufficient to explain the carcinogenic response in the Oldiges et al. study and that the latter study could not be used to define a carcinogenic potency for cadmium pigment.

On the basis of their study results, Konig et al. were of the opinion that the observed lung tumor response in the Oldiges et al. study:

cannot be attributed solely to the effect of CdS * * * The real contribution of the CdS particles to the observed lung tumor rate after inhalation of a mixture of $CdSO_4$ and CdS depends exclusively on the bioavailability or solubility of CdS particles retained in the lungs (Ex. L–140–27–B).

Konig et al. then cited studies by Klimisch et al., whereby they used a dry dispersion technique to exposed rats to CdS aerosols. This technique of preparation and administration of CdS make it unlikely that photodecomposition will occur because moisture and light are not present together. The study showed that Cd was retained in the lungs and was bioavailable since it was found in the kidneys.

Konig et al. also cited inhalation studies with rats and monkeys that measured pulmonary retention (Oberdörster and Cox, 1989) and concluded that the study "clearly showed" the bioavailability of CdS retained in the lungs. CdS in these latter experiments was suspended in ethanol and the exposure to the aerosol lasted for only 10 minutes. Since CdS in ethanol is much more stable than in water, Konig et al. assumed that almost no $CdSO_4$ was inhaled by the animals in the study and concluded:

* * * because of the high carcinogenic potency of Cd^{++} ions in the lungs also very small amounts of dissolved CdS could lead to a tumor response * * * and therefore inhalable CdS has to be regarded as a probable human carcinogen. (L–140–27–B)

* * * because of the low solubility of CdS in the lungs and the relatively long biological half-time of inhaled particles in the human lung compared to the rat lung the carcinogenic risk of CdS dust for humans could be higher than expected on the basis of the rat data. (Ex. L–140–27–B)

The study by Ulicny and Gagliardi shows low *in vitro* solubility of CdS pigment following 30 days of suspension in a solution with a ph of 4.0—a ph similar to that in alveolar macrophages of the lung (Ex. 144–1). The study by Klimisch and Gembardt evaluated the clearance and excretion of CdS and its bioavailability in terms of renal uptake in Wistar rats (Ex. 151). They did not measure liver uptake. A dry dispersion technique was used to expose the animals by inhalation to 0.3 mg/m^3 $CdCl_2$, 0.2 mg/m^3 CdS, 1 mg/m^3 CdS and 8 mg/m^3 CdS. Including controls, five groups of 60 animals were exposed for up to 10 days and followed post exposure for up to three months. For $CdCl_2$, renal accumulation was 35% of lung clearance. For CdS, renal accumulation was 1% of lung clearance. This study again shows the bioavailability of cadmium as a result of inhalation exposure to CdS, however, the amount of accumulation is low compared to the that of $CdCl_2$. Nevertheless, the solubilization and bioavailability of cadmium from inhalation of CdS has been demonstrated in several studies.

Although the results by Konig et al. show slightly less photodecomposition as compared to the results by Glaser et al. from an aqueous suspension and aerosol related to 90 $\mu g/m^3$ of CdS, they nevertheless confirm the findings in the study by Glaser et al. (1991) who observed that CdS will be solubilized to a significant degree when kept in an aqueous suspension even under low light conditions over an extended period of time and that lower concentrations of CdS suspensions will lead to relatively higher solubilization rates.

Dr. Oberdörster considered the issue of CdS carcinogenicity partly from the standpoint of evaluating the lung cancer response in rats observed in the Oldiges et al. inhalation study (Ex. 141). Because of high mortality necessitating cessation of exposure in the groups of animals exposed to the three highest concentrations of CdS (270, 810 and 2430 $\mu g/m^3$), Dr. Oberdörster evaluated lung cancer response in the lowest CdS exposure group (90 $\mu g/m^3$). In order to maximize the estimate of CdS pigment that may have become solubilized in the carcinogenicity study by Oldiges et al. (Ex. 8–964–D), Oberdörster used the data from Glaser et al. (Ex. L–140–14) rather than data from Konig et al. (Ex. L–140–27–B) and therefore assumed that 50% (rather than 38%) of CdS would photodecompose to $CdSO_4$ at the 90 $\mu g/m^3$ exposure level. Thus, the possibility exists that the lung cancer response rate in the Oldiges et al. study (75% in males and 85% in females) may have resulted from combined exposure to CdS and $CdSO_4$ of 45 $\mu g/m^3$ each. When these results were compared to the dose response data for $CdCl_2$ and lung cancer in the Takenaka study, Dr. Oberdörster was of the opinion that this high tumor response rate in the CdS exposed animals could have resulted from the 45 $\mu g/m^3$ of $CdSO_4$ that was produced by photodecomposition. On the other hand, he noted that animals exposed to 90 $\mu g/m^3$ of $CdSO_4$ had a tumor response rate similar to those exposed to 90 $\mu g/m^3$ CdS, i.e., 90 $\mu g/m^3$ of either cadmium compound resulted in the same cancer response. For this reason, he was also of the opinion that the tumor response rate in the group of rats exposed to 90 $\mu g/m^3$ of CdS could have also been the result of the remaining exposure of 45 $\mu g/m^3$ of CdS in combination with $CdSO_4$ if the effects of both compounds were additive. In other words, Dr. Oberdörster was also of the opinion that both cadmium compounds may have been responsible for the high tumor rate observed in the Oldiges et al. study since the high tumor rate placed this value in the flat part of the exposure response curve. Thus, he felt that evidence for the carcinogenicity of CdS could not be determined conclusively from this study.

Dr. Oberdörster also considered the issue of CdS carcinogenicity by evaluating the tumor response observed in rats as a result of administration of various cadmium compounds through intratracheal instillation in the Pott et al. (1987) study. Three separate dose levels for each cadmium compound were used in this study (Ex. 8–757). Animals were exposed to a total of 20 μg, 60 μg or 135 μg of $CdCl_2$ or $CdSO_4$ and to a total of 630 μg, 2500 μg and 10,000 μg of CdS. These doses of CdS would result in approximately 60 μg, 70 μg and 100 μg of $CdSO_4$ being formed through photodecomposition (Ex. 141). In his analysis, Dr. Oberdörster estimated the amount of CdS that would have photodecomposed to $CdSO_4$ in the Pott study based upon the Konig et al. (1991) study.

Note: Dr. Oberdörster overestimated the actual amount of CdS that would photodecompose to soluble $CdSO_4$ in his analysis because he assumed that the CdS suspension was exposed to light for 24 hours when he had information that Dr. Pott had kept the suspension in a dark refrigerator over night.

Dr. Oberdörster compared cancer response in the low and middle dose groups because there was early mortality in the high dose groups—over 50% of the animals in the high dose groups had died before the first tumor was observed in the study.

The tumor response (5.1%) in the low dose group of CdS exposed animals was not significantly different from the tumor response of the pooled low dose groups exposed to $CdCl_2$ and CdO (2.7%) or to the tumor response (6.2%) observed in the pooled middle dose groups of $CdCl_2$ and CdO exposed animals. Dr. Oberdörster then calculated that the tumor response (22.2%) in the mid-dose group exposed to CdS (equivalent to about 70 μg of soluble $CdSO_4$) was: (1) Significantly greater than the tumor response (5.1%) in the low dose CdS group (equivalent to 60 μg of soluble $CdSO_4$) and (2) significantly greater that the tumor response (6.2%) with data combined for the mid-dose groups exposed to 60 μg of soluble $CdCl_2$ or CdO.

Thus, in the presence of CdS, an increase of slightly less than 10 μg of

exposure to $CdSO_4$ (60 to 70 μg) significantly increased the tumor response from 5.1% to 22.2%. In addition, exposure to slightly less than 70 μg of $CdSO_4$ in the presence of a high dose of CdS yielded a significantly higher tumor response (6.2% versus 22.5%) than observed with exposure to 60 μg of soluble $CdCl_2$ or $CdSO_4$. In Dr. Oberdörster's opinion, this significantly increased tumor response as a result of only a slight increase in exposure to $CdSO_4$ in the mid-dose CdS group as compared to the low dose CdS group, or in comparison to the mid-dose $CdCl_2$ or CdO group could not have been the result of exposure to only an additional 10 μg of $CdSO_4$. Therefore, in Dr. Oberdörster's opinion, exposure to CdS was the most likely cause of the increase in lung cancer in the mid-dose group exposed to CdS in this study. Thus, the Pott study provided evidence of a qualitative carcinogenic response as a result of exposure to CdS. Dr. Oberdörster stated:

> * * * no firm conclusion about the pulmonary carcinogenicity can be drawn from the results of the study by Glaser et al. (1990). However, when the inhalation study and the instillation study are viewed together the evidence for carcinogenicity of CdS becomes stronger. (Ex. 141).

The Pott study, however, in Dr. Oberdörster's opinion could not be used to provide quantitative evidence of cancer potency because the cadmium compounds were administered by intratracheal instillation. Dr Oberdörster was of the opinion that CdS is probably less potent as a carcinogen in rats than the other cadmium compounds tested. He stated "to determine how much less this carcinogenic potency is requires a far better knowledge of the underlying molecular and cellular mechanisms of cadmium carcinogenicity than we have at present.

On the basis of their experimental results as presented above, Glaser et al. stated that:

> CdS solubilization may have contributed to the high lung tumor incidences in the CdS exposed rats. However, CdS particles still have a carcinogenic potential to the lung of rats as indicated by the results of Pott et al. (1987), who found an increased lung tumor incidence in rats after repeated intratracheal instillation of CdS particles. (Ex. L-140-14)

Dr. Heinrich of the Fraunhofer Institute in Hannover also commented on the carcinogenic potential of CdS (Ex. 142). Based upon two lines of reasoning, he was of the opinion that CdS is carcinogenic. First, he noted that rats given two intraperitoneal injections of 0.125 mg of Cd as CdO developed a tumor rate of only 6.4% in the 1987 Pott et al. study (Ex. 8-757). He then stated that the high tumor rate (67%) resulting from 50 mg of cadmium as CdS in the study by Pott could only be explained by a high amount of CdS becoming solubilized in the peritoneal cavity over time. He reasoned that if the 50 mg suspension of cadmium as CdS had already contained appreciable quantities of cadmium ions at the time of administration, the animals would have shown toxic effects. Second, the findings of Konig et al. (Ex. L-140-27-B) of about 40% Cd^{++} ion formation in aerosol generated from the 90 $\mu g/m^3$ CdS exposure in relation to the cancer incidence in rats exposed via inhalation to 90 $\mu g/m^3$ of CdS in the Oldiges et al. study (8-694-D) indicated to Heinrich that about 60% or 56 $\mu g/m^3$ of CdS was inhaled by rats in the Oldiges et al. study. As a result, he estimated that the amount of cadmium deposited in the rat lung per day as CdS would have been 2.1 μg. According to Heinrich, only 25% of this amount of cadmium has to be biologically available to reach the same lung burden with cadmium ions and possibly the same tumor rate (15.4%) as the rats exposed to 13.4 μg Cd/m^3 as $CdCl_2$ in the Takenaka et al. study. As a result of the above observations, Heinrich concluded:

> Thus there is no doubt that CdS retained in the lung will dissolve to some extent depending on the residence time or biological halftime of the inhaled CdS particles in the lung. Therefore, inhalable CdS aerosol has to be regarded as a probable human carcinogen. The longer the residence time of the CdS particle in the lung the more CdS becomes dissolved and the higher will be the carcinogenic potency. As we know that the biological halftime of particles with low solubility in the human lung is about ten times longer compared to the rat lung, the carcinogenic potency of inhaled CdS aerosols is expected to be higher for humans than for rats. (Ex. 142)

In other words, the same dose of CdS to the human lung may cause a greater carcinogenic response than in the rat lung because of longer retention time in the human lung. However, this does not imply that CdS would be a more potent carcinogen than other more soluble cadmium compounds based on the ionic theory of carcinogenesis. Indeed, DCMA (Ex. 144-20) pointed out that all of the cadmium compounds had a similar retention time in the rat lung and that the study by Dr. Oberdörster and Cox (Ex. 31-A) indicated that all of the cadmium compounds are retained in the lungs of primates 10 times longer than in rodents.

Thus, it seems reasonable to assume that the steady state concentration and the resulting retained dose of CdS particles from a comparable exposure concentration will be higher in the human lung than in the rat lung. Moreover, the longer residence time of CdS particles to be released in the human lung means that there is more time than in the rat lung for cadmium ions to be released by dissolution from the CdS particles (Ex. 142). Both of these biological factors lead Dr. Heinrich to conclude that from a comparable exposure concentration, the resulting carcinogenic effect of CdS will be higher in the human lung than in the rat lung (Ex. 142) even though the overall carcinogenic effect of CdS may be less as compared to other more soluble cadmium compounds.

Based upon the ionic theory of carcinogenesis for cadmium compounds and data related to solubility and bioavailability of CdS in rats, Dr. Heinrich (Ex. 142), Dr. Oberdörster (Ex. 141) and Drs. Konig et al. (Ex. L-140-27-B) were all of the opinion that CdS-exposed rats are likely to develop a lower lung tumor rate than $CdCl_2$ or CdO-exposed rats. Neither Dr. Heinrich nor Dr. Oberdörster, however, could not give an estimate of the carcinogenic potency of CdS to humans because of lack of knowledge of the mechanisms involved. For example, Dr. Heinrich stated that we do not:

> * * * know how many cadmium ions are actually necessary to induce the observed carcinogenic effect. We also do not know whether metallothionein-bound cadmium ions in the lung can be remobilized and are thus also available for a carcinogenic effect. (Ex. 142)

With regard to carcinogenic potency of CdS, Dr. Oberdörster stated:

> To determine how much less this carcinogenic potency is requires a far better knowledge of the underlying molecular and cellular mechanisms of cadmium carcinogenicity than we have at present. I can think of several hypothetical mechanistic scenarios which would implicate CdS as being a direct or indirect pulmonary carcinogen. (Ex. 141)

Dr. Oberdörster went on to say that if ionic cadmium is the ultimate carcinogen, then long term in vivo solubilization rates in the lung may permit the estimate of a potency factor for bioavailability of Cd^{++}. If, on the other hand, an intrinsic toxic particulate effect contributes to the carcinogenic effect of CdS as it may do with respect to toxic effects in the lungs, then in vivo solubility is not a good indicator of carcinogenic potency. He also stated the possibility of a combined effect of solubilized cadmium on further in vivo CdS solubilization and retention due to effects on lung cell function as a possible mechanism.

In summary, DCMA requested a separate health standard for cadmium pigments (Ex. 144–20). The basis for this opinion is that the scientific studies of carcinogenicity by Oldiges et al. and by Pott et al. are flawed because the CdS administered to the animals was subjected to light and as a result the material photodecomposed to $CdSO_4$, which was responsible for the cancer response.

After reviewing the new photodecomposition studies and comments about them as mentioned above, OSHA is of the opinion that the photodecomposition of CdS to $CdSO_4$ may have played a role in the cancer response observed in the Oldiges et al. and Pott et al. studies. However, photodecomposition of CdS to $CdSO_4$ could not account for the tumor response observed in the mid-dose group of the Pott et al. study as pointed out by Oberdörster (Ex. 141) and discussed above. If CdS was responsible for the significant increase in the cancer response observed in the mid-dose group, it is reasonable to conclude that CdS has a carcinogenic potential and contributed to the cancer response observed in the inhalation cancer study by Oldiges et al.

After reviewing all of the studies and comments on the issue of CdS carcinogenicity, OSHA agrees with the commentors that the CdS preparations used in animal carcinogenicity studies photodecomposed to varying degrees which depended upon the concentration administered and the amount of light and moisture present. The exact role of this photodecomposition in the quantitative carcinogenic response observed in the various cancer studies, however, cannot be determined. Nevertheless, evidence was presented during the rulemaking that CdS is a probable human carcinogen. This opinion of OSHA is derived from a combination of the following observations:

(1) The analysis of Dr. Oberdörster showing that an increase of only 10 μg of $CdSO_4$ in the presence of CdS resulted in a statistically significant increase in lung tumor response in the Pott et al. study;

(2) The Oldiges et al. study demonstrating a significant increase in lung cancer in rats exposed to CdS by inhalation;

(3) The above mentioned analysis by Heinrich indicating that the lung tumor response among animals given 50 mg of cadmium as CdS in the Pott et al. study can only be explained by a high solubility of CdS in the peritoneal cavity over time;

(4) Study results indicating that administration of CdS leads to absorption into the body;

(5) Lung retention of CdS aerosol is estimated to be 10 times greater in the human lung than in the rat lung and increases the likelihood of systemic absorption in humans.

With the exception of Mr. Ulicny, all of the investigators involved in the actual research related to CdS photodecomposition or carcinogenicity who offered comments (Glaser et al.; Konig et al.; Heinrich; Oberdörster) were of the opinion that CdS was carcinogenic even though photodecomposition to $CdSO_4$ may have played a role in the carcinogenic response observed in the animal cancer studies (Exs. L–140–14; L–140–27–B; 142; 141). None of the latter group of investigators was of the opinion that CdS was not carcinogenic.

The animal inhalation studies with the various cadmium compounds by Oldiges et al. indicate a similar carcinogenic response even though the photodecomposition studies raise the possibility that part of the cancer response with CdS may have been due to the photodecomposition of CdS to soluble $CdSO_4$. The analysis of the Pott et al. data by Dr. Oberdörster indicates that a large part of the carcinogenic response in the animals had to be attributed to CdS since it could not be attributed solely to $CdSO_4$ (Ex. 141). Thus, it is also possible that a large portion of the carcinogenic response observed in the Oldiges et al. inhalation study of CdS could be attributed to CdS. Therefore, it is also reasonable to conclude that the cancer response of rats in the Oldiges et al. inhalation study could not be attributed entirely to the formation of ionic cadmium through photodecomposition. How much of the cancer response may have been due to the photodecomposition, however, cannot be determined with the data currently available because information on molecular and cellular mechanisms involved in the carcinogenicity of the various cadmium compounds is not known.

It was pointed out that an intrinsic toxic particulate effect could contribute to the carcinogenic effect of CdS and if this is so, in vivo solubility is not a good indicator of carcinogenic potency of cadmium pigments. It was also pointed out that CdS may have acted in an additive manner with the amount of $CdSO_4$ formed through photodecomposition to induce cancer.

Evidence also indicates that CdS will be retained in the human lung 10 times longer than in the rat lung making it likely that the potency from inhaled CdS will be greater for humans than for rats. If one accepts the ionic theory of cancer for cadmium compounds, CdS pigments may be less carcinogenic, but it is not possible to determine the magnitude of the difference in potency when the results are extrapolated to humans. An intrinsic particulate effect could play a role in the development of cancer with the cadmium pigments and there could also be a combined effect of solubilized cadmium on further in vivo CdS solubilization and retention in relation to lung function.

Thus, OSHA is of the opinion that CdS is an occupational carcinogen. With the data currently available, however, it is not possible to determine whether cadmium sulfide has a different carcinogenic potency from other cadmium compounds though it is possible that it may be less potent. Therefore, with regard to carcinogenicity, CdS will be treated similar to other cadmium compounds.

DCMA (Ex. 144–20) has argued that a conclusion that CdS should be regulated as an occupational carcinogen does not conform with OSHA's Cancer Policy. However, in addition to the evidence of carcinogenicity presented above, sec. 1990.111 (c) of the Cancer Policy (45 FR 5002–5296, Jan 22,1980) allows the Agency to regulate groups of substances, or combinations of substances, or mixtures of substances found in the workplace. Thus, OSHA may regulate a group of substances on the basis of the scientific evidence available on a single member of the group. In the arsenic standard, OSHA regulated all pentavalent arsenic compounds along with all trivalent arsenic compounds as carcinogens even though evidence of carcinogenicity for the former compounds was based on a single study of pentavalent arsenic exposure which was limited in study design and methodology. In the arsenic standard, OSHA relied upon expert opinion about the study results for the carcinogenicity of pentavalent arsenic, the evidence on the carcinogenicity of trivalent arsenic compounds, as well as on the Supreme Court's benzene decision (I.U.D. v. A.P.I. 448 U.S. 607) that OSHA was free to use conservative assumptions to err on the side of worker protection. Inclusion of pentavalent arsenic compounds in the arsenic standard was upheld by the Court of Appeals in ASARCO, Inc. v. OSHA (746 F. 2d 483 (1984)), which agreed that it was appropriate to utilize evidence of the carcinogenicity of trivalent arsenic compounds in determining the carcinogenicity of pentavalent arsenic compounds. Thus, OSHA believes that it

has a scientific basis as well as a judicial basis for including CdS in the current standard and for establishing the same PEL for cadmium pigments that will be set for all other inorganic cadmium compounds. In any event, OSHA notes that all of the inorganic salts of cadmium, including CdS, tested for carcinogenicity by inhalation in the rat produced a highly carcinogenic response.

As discussed in the section of this preamble dealing with CdS carcinogenicity, record evidence and expert opinion leads the Agency to conclude that CdS, in and of itself, is an occupational carcinogen. The final issue raised is whether or not CdS has the same carcinogenic potency as the other cadmium salts. Although the cancer test results showed a similar tumor response for CdS as for other cadmium compounds tested, because of the possibility of photodecomposition, several experts testified that it is not possible with scientific certainty to determine the relative carcinogenic response that could be attributed to CdS as distinguished from $CdSO_4$. Dr. Oberdörster, for example, stated that an additive effect between CdS and $CdSO_4$ in the carcinogenic response cannot be excluded and that until more and better data become available, it would not be advisable to establish a different standard for CdS (Ex. 141). Thus, record evidence and expert opinion lead the Agency to conclude that CdS should be considered an occupational carcinogen and have the same PEL as that established for other cadmium compounds.

3. Evidence in Humans—Introduction

Extensive study of five cohorts with occupational exposure to cadmium has found an excess of lung cancer among cadmium exposed workers (Ex. L–140–50). The mortality experience of these workers has been studied repeatedly. The five cohorts are comprised of workers at a cadmium smelter in the U.S. (Thun, Exs. 4–68; 8–658a; Lemen, Ex. 4–51 and Varner, Ex. 8–649); workers at two cadmium battery plants in the United Kingdom (Armstrong and Kazantzis Ex. 8–603; Kipling and Waterhouse, Ex. 4–45; Sorahan, Ex. 4–65; and Sorahan, Ex. 12–12–A); workers from 17 different plants using cadmium in the United Kingdom (Armstrong and Kazantzis, Ex. 8–603; Armstrong and Kazantzis, Ex. 8–565; and Kazantzis et al., Ex. 8–684); workers at a cadmium-alloy plant in the United Kingdom (Holden, Ex. 4–39; Armstrong and Kazantzis, Ex. 8–603); and workers at a nickel-cadmium battery plant in Sweden (Kjellstrom et al., Ex. 4–48; Elinder et al., Ex. 4–25; Jarup et al., referenced in L–140–50). Evaluation of these data is complicated by the fact that the same populations have been examined repeatedly, sometimes by different groups of investigators. For example, the cohort of workers from 17 plants included members of the the cohort at the two cadmium battery plants (Exs. 8–603 and 12–12–A).

Elinder et al. evaluated 13 studies of these cohorts and concluded that in several studies, workers with high exposures were combined with workers with low exposures into one exposure group. This would reduce the ability of these studies to detect an effect due to cadmium exposure (Ex. 4–25). In addition, Elinder concluded that in the largest study (Ex. 8–684), most workers had such low cadmium exposures that cadmium-associated cancer would not be induced. After evaluating the studies, Elinder combined the data from them and found an overall lung cancer SMR of 121 (Obs.=195; Exp.=161.4; p=0.008, two-tailed).

Elinder also found that 12 of the 13 studies reported excess cancers of the prostate, and in 4 of these, the excesses were statistically significant. Elinder noted that the median SMR for prostate cancer from all of the studies was 167, but when the number of observed and expected cases are combined for the most recent updates of the 6 independent studies (7 of the 13 studies were updates of earlier studies), the statistically significant SMR for prostate cancer for all cohorts is 162 (Obs=28, Exp=17.2, $p<.02$, two-tailed).

Elinder concluded, "Our interpretation is that the accumulating data on the mortality of cadmium workers with high exposure levels in the past (above 0.3 mg/m^3) support an association between lung cancer and cancer of the prostate and exposure to cadmium," (Ex. 4–25). Thun et al. subsequently evaluated studies of these same five cohorts including updates of studies of four of the five cohorts (Ex. L–140–50). The authors' analysis of the prostate cancer data lead them to conclude that while mortality from prostate cancer is slightly increased in several of these industrial cohorts, the number of excess cases is small and there is no clear dose-response relationship with exposure. Several other researchers have concluded that the evidence for an association between cadmium exposure and prostate cancer is limited or decreasing (Exs. 19–43–A and 19–29).

Analyzing the lung cancer data from these studies, Thun et al. found that these updates reported a statistically significant increase in mortality from lung cancer in cadmium smelter workers, with two or more years of employment (SMR=137, Obs=24, Exp=10.76, 95% CI= 143–332 (Thun, Ex. 33)); a statistically significant increase in mortality from lung cancer in nickel-cadmium battery workers in the U.K. (SMR=130, Obs.=110, Exp.= 84.5, 95% CI=107–157 (Sorahan, Ex. 12–12–A)); a statistically significant increase in mortality from lung cancer in workers at 17 plants combined in the U.K. (SMR=115, Obs.=277, Exp.=240.9, 95% CI=101–129 (Kazantzis, Ex. 8–684)); and a statistically significant increase in mortality from lung cancer in Swedish nickel-cadmium battery workers (SMR=241, Obs.=14, Exp.=5.8, 95% CI=132–405 (Jarup et al., referenced in Ex. L–140–50)). Thus, in each of these updates a statistically significant excess of lung cancers was observed.

These studies provide qualitative evidence of the carcinogenic effects of cadmium on the human lung. In several of these studies, there are indications of a dose-response relationship between cadmium exposure and risk (Ex. L–140–50). For example, in three cohorts (Exs. 33, 12–12–A, and 8–684), the SMR for lung cancer increases either with length of employment or cumulative exposure to cadmium (Ex. L–140–50).

4. Studies of the U.K. Nickel-Cadmium Battery Factory Cohort

One of the earliest cohort studies was by Kipling and Waterhouse who observed four cases of prostate cancer among a cohort of 248 men employed in a British nickel-cadmium battery factory (Ex. 4–45). Exposure was to cadmium oxide dust. The observed number of prostate cancers was more than seven times greater than the expected number of protate cancers (Exp=0.58, p=.003] calculated using incidence rates from a regional cancer registry.

In a subsequent study of these workers, Sorahan and Waterhouse observed a statistically significant excess of respiratory cancer (Obs=89; Exp=70.2; SMR=127; $p<.05$)(Ex. 4–65). An excess of prostate cancer was again observed, but this time was not statistically significant (Obs=8; Exp=6.6; SMR=121).

To assess the relationship between cadmium dose and mortality, the authors devised two measures of cadmium exposure. The first measure was "cumulative duration of employment in high exposure jobs," and the second measure was "cumulative duration of employment in high or moderate exposure jobs." Using the method of regression models in life tables, the authors found that

cumulative duration of employment in high exposure jobs was significantly related to prostate cancer mortality but only when the four original cases described by Kipling and Waterhouse were included in the analysis. The measure cumulative duration of employment in high exposure jobs was not statistically significantly associated with lung cancer mortality, but the measure cumulative duration of employment in high or moderate exposure jobs did show a statistically significant relationship to lung cancer mortality. The authors cautioned, however, that this observed effect could be confounded by oxyacetylene fume exposure.

Workers at this factory were studied once again by Armstrong and Kazantzis, who conducted a case-control study of workers who had died of prostate cancer, renal cancer, bronchitis or emphysema, or nephritis or nephrosis (Ex. 4–19). Cases were selected from three cohorts of British workers exposed to cadmium. All of the cohorts had been studied previously. Cohort C1 was comprised of workers from a lead-zinc-cadmium smelter previously studied by Armstrong and Kazantzis (Ex. 8–505). Cohort C2 was comprised of workers from the nickel-cadmium battery factory studied by Sorahan and Waterhouse (Ex. 4–65). Cohort C3 was comprised of workers from a copper-cadmium alloy plant previously studied by Holden who had found statistically significant excess of prostate cancers (Ex. 4–40). Cases consisted of workers who had died of prostate cancer, chronic respiratory disease or renal disease. Only men born before 1940 with at least one year employment before 1970 were included. For each case, 3 controls were selected matched by plant, age, and, as nearly as possible, date of birth.

The authors divided these cohorts into three groups: always low cadmium exposure; ever medium cadmium exposure; and ever high cadmium exposure. They found that the odds of prostate cancer for the ever medium or ever high exposure groups were elevated relative to the always low exposure groups (1.55 and 1.35 respectively), but neither of these odds ratios were statistically significant. The authors noted, however, that the small number of prostate cancer cases makes interpretation of this finding difficult.

In 1987, Sorahan updated his study of the nickel cadmium battery workers (Ex. 12–12A). Twenty-two additional deaths from lung cancer were reported. According to the author, there was some evidence of an association between risk of death from lung cancer and duration of employment in high or moderate (or slight) exposure jobs for "early workers" (i.e. first employed before 1946), but none for "late workers" (i.e. first employed after 1946). A significant increase in lung cancer was observed for the entire study cohort (110 Obs., 84.5 Exp., $p<.01$). Sorahan did not report a statistically significant increase in lung cancer for his cohort when workers were divided into "early workers" and "late workers," but OSHA's analysis shows that there was a significant excess of lung cancers for the "late workers" (45 Obs., 33 Exp., $p<.05$—one tail).

Among "late workers," the SMRs for lung cancer were observed to increase with years from first employment. Because this trend was not observed for "early workers," Sorahan suggested that the there might be selection bias for the "early workers" and that this sub-cohort may be incomplete. The study's inability to demonstrate a significant relationship between duration of employment and lung cancer risk, however, does not mean that there is no association between cadmium exposure and lung cancer risk. Duration of exposure may not be a surrogate for dose, particularly when the length of exposure periods are not adjusted for the particular years in which the exposure occurs. The observed excess of lung cancer deaths among the "late workers" supports an association between cadmium exposure and lung cancer.

5. Studies of the 17 U.K. Plant Cohort

Ades and Kazantzis conducted a study of lung cancer in non-ferrous smelter workers (Ex. 12–14C). This cohort of men employed in a lead-zinc-cadmium smelter was part of Cohort C1 in the Armstrong and Kazantzis study described above (Ex. 4–19). The authors found a significant excess of lung cancer deaths among the entire cohort (182 Obs., 146.2 Exp., $p<.005$). In subcohorts of workers, a significant excess of lung cancer deaths was observed for workers with 20 to 29 years of employment (44 Obs., 23.1 Exp., $p<.005$) and for workers with 40 or more years of employment (8 Obs., 2.74 Exp., $p<.02$).

SMRs for lung cancer death were observed to increase with duration of employment for the cohort. This linear trend was statistically significant. The risk of lung cancer for workers with more than five years of employment relative to the risk for workers with less than five years of employment was also observed to increase with duration of employment. Using a matched logistic regression analysis, the authors were able to associate this increasing risk with exposure to arsenic and lead but not cadmium. This finding, however, could be due in part to the study protocol for choosing controls. Cases and controls were matched by date of hire, but because controls were required to have ten years of follow-up and to survive the matched case, cases and controls may have been inadvertently matched on cadmium exposure as well.

The entire Armstrong and Kazantzis cohort was studied again by Kazantzis and associates (Ex. 8–684). In this update, the authors followed the workers for an additional five years. Seventy-five additional cases of lung cancer were observed, resulting in a significant excess of mortality due to lung cancer for both the additional five year period (SMR=134; 95% CI=103–164) and the entire study period (Obs=277; Exp=240.9; SMR=115; 95% CI=101–129).

The increased lung cancer risk occurred mainly among those first employed before 1940, and the risk increased with length of employment and length of follow-up. The majority of lung cancer deaths were among workers employed in the non-ferrous smelter studied by Ades and Kazantzis. This worksite provided over 60% of the total study population, but its workers' exposures were characterized only as low or medium. No exposures in the smelter were characterized as high.

Over the entire study period, there was a statistically significant excess of mortality due to stomach cancer (Obs=98; Exp=70.6; SMR=139; 95% CI=111–166). Of the 98 deaths observed, 22 occurred during the five years of added follow-up, giving a statistically significant excess of stomach cancer mortality for that five year period (SMR=179; 95% CI=112–271).

Dr. Kaztanzis testified that there were other major illnesses, in addition to cancer of the lung, considered a priori to be possibly related to cadmium exposure that needed to be evaluated in this large cohort study. These included chronic bronchitis (chronic obstructive airway disease) and emphysema, among others (Tr. 6/8/90).

According to Dr. Oberdörster, who testified at the hearing, OSHA did not discuss the important finding of the Armstrong and Kazantzis study, that there was a high risk of dying from bronchitis in the group of "ever high" Cd-exposed workers.

According to Dr. Oberdörster, this is an important health effect of Cd exposure, reconfirmed in an updated study by Kazantzis, and it deserves more attention (Tr. 6/6/90, pp. 153–246) because: "Increased cell proliferation rates which can be assumed to be

present in the workers with chronic bronchitis could indeed be an important risk factor in carcinogenesis (Ex. 31, Attachment D)." Furthermore, Dr. Oberdörster stated, "Dying from bronchitis is comparable to dying from lung cancer." (Ex. 31, p. 4)

The update included the diseases considered to be important by Dr. Kazantzis. The results of the study confirmed a significant excess risk from bronchitis related to intensity of exposure. The SMR for workers classified as having "ever high" exposures was 382 (Obs.=13; Exp.=3.4, 95% CI=203–654). The SMR for workers classified as having "ever medium" exposures was 146 (Obs.=25, Exp.=17.1, 95% CI=94–215. The SMR for workers classified as having always low exposures was 123 (Obs.=140, Exp.=114.3, 95% CI=102–143). The bronchitis SMR for the entire cohort was statistically significantly elevated (SMR=132, Obs.=178, Exp.=134.9, 95% CI=113–151).

In response to questions during the hearing about the marked excess of mortality from bronchitis which showed a strong relation to both intensity and duration of exposure that was observed in his follow-up study, Dr. Kazantzis agreed that the dose response is cadmium-exposure-related. Dr. Kazantzis stated that:

> I find it very difficult to account for that in any other way other than the cadmium exposure * * * our study has * * * a very high proportion of low exposed workers, nevertheless, we have found this very marked dose response relationship. (Tr. 6/8/90)

The Cadmium Council has argued that the studies by Kazantzis "failed to establish a clear association between cadmium exposure and lung cancer," in part because the studies failed to adequately control for exposure to other carcinogens such as arsenic and nickel (Ex. 19–43). The Council questioned the link between cadmium exposure and prostate cancer because no cases of prostate cancer were observed in the medium- or high-exposure groups. The Kazantzis 5-year update also found no prostate cancer in these exposure groups (Ex. 8–684, p. 18).

A new update of this cohort is currently underway (Ex. L–140–50, pp. 701–702). According to Dr. Kazantzis:

> The mortality experience of the cohort is currently being followed up for an additional 5-year period. Preliminary analysis of mortality from lung cancer for the first three of five years confirmed a significantly increased lung cancer risk for the total study period from 1942–1987, but a significant excess lung cancer risk was no longer seen in the high exposure group (Kazantzis, 1990).

At present, however, this study has not been published and the paper has not been submitted into the record for analysis of the methodology used in the study.

6. Studies of the Swedish Cadmium-Nickel Battery Factory Cohort

In an update of an earlier study by Kjellstrom et al (Ex. 4–48), Elinder et al examined the mortality experience of 545 male workers at a Swedish cadmium-nickel battery factory (Ex. 4–25). While no statistically significant excess of mortality due to any type of cancer was observed, the authors reported that the SMRs for cancers of the lung, prostate, and bladder increased with time since initial exposure (i.e. latency) among workers with at least 5 years of exposure. Thus, for lung cancer, the SMR, was 133 for the entire cohort, but for workers with at least five years of exposure, the SMR was 163 after 10 years latency and 175 after 20 years latency. For prostate cancer, the SMR was 108 for the entire cohort, but for workers with at least 5 years of exposure, the SMR was 125 after 10 years latency and 148 after 20 years latency. For bladder cancer, the SMR was 181 for the entire cohort, but for workers with at least 5 years of exposure, the SMR was 222 after 10 years latency and 250 after 20 years latency.

This study was updated in 1990 by Jarup et al., (referenced in Ex. L–140–50). A statistically significant increase in lung cancer mortality was reported among nickel-cadmium battery workers, using regional rates and 20 years latency (SMR = 232).

7. Studies of Two U.K. Copper-Cadmium Alloy Plant Cohorts

A mortality study of 330 men employed in two factories manufacturing copper alloys was conducted by Holden in 1980 (Ex. 4–39). Plant A was in operation from 1922 to 1966, and plant B was in operation since 1925. Holden reported that 104 men in his cohort had been medically evaluated over time, and in 1953, 22% were found to have chronic cadmium poisoning; eleven workers had both emphysema and proteinuria; eight had proteinuria alone; and, four had emphysema alone. Holden's mortality study indicated that in plant B, the respiratory cancer SMR [International Classification of Diseases, 8th Revision (ICD–8); ICD 160–163] was 222 (Obs.=8; Exp.=4.5) using the population of England and Wales as a comparison population. When death rates for the urban district in which the plant is located were used, the SMR was 167 (Obs.=10; Exp.=6).

The mortality experience of these workers was subsequently followed up by Armstrong and Kazantzis in 1982 in a report to the International Lead Zinc Research Organization (Ex. 8–603). In that report, the authors included those cases from the study performed by Holden which satisfied the selection criteria of the Armstrong and Kazantzis study. The lung cancer SMRs for this group of workers were 87 for the control group, 114 for the medium exposure group, and 72 for the high exposure categories. The mortality experience of these workers was combined with that of workers from 16 other plants. The results of the follow-up study are included in the discussion of the studies of the 17 U.K. plant cohort above.

8. Studies of the U.S. Cadmium Smelter Cohort (Globe)

One of the strongest studies supporting the evidence of the carcinogenicity of cadmium in humans comes from the mortality study of cadmium smelter workers at the Globe plant in Denver, Colorado. Previous studies of workers in this plant were conducted by Varner (Ex. 8–649) and by Lemen et al. (Ex. 4–61).

This population was first studied by Lemen et al. (Ex. 4–61) who found a statistically significant excess of deaths due to malignant neoplasms (i.e. cancer). Lemen's study population consisted of 292 white male workers with a minimum of two years employment between 1940 and 1969. Of these workers, 27 died of malignant neoplasms whereas only 17.57 deaths from this cause were expected (SMR=154; p=.05). Twelve of the 27 deaths were due to respiratory cancer whereas only 5.11 were expected (SMR=235), and this excess was also statistically significant ($p<.05$). Focusing of the lung cancer incidence, Lemen found that the rates increased with time since first exposure and that the highest rates were observed in workers with more than 30 years of follow-up. Lemen also found an excess of deaths due to prostate cancer, but this excess was statistically significant only when the analysis was restricted to workers with at least 20 years since first exposure (Obs=4; Exp=1.15; SMR=347; $p<.05$). Lemen's study was followed by a study by Varner (Ex. 8–649). The Varner cohort consisted of 644 workers with at least six months of employment at the Globe smelter between 1940 and 1969. The cohort was followed through 1981. Mortality data was analyzed using Standardized Cause Ratios (SCRs). Statistically significant excesses of mortality due to lung cancer, urinary tract cancer, specific bladder

cancers, and total cancers were observed. Mortality due to prostate cancer was elevated, but the excess was not statistically significant.

Cumulative cadmium exposures were estimated for each member of the cohort using personal monitoring measurements made from 1973 through 1976. Exposures measured during this period were assumed to be constant for the entire period of study. The cohort was divided into a low exposure group (0–4 mg/m^3-years), a middle exposure group (5–15 mg/m^3-years), and a high exposure group (16+ mg/m^3-years). The observed SCRs for lung cancer deaths for each exposure group were: 95 for the low dose group, 159 for the middle dose group, and 332 for the high dose group. The observed SCRs for all cancer deaths for each exposure group were: 108 for the low dose group, 123 for the middle dose group, and 168 for the high dose group. A dose-response relationship was observed between cadmium exposure and lung cancer and between cadmium exposure and total cancers.

Varner attributed the observed excess of lung cancer deaths to arsenic exposure and cigarette smoking but did not present any data on smoking and arsenic exposures by dose group. There was, therefore, little reason to assume that these confounders did not affect all three exposure groups to at least some, if not the same, degree. There was no evidence that smoking was more common among cadmium workers than among the general population and therefore that the observed lung cancer excess was associated with increased smoking.

Varner's study was followed up by Thun et al., (Ex. 4–68). Originally, Thun followed 602 white males who had spent at least 6 months in a production area of the smelter between 1940 and 1969. Workers were followed through 1978. The mortality status of all but 12 workers (2%) was determined; 411 were still alive (69%) and 179 had died (29%). Deceased workers for whom no death certificate was located were assumed dead, as specified in the protocol, with the cause of death unknown. Persons lost to follow-up were assumed to be alive.

From 1886 to 1919, the Globe plant was a lead smelter, and from 1920 to 1926, it was an arsenic smelter. Twenty-six of the 602 workers had been hired prior to 1926. These workers were omitted from subsequent analyses. Most analyses were limited to the remaining 576 workers.

Worker exposures were estimated by Smith et al., who based his estimates on historical area monitoring data adjusted to reflect the actual exposures of workers wearing respirators (Ex. 4–64). Using Smith's exposure estimates and company personnel records, Thun calculated cumulative dose estimates for each worker in his cohort.

Thun analyzed his data using a modified life-table method developed by National Institute of Occupational Safety and Health (NIOSH). Expected rates were calculated from the U.S. population and were adjusted for age, sex, race, and calendar time. Both standardized mortality ratios (SMRs) and standardized risk ratios (SRRs) were examined. To analyze his data by cumulative exposure, Thun divided his cohort into three groups chosen prior to analysis of the data. These groups corresponded to the recommended exposure limits that were in existence at the time the study was conducted. The low dose group consisted of workers with cadmium exposure at 584 μ/m^3-days or less, the equivalent to forty years of exposure at less than or equal to 40 μ/m^3. This cumulative dose corresponded to the NIOSH recommended exposure level at that time. The upper limit of the middle dose group, i.e., 40 years of exposure between 41 and 200 μ/m^3, was chosen to correspond to the upper limit allowed by OSHA. The high dose group was chosen as 40 years of exposure at greater than 200 μ/m^3. Thun also identified for separate analysis a subset of the low exposure group of his cohort in which the 40-year TWA equivalent exposures ranged from 21–40 μ/m^3.

Thus, the update of this cohort by Thun et al., (Exs. 4–68 and 8–658a) included estimates of cadmium exposures and an evaluation of the mortality experience of the workers in the cohort by SMRs per dose group. An excess of lung cancer mortality was observed in relation to cadmium exposure.

Forty-three percent of the workers had less than 2 years of employment. Follow-up time was long; 82.5% had more than 20 years of follow-up and 66.3% had more than 30 years of follow-up. Among the entire cohort of 602 workers, a statistically significant excess of deaths due to respiratory cancer (Obs=20; Exp=12.15; SMR=165; CI=101–254) and deaths due to non-malignant gastrointestinal disease (Obs=9; Exp=2.35; SMR=383; CI=175–727) was observed. All deaths due to lung cancer occurred in workers with more than two years of employment. When the analysis was restricted to the 576 workers hired after 1926, the excess of lung cancer death was no longer statistically significant (Obs=16; Exp=10.88; SMR=147). When the analysis of these 576 workers was further restricted to those workers with two or more years of employment, the observed excess was statistically significant (Obs=16; Exp=7.00; SMR=229; CI=131–371).

Analysis of all the 576 workers hired after 1926 indicated that the incidence of lung cancer death increased with dose. A statistically significant dose-response relationship existed between cumulative exposures to cadmium and lung cancer mortality. Among the low dose group, there was a non-significant deficit, i.e. lower than expected, of lung cancer deaths (Obs=2; Exp=3.77; SMR=53; p=0.28; SRR=0.48; See Table VI–14). Among the subset of the low exposure group with exposures equivalent to 21–40 μ/m^3 over 40 years, the lung cancer SMR was 100 and the SRR was 96. For the middle dose group, a non-significant excess of lung cancer was observed (Obs=7; Exp=4.61; SMR=152; SRR=1.55). For the high dose group, the excess of lung cancer deaths was statistically significant (Obs=7; Exp=2.5; SMR=280; CI=113–577; SRR=3.45). Thun reported that this dose-response trend was also observed when the analysis was restricted to workers with more than 20 years since first exposure. The regression slope of the SRR for lung cancer was statistically significant indicating that an increase in cadmium exposure is producing a real increase in the risk of lung cancer.

Thun et al., also observed a significant increase in death from non-malignant gastrointestinal disease (NMGID), 9 observed versus 2.35 expected. The death certificates for six of these individuals suggested peptic ulcer disease. For those hired after 1926, there was a significant linear trend between increased cadmium exposure and the SRR from NMGID. The authors thought this observation was noteworthy in light of previously reported associations between cadmium exposure and severe gastrointestinal irritation in humans.

A non-statistically significant excess of genitourinary cancer was observed for the entire cohort first employed after 1926 (Obs=6; Exp=4.45; SMR=135; CI=49–293). Three of these deaths were from prostate cancer. The observed mortality from prostate cancer exceeded the expected, but the excess was not statistically significant (Obs=3; Exp=2.2; SMR=136). There were two other cases of prostate cancer, however, which Thun did not include in his analysis. One of these was a death from prostate cancer which occurred in a guard who had not spent 6 months in a production area of the smelter. The second case was not included because

prostate cancer was not the underlying cause of death.

Subsequent to the publication of his study in 1985, an analysis based on an updated cohort was presented by Dr. Thun at a workshop on cadmium and cancer in London, England (Ex. 8–658a). The updated study of the same Globe cadmium smelter included an evaluation of the mortality experience of the cadmium workers through 1984 (Ex. 8–658a). The extended follow-up study included 625 white male workers with six or more months in a production area between 1940 and 1969. The cohort was essentially the same as that previously described except for the addition of 23 new workers who met the eligibility criteria. These additional new workers included in the follow-up through 1984 were identified through further examination of the records of the Globe facility (Tr. 6/7/90, p. 108).

Forty-three percent of the workers had less than 2 years of employment. Follow-up time was long; 65% had more than 20 years of follow-up. By December, 1984, 234 workers were deceased; this represented fifty-five additional deaths since the previous NIOSH study. Thun et al., found that, among workers with two or more years of employment hired after 1926, a statistically significant excess of deaths due to respiratory cancer persisted (Obs=24; Exp=10.7; SMR=223; CI=143–332). No lung cancer deaths occurred among workers who were employed for less than two years. The excess of deaths from lung cancer was statistically significant for the new period of observation, 1979–84 (Obs=8; Exp=3.19; SMR=251; 90% CI=108–494) (Ex. 8–658a). The excess of deaths due to prostatic cancer was statistically non-significant (Obs=4; Exp=2.35; SMR=170; CI=46–436).

Vital status was known for all but fifteen members, or for 98%, of the updated population study (8–658a). Deceased workers with no death certificates were assumed dead, as specified in the protocol, with the cause of death unknown. Persons lost to follow-up were assumed to be alive. Vital status determination was, therefore, adequate for epidemiological analyses.

With the updated cohort, Thun again analyzed his data using a modified life-table method developed by NIOSH, with expected rates being calculated from the U.S. population, and adjusted for age, sex, race, and calendar time. To analyze his data by cumulative exposure, Thun again divided his cohort into the same three groups. The results, like the earlier study, indicated that the incidence of lung cancer death increased with cadmium exposure. The follow-up study had eight additional cases, more stable exposure estimates, and its findings were consistent with the earlier study. Among the low dose group, there was a nonsignificant deficit of lung cancer deaths (Obs=2; Exp=6.06; SMR=33; p=0.06). For the middle dose group, with cadmium exposures that ranged from 41 μ/m^3–200 μ/m^3 for a forty year TWA equivalent, there was a statistically significant excess of lung cancer (Obs=13; Exp=6.80; SMR=191, p<.05). For the high dose group, the excess of lung cancer deaths was also statistically significant (Obs=9; Exp=3.32; SMR=271; p<.02). The observation that frequency of lung cancer increased with the dose or level of exposure lends support to a causal interpretation between lung cancer and exposure to cadmium.

Thun included two additional analyses in the updated report. The first of these was a comparison of the three original dose groups with SMRs that were calculated using local Colorado lung cancer death rates as the referent population. Among the low dose group, there was a nonsignificant deficit of lung cancer deaths (Obs=2; Exp=4.37; SMR=46; p=0.19). For the middle dose and high dose groups, the SMRs are 35–40% higher than in the analysis using the U.S. rates. In the middle dose group, the SMR was 263 (Obs=13; Exp=4.95; p<0.005, one-sided), and in the high dose group the SMR was 373 (Obs=9; Exp=2.42; p<0.005 one-sided). This indicates that the lung cancer risks estimated using national death rates as the comparison population may be an underestimate of the true risk.

In its comparison of results from different epidemiological studies, OSHA relied upon the SMRs calulated using expected death rate derived using national death rates. Thun did the same in most of his analyses, primarily to facilitate comparability of results between the different epidemiological studies.

In the second analysis, Thun provided a more detailed breakdown of dose-response, including six exposure strata developed by dividing each of the three previous strata in half. SMRs for lung cancer were developed using a comparison with the U.S. mortality; the resultant slope was linear and was comparable to the results of original analyses.

Studies of the Globe workers are particularly useful for assessing the carcinogenicity of cadmium in humans for four reasons. First, the cohort was highly exposed to cadmium. Second, information was available for the prolonged follow-up of lung cancer (85% of the workers had 20+ years of follow-up). Third, extensive exposure information was available from good industrial hygiene records which could be linked to work histories. This allowed the computation of cumulative individual exposures to cadmium for each worker included in the cohort. Finally, additional information was available on tobacco smoking habits of workers and on arsenic exposures at the workplace. This allowed some control for the potential confounding effects of these known risk factors for lung cancer.

> Dr. Thun noted that: * * * for a small study, the strength of the exposure, the intensity of the exposure is one of its major advantages. The second has been the opportunity for prolonged follow-up, and * * * 85 percent of the cohorts have had at least 20 years observation since first exposure to cadmium, and the entire cohort has had 15 years. (Tr. 6/7/90, p. 89)

Because Thun's analyses of the Globe workers showed the clearest association between cadmium exposure and lung cancer, it was his work which drew the most comments during the rulemaking.

a. *Power.* In commenting on the proposed cadmium rule, Environ noted that from the standpoint of the size and power, Thun's study does not compare favorably with some of the other epidemiologic studies that have been conducted (Ex. 12–41). The power of a study relates to its ability to detect an effect. In so far as Thun's cohort was relatively small, Environ's observation is correct. The power to detect a true excess relative risk of 2.0 or greater was 0.893 or 89% when the experience of the entire cohort was considered. When the analysis was limited to the experience of workers employed from 1926 on, the power to detect a doubling of risk was 0.86 or 86%. The probability of detecting a smaller increase in risk is even smaller. For example, the power to detect a true excess risk of only 1.5, the power was only 0.44.

In general, power calculations are used to evaluate possible reasons why a study failed to show an increased risk of a particular cause of death. When a study is conducted and the results show an increased risk of a particular cause of death, as did Thun's study, the hypothetical probability of the study to detect an excess is irrelevant and a power calculation is not necessary. Therefore, the power of the Thun study is not an issue.

b. *Case status.* Another issue raised by Environ was whether two deaths observed in the Thun update should have been considered lung cancer cases based upon a recording of information on the death certificate (Ex. 19–43; 12–

41). Lung cancer was listed on the part of the death certificate under "other significant conditions" for both of these cases, but the immediate cause of death was coded as metastatic brain disease for one case and pneumonia for the other case (Ex. 8–658a).

As Dr. Thun indicated, the death certificate information was somewhat ambiguous for these two cases in the update. The hospital records for both of these individuals indicated that lung cancer was the underlying disease. Two of three nosologists were of the opinion that the underlying cause of death on the death certificate should have been coded to lung cancer. Thus, there is some disagreement as to the correct coding of the cause of death for these two individuals for purposes of epidemiologic study. Thun considered the coding of these two deaths to be ambiguous because metastatic brain disease could theoretically originate in the lung or, theoretically, in the brain, even though metastases from a primary cancer in the lung are common while metastases from a primary brain tumor are exceedingly rare (Ex. 8–658a).

Regarding the appropriateness of the inclusion of these two cases in a study of lung cancer, another commentor stated that no one was,

"* * * questioning the fact that (these) two men * * * died as a consequence of lung cancer (SCM Chemicals; Ex. 12–33–D)." The question is one of comparability of lung cancer cases with the referent population.

Thun et al., concluded that, although some disagreement existed among nosologists about appropriate coding methodologies for cause of death, in the analyses of the data by exposure group it would be appropriate only to include these two cases of lung cancer in internal comparisons within the cohort unless similar cases were included in the compilation of vital statistics upon which expected rates of death were based (8–658a). However, as Thun also reported, if the two lung cancer cases were subtracted from the appropriate dose group, the dose-response relationship and the trend would remain basically the same (Tr. 6/7/90 p. 94). In comparisons with the external U.S. population (Ex. 33) as Thun indicated (Ex. 8–658a) even if these two cases are excluded, the excess of lung cancer is still statistically significant among workers in the update employed for two or more years (Obs=22; Exp=10.76; SMR=204; CI=128–310).

c. *Deficit of lung cancer in the low dose group.* Several commenters stated that the finding of a deficit of lung cancer deaths in the low dose group demonstrated that there was no carcinogenic risk from cadmium exposures below 40 μ/m^3, since:

> * * * the statistically significant excess occurred only for a cumulative exposure equivalent to 40 years of exposure above the current OSHA PEL of 200 μ/m^3 (SCM Chemicals; Ex. 19–42A).

Further:

> This (deficit) would indicate that there is a difference between workers exposed to high levels of cadmium and workers exposed to low levels of cadmium (Big River Zinc Corporation; Ex. 19–30).

Mr. George M. Obeldobel, Vice President and General Manager of Big River Zinc Corporation (BRZ), the third largest zinc producer in the U.S. and the largest cadmium producer in North America, took exception to the Thun study as evidence of the carcinogenicity of cadmium in humans:

> * * * the data showed a strong difference between workers exposed to low levels and high levels of cadmium, i.e., workers exposed to the equivalent of 40 years exposure at:
> (a) 21–40 $\mu g/m^3$ respirable cadmium, showed only two cases of lung cancer versus an expected 3.77 cases (again, *less than the general population*).
> (b) 41–200 $\mu g/m^3$ respirable cadmium, showed seven cases versus an expected 4.61 cases. (Ex.19–38).

Dr. Thun addressed this issue in his testimony:

> The deficit is an artifact because this population of workers * * * is being compared with the U.S. population. The deficit is * * .* not from any protective effect of low levels of cadmium exposure (6/7/90, p. 187).

Furthermore, Dr. Thun continued:

> This finding * * * should not be interpreted as showing a "safe" level of cadmium exposure (Ex. 33 p. 13).

Thun indicated that there are at least three factors which could explain the finding of a deficit in the low dose group:

(1) The healthy worker effect;

(2) Race status of the referent population; and

(3) Smoking.

These factors are discussed in detail below as they pertain to both the finding of a deficit in the low dose group and the finding of excess lung cancer deaths among cadmium exposed workers in general. As discussed in section VI (QRA), OSHA notes that the deficit is not statistically significant and may, therefore, be attributed to random fluctuation.

i. *Healthy worker effect.* The "healthy worker effect" is evidenced by studies which show that active workers experience a mortality risk less than that of the general population which includes sick, disabled, and institutionalized persons. Workers tend to be healthier than the general population. Comparison of mortality among workers to that of the general population would bias the results toward an underestimation of risk.

OSHA received comment on the appropriateness of attributing a "healthy worker effect" (HWE) to cancer SMRs. The Cadmium Council (Ex. 119) stated that the healthy worker effect (HWE) could not sufficiently explain the deficit in the low dose group since this effect has little application to cancer. In the post hearing brief by the Cadmium Council, the studies on the HWE put forth by OSHA (Ex. 8–677; Ex. 50 a and b) were questioned as to their relevance to cancer mortality or were faulted for being studies of veterans, whose comparability with workers had not been established.

According to a study by McMichael (Ex. 8–677), the HWE may not apply equally to all causes of death. As McMichael stated, "* * * if one attempts to improve the meaningfulness of an SMR by adjusting for the HWE, allowance must be made for variation between different * * * causes of death (Ex. 8–677)."

McMichael conducted analyses of data generated by Milham (1974) in a study of carpenters and joiners. McMichael's conclusion was that the HWE does tend to create lower SMRs (60–90%) among cohorts of workers when the U.S. population is used as a referent population. In two other submissions to the docket on the HWE, the issue of the applicability of the HWE to cancer SMRs, in particular, was further examined. The first of these, a study by Dr. Monson (Ex. 50–A), suggests that a HWE lasts for about 15 to 25 years after first exposure, depending on the cause of death and the occupational group being followed.

Dr. Monson stated:

> * * * it has long been observed that groups of employed persons have mortality rates that are lower than the general population. This favorable mortality experience has been termed the healthy worker effect (HWE). Uncertainty about the strength and extent of the HWE has led to uncertainty in interpreting data from studies in which the mortality rate of an employed group is compared with the mortality rate of the general population. (Ex. 50–A.)

Monson studied ten groups of workers in order to evaluate the strength of the HWE on various causes of death. He noted that while the healthy worker effect was relatively weak in comparison to causal excesses, and that there was a difference between the

strength of the HWE for different causes of death, there was, nonetheless, no evidence of a lack of HWE on cancer SMRs.

A second study by Drs. Sterling and Weinkam (Ex. 50b) examined the extent, persistence, and constancy of the HWE by selected causes of death including cancer. Sterling and Weinkam chose to evaluate the data from the Dorn Study of Mortality Among U.S. Veterans because: (1) Veterans who were selected to serve in the armed forces qualified for such duty because they had health status comparable to that of workers seeking employment; and (2) subsequent to termination of service, not all veterans would enter the same occupation. Thus, the high risks of disease among veterans from occupational exposures in hazardous occupations in each cause-specific-death group would tend to be balanced by the inclusion, in the same group, of veterans with low risks of disease from non-hazardous occupations. As a result, the influence of confounding from job exposures on the evaluation of the HWE would be minimal. Sterling and Weinkam observed a persistent HWE for all causes that did not substantially weaken over time. For lung cancer specifically, the HWE persisted at least through age 74 years. For ages 70–74, the lung cancer mortality ratio was 0.72; it was less than this for younger aged veterans.

For the reasons stated by Sterling and Weinkam, OSHA considers the choice of the study group by Sterling and Weinkam to be an adequate and suitable reference group for assessing the influence of the HWE on specific causes of death, including cancer.

Overall, based on the above mentioned references, the HWE appears to be relevant to cancer SMRs, and thus is relevant to Dr. Thun's study of cadmium exposed workers though the strength of the effect may differ for different cancer diagnoses and depends upon other factors relevant to the cohort under study such as age at time of hire.

OSHA agrees with the Cadmium Council that, in and of itself, the HWE may not be sufficient to explain the finding of a deficit of lung cancer in the low dose group in the Thun study. However, the HWE in conjuntion with the lower rates of smoking and lower background lung cancer death rates of the exposed population, plus statistical variability may all combine to account for the deficit of lung cancer mortality.

ii. *Hispanic surname.* Reduced tobacco use among workers is another plausible explanation for the deficit of lung cancer SMR observed in the low dose exposure group. This does not mean that the low dose group smoked less than the other exposure groups. Rather, smoking in all of the exposure groups was less than the general population, and, as Dr. Thun concluded, the HWE was therefore much more extreme (Tr. 6/7/90; p. 102). Dr. Thun based this conclusion on the fact that slightly less than 40% of the workers at the Denver cadmium plant had Hispanic surnames. Hispanics, in general, are known to smoke less than other white males and thus to have lower rates of lung cancer than other U.S. white males. As Dr. Thun stated, "Several studies have shown low rates of lung cancer among Hispanic males in the Southwest, and particularly in Denver (Tr. 6/7/90, p. 98)."

Dr. Thun's conclusion is supported by a study by Dr. Savitz, (Ex. 57–N), who found that in Denver between 1969 and 1971, Hispanics had a lung cancer incidence that was less than that of other white males. Cancer incidence rates for persons of Spanish surname and other whites in the Denver area were derived for two time periods, 1969–71 and 1979–81. Lung cancer death rates among males with Spanish surnames increased from 23.1 per 100,000 person-years in 1969–71 to 45.6 in 1979–81, as compared to other white males whose rates increased from 57.0 to 68.9 in the same time period. While lung cancer was substantially less common among those with Spanish surnames compared to other white men, there was a convergence of the rates. The convergence of the rates could be attributed, according to the author, to, among other things, acculturation of persons with Spanish surnames, the imperfection of Spanish surname as an indicator of ethnicity, or systematic error due to miscounting of illegal immigrants. While acculturation could explain the change in trends, the authors concluded that Spanish surname was not likely to explain the convergence of rates. Spanish surname identifiers appeared to be consistent for both cases and the reference population across the two time periods. The systematic error in enumeration of immigrants, however, would tend to inflate the cancer rates, since the referent population would be less likely to be counted correctly than would the cancer cases.

By comparing the death rates among the Globe cadmium workers, a group that included a mix of workers with Hispanic and non-Hispanic surnames, to U.S. white male lung cancer death rates, the expected number of lung cancer deaths would be overestimated, and the occupational effect of cadmium on lung cancer would be underestimated. The percent of the workers with Hispanic surnames in the low dose group was 38.5%; the percent of the workers in the middle dose group with Hispanic surnames was 41.5%; and, the percent of the workers in the high dose group with Hispanic surnames was 32.2% (Ex. 33). The mixture of cadmium workers with Hispanic and non-Hispanic surnames was similar between the three dose groups. To the extent that Hispanic surname reflects ethnicity, and that Hispanics smoke less and have lower lung cancer death rates than U.S. white males, it is unlikely that differences in ethnic group would have caused a significant impact on the SMRs between dose groups, i.e., in the low dose group alone. Thus, it appears as though Dr. Thun's suggested use of Hispanic surname is a plausible method by which to estimate the effect of ethnicity on the lung cancer SMRs in his cohort.

An additional study of the impact of differences in lung cancer mortality between Hispanic and non-Hispanic workers at the Globe plant was carried out by the National Institute for Occupational Safety and Health (NIOSH) (Ex. 79). NIOSH presented a lung cancer mortality analysis based upon the most recent follow-up of the Thun et al., cadmium cohort through 1984. The life table analysis used in this assessment was stratified into four cumulative dose categories, i.e., ≤ 584, 585–1460, 1461–2920, and ≥ 2921 mg/m^3-days) and three "time-since-first-exposure" categories, i.e., <10, 10–19, and 20+ years. Separate life-table analyses were performed for members of the cohort with Hispanic and non-Hispanic surnames. For the lung cancer SMRs, U.S. rates for white males were used as the referent group.

The results from the life-table analysis indicated that lung cancer mortality was similar to Dr. Thun's findings, i.e., lung cancer SMRs were not significantly elevated for the entire cohort (SMR=149; Obs=24; Exp=16.07; 95% CI=95, 222; p=.076, 2 tailed test). However, among white males, lung cancer mortality was significantly elevated (SMR=211; Obs=21; Exp=9.95; 95% CI=131,323; p<.01). A deficit of lung cancer mortality was found among Hispanics (SMR=49; Obs=3; Exp=6.12) as would be expected if the referent rates for U.S. white males reflect people who smoked more than people with Hispanic surnames. Lung cancer mortality increased with cumulative exposure to cadmium, and was significantly elevated in the highest exposure group for the combined cohort (SMR=272; Obs=9; Exp=3.3; p<.05) and for the three highest exposure groups among

non-Hispanics. A significant excess of lung cancer mortality was also observed among workers in the longest "time-since-first-exposure" category for the combined cohort (SMR=161; Obs=21; Exp=12.97; $p<0.05$, two-tailed test) and for non-Hispanics (SMR=233; Obs=19; Exp=8.13; $p<.01$, two-tailed test). The finding of a statistically significant excess of lung cancer among non-Hispanics, and a deficit among Hispanics, further strengthens Dr. Thun's conclusions that the deficit of lung cancer in the low dose group could, in fact, result from an excess of workers with Hispanic surname in the cohort in comparison with the referent population.

The issue of the use of the percent of Hispanic workers in the exposed population to evaluate the confounding effects of smoking was questioned by the Cadmium Council during the reopening of the record (Ex. 144–16). According to the Cadmium Council, during an IARC Symposium in 1991, information was provided that Hispanics who smoke do so with the same frequency as non-Hispanics. The difference is only that workers with Hispanic surnames tend to underreport smoking habits (Ex. 144–16). This opinion by the Cadmium Council was apparently based upon a document prepared by Dr. Lamm, in which Dr. Lamm summarized the results of the IARC International Symposium (Ex. 144–7). No document which represented IARC's formal conclusions was submitted to the OSHA docket. However, if people with Hispanic surnames do in fact underreport their habits, it is not possible to determine whether the underreporting itself could account for the differences in smoking observed between white males and males with Hispanic surnames in the Thun cohort. If smoking habits between white males and males with Hispanic surnames are indeed similar, nonetheless, lung cancer rates in general are lower among males with Hispanic surnames than among white males (Ex. 57–N). The important factor in the analysis by Thun et al., is that the proportion of males with Hispanic surnames included in each dose category was approximately equal. Thus, any potential confounding effect of the inclusion of a large number of males with Hispanic surnames was equally distributed over dose categories, yet the potential confounding effects did not override the dose-response relationship observed between lung cancer excesses and cadmium exposures.

iii. *Smoking.* Thun provided direct and indirect evidence for his position that the workers in his study smoked less than the general U.S. population by noting the absence of elevated rates of death for other smoking-related diseases in his cohort. As Dr. Thun stated, "(Cardiovascular disease) * * * is often a good marker of smoking habits (Tr. 6/7/90, p. 101)." Dr. Thun found that death rates from cardiovascular disease were about two-thirds that of the general population (SMR=65; Obs=56, Exp=85.7).

Dr. Kazantzis, who testified as an expert witness for the Cadmium Council, agreed that indirect evidence such as the finding of a significant deficit of major diseases related to cigarette smoking, such as cerebral-vascular disease and other cardiovascular diseases, would be a factor that must be taken into consideration in evaluating the relationship between smoking and lung cancer excesses. In the absence of direct evidence on smoking habits of members of a study cohort, Dr. Kazantzis agreed that such indirect evidence might argue against cigarette smoking as the major factor associated with observed excess lung cancer (Tr. 6/8/90).

Furthermore, the HWE could have affected, and thus lowered, the SMRs for ischemic heart disease in this occupational cohort because heart disease is more likely to be selected against in the recruitment and retention of active workers (Ex. 8–677). Thus, it would appear that smoking was not so prevalent among cadmium workers in the Thun study that its effects would override the HWE on heart disease rates. Dr. Thun stated that:

> * * * one of the implications of the lower smoking habits of this population [the Denver cadmium workers] is that one should not interpret SMRs below 100 in the low dose group as * * * a safe or threshold level for cadmium * * * [W]hat those levels reflect is a lower background risk of lung cancer among these workers due to * * * less smoking than the U.S. general population * * * (Tr. 6/7/90, p. 102)

Dr. Thun also evaluated direct evidence on smoking habits obtained from a 1982 questionnaire. Responses were provided by surviving workers or their next of kin, and were supplemented by medical records. These responses showed that although the majority of Hispanic workers smoked, most were light smokers. These light smokers reported smoking fewer cigarettes per day than white males. As for other white male workers at the plant, if anything, they smoked slightly less than white males in the general U.S. population (Tr. 6/7/90, p. 100). As Dr. Thun indicated, use of the data from the questionnaire was somewhat limited because the questionnaire obtained smoking information on only 43% of the overall cohort, and the missing information pertained primarily to the low and medium dose groups (74% and 47%, respectively). Without comparable smoking information for each of the dose groups, controlling for smoking based on the direct evidence from the questionnaire might produce biased results, either towards over or underestimating the effects of smoking on the SMRs for each dose group.

There have been differences of opinion as to the value of smoking data and different estimates of the number of packs smoked (Tr. 6/7/90, p. 183; Ex. 8–658a). Lack of data on smoking in the low dose groups, however, made these data less valuable than data on Hispanic surnames because workers with Hispanic surnames were evenly distributed in the three exposure groups.

Dr. Thun stated that the use of an internal analysis would yield a valid estimate of the effect of occupational exposure (Tr. 6/7/90, p. 72). Such an analysis was conducted by NIOSH for risk assessment purposes (Ex. 79). In this study, NIOSH presented results from modelling of the dose-response relationship between cadmium exposures and lung cancer mortality and projected risks associated with varying levels of cadmium exposure. (See Poisson regression models fitted to the "5-year lagged analysis.") The parameter estimates for the categorical model represented the effect of each category relative to the low dose category (<584 mg/m^3-days). The issue of the use of internal controls by NIOSH will be dealt with further under the Quantitative Risk Assessment Section.

OSHA received several comments on NIOSH's analysis. During the 1992 IARC International Symposium, the NIOSH analysis was questioned as to whether it provides a biologically reasonable explanation of the data (Ex. 144–16). However, this comment was not from a formal document of the IARC International Symposium (Ex. 144–7).

A similar issue was raised by Dr. Starr during the hearing (Ex. 38). Dr. Thomas Starr commented that "OSHA should redo its analysis with the individual person-year information collected by Thun et al.," noting that the latter data were only very crudely characterized by the median cumulative exposure for each category (Ex. 38). He also recommended that "OSHA should reanalyze the Thun et al., (Ex. 4–68) data with the multistage dose-response approach model utilizing an approach similar to that described by Crump and Howe (1984)." The NIOSH risk

assessment and subsequent addendum (Exs. L–140–20, L–163) incorporated both of these recommendations. OSHA's use of additional models is further discussed in its section on quantitative risk assessment. (See section VI.)

iv. *Conclusions.* In summary, OSHA notes that the finding of a deficit in lung cancer in the low dose group may have resulted from other factors, such as the healthy worker effect, lower smoking rates, and Hispanic ethnicity as noted by Dr. Thun. The deficit should not be interpreted as an absence of lung cancer risk at doses of cadmium less than 40 μ/m^3.

d. *Smoking and Arsenic in the Thun Cohort.* The roles of smoking and arsenic as causes for the excess lung cancers observed in the Thun study were the focus of many of the comments received by OSHA. These concerns were primarily related to the findings of a study by Lamm et al., 1988, which purported to show that there was no link between cadmium exposure and cancer (Exs. 19–43E, 12–13a, 12–33d, and 12–33e). For example, the Cadmium Council reiterated its earlier argument that the Thun study failed to control for smoking, citing the case-control study by Dr. Lamm which, in the Council's view, demonstrated an association between smoking and cancer but not between cadmium and cancer. The Cadmium Council also stated that ENVIRON peer-reviewed the Lamm study and "endorsed its conclusions". Several other commenters made observations similar to those of the Cadmium Council (Ex. 19–43; 12–33e).

i. *Lamm's case-control analysis.* Dr. Lamm conducted a case-control study (Exs. 19–43e and 144–7b), in which he attempted to replicate the data used in the mortality study by Thun et al., (Ex. 144–7b). Dr. Lamm identified 599 of the 602 white males in the Thun et al., study (144–7b), which included all of the lung cancer cases previously identified in the Thun et al., study. Eligibility for both the Thun et al., and the Lamm case-control studies was the same. The workers had to have been employed over six months in the cadmium smelter production areas "* * * during 1940–1969" (144–7a). Dr. Lamm used a "nested" case-control design of 25 cases of lung cancer matched with 75 controls from the entire cohort of 602 workers included in the Thun et al., study.

The case-control study was used to evaluate lung cancer and the contribution of arsenic and smoking as well as cadmium to the lung cancer deaths (Ex. 19–43e). Dr. Lamm matched cases with controls on age, race, sex, and date-of-hire (Ex. 144–7b). Cadmium exposures for both cases and controls were estimated using NIOSH's original exposure estimates, which Thun calculated for each employee at his worksite. Smoking histories were obtained by company personnel from interviews and company records for about 43% of the cohort (Ex. 19–43e).

Based on data from 597 workers in this plant, Lamm identified three time periods of potential arsenic exposure (Ex. 12–33e), or period-of-hire risk factors (Ex. 144–7b). Based on 25 cases of lung cancer and 75 controls, and using the cadmium exposures developed by Thun et al., the arsenic feedstock data, and the previously identified period-of-hire risk factors, the relationships between lung cancer deaths and cadmium exposures, smoking, arsenic, and period-of-hire, respectively, were independently evaluated.

ii. *The smoking argument.* Based on the amount of tobacco consumed (pack-years per employee), Dr. Lamm found that the relative case-to-control smoking history, for workers with known smoking history, was 2.5, with a range from 1.6–6.3 (Ex.12–33-e). When Dr. Lamm categorized workers as ever/never smoked, the odds ratio for smoking as a lung cancer risk factor was 8.2 (Fisher's exact test two-tailed; $p=0.047$; 95% CI: 1.04 to 367.05). Based upon these analyses, Lamm concluded that cigarette smoking was responsible for the elevated lung cancer risk observed among the cohort (Ex. 12–33-e).

Dr. Thun stated that the missing data on smoking (available, for example, for only 57% of controls; see Section VI—QRA.) made it invalid to use these individual smoking histories in case control analyses (Tr. 6/7/90; p. 101). While smoking clearly affects lung cancer rates in general, it does not account, in and of itself, for the lung cancer excesses observed in Thun's study, based on Dr. Lamm's analysis. Dr. Thun indicated that the preferred evaluation of smoking status and its effects on lung cancer death rates would be to use Hispanic surname or an internal analysis to control for both the confounding due to the HWE and smoking.

OSHA is of the opinion that the smoking data from the questionnaire survey were limited and should not have been used alone in the case-control study to evaluate the effects of smoking. If smoking were a main cause of lung cancer, one would not expect a deficit of lung cancer in the low dose group. Smoking would elevate these rates, too.

iii. *The arsenic argument.* A second analysis by Dr. Lamm entailed examing lung cancer deaths (SMRs) for the entire Thun et al., cohort, including workers employed before January 1, 1926 (Ex. 19–43e; Ex. 12–33e; Ex. 144–7b). For this analysis, Dr. Lamm merged data from the Thun et al., study with data from the plant owners. Mean arsenic concentrations in the feedstock for various time periods were calculated based on a 10% sample of arsenic feedstock records (Ex. 19–43e). Dr. Lamm indicated that there were three critical calendar time periods of potential arsenic exposure based on the arsenic exposure concentration in the feedstock. These three periods were characterized as: prior to 1926, very high; 1926–39, high; and 1940–69, moderate to low. The reductions in exposures by calendar time period resulted from changes in plant processes. Arsenic exposures, it was assumed by Dr. Lamm, occurred uniformly throughout the plant.

Dr. Lamm then examined the SMRs for lung cancer by period of hire. He found that for workers hired prior to 1926, the SMR was 492 (Obs=3, Exp=0.61); for workers hired between 1926 and 1939, the SMR was 283 (Obs=6, Exp=2.12); and, for workers hired between 1940–69, the SMR was 88 (Obs=8, Exp=9.08). A full discussion of the lung cancer response among workers hired prior to 1940 is included in Section VI—QRA. Dr. Lamm concluded from these findings that the lung cancer risk appeared to reflect arsenic exposure confounded by cigarette smoking. Addressing Dr. Lamm's conclusions, Dr. Thun stated that:

> The conclusions (by Dr. Lamm) * * * go well beyond the data presented * * * the first conclusion implies that the average arsenic concentration in feedstock being processed by the Globe plant is 5%. This statement is incorrect * * * in actuality, the mean annual arsenic concentration (geometric mean) of the feedstock after 1927 averaged between 2–3% with the exception of the year 1930 (5.6%) and 1931 (4.9%). Lamm and co-workers also imply that arsenic exposure is generalized throughout the plant. In fact, arsenic exposure is limited to the early steps of the process, in the sampling, calcine, and roasting areas * * *. In our opinion, arsenic exposure may have contributed to the excess of lung cancer deaths at the Globe plant, but this contribution has been overstated by the spokesmen for the cadmium industry. (Ex.8–645.)

Furthermore, Dr. Thun commented that the feedstock data that Dr. Lamm used was:

> * * * based * * * upon visual impressions of records of arsenic in feedstock entering the plant. Dr. Lowell White, a former employee of the company, compiled the estimates of arsenic concentration, by year * * *. We (NIOSH) have obtained the records of arsenic

in feedstock from the company and have analyzed the data through 1958 * * *. The calculated geometric means do show slightly higher values during the years 1930–38 than thereafter, but the averages are lower than those estimated by the company scientists. (Ex. 8–658a.)

In other words, as Dr. Thun indicated during the hearings:

(Dr. White) sort of eyeballed the sample of records. But we obtained the actual records and analyzed them and determined the geometric mean and the percentage of arsenic in feedstock that was actually present is shown * * * under NIOSH calculations. (Tr. 6/7/90, p. 104).

Mr. George M. Obeldobel, Vice President and General Manager of Big River Zinc Corporation (BRZ), the third largest zinc producer in the U.S. and the largest cadmium producer in North America, took exception to the Thun study on the carcinogenicity of cadmium in humans:

Without including the * * * 26 workers [who had worked at the smelter prior to 1926 when the smelter functioned as an arsenic smelter] * * * the excess of lung cancer death was not statistically significant, suggesting that arsenic played a large confounding role in the data. (Ex. 19–38).

Although the lung cancer SMR was not statistically significant for the total cohort hired after 1926 (SMR=147; Obs=16; Exp=10.87; 95% CI=84,239), according to the Thun study, lung cancer mortality was significantly elevated among workers with two or more years of exposure.

The fact that the lung cancer SMR for the total cohort was not significant, however, does not indicate that the arsenic exposures had a more significant effect than anticipated by Dr. Thun. Dr. Thun excluded workers hired prior to 1926 to control the effects of arsenic exposure within the cohort. The true effect of excluding these workers hired prior to 1926, as Dr. Thun indicated, would be to reduce the potential confounding among the cadmium workers for arsenic, not to entirely eliminate its effect.

The continuing controversy about the exposure assessment used by Dr. Thun and the potential for arsenic confounding, centered, in part, around whether or not the arsenic exposures in the plant were similar for all cadmium exposed workers, (i.e. whether the amount of arsenic per worker was similar between dose groups in the dose-response analysis).

As Dr. Thun has stated:

* * * the arsenic exposure occurred only in departments that processed incoming feed material: sampling, mixing, roasting, and calcine furnace area. Other stages of the process are housed in separate buildings where workers were exposed to cadmium but not to arsenic. It's important to emphasize the localized areas of arsenic exposure at this plant which differ from the more generalized exposure in arsenic and copper smelters. Company representatives have drawn analogies between the Globe plant and the Tacoma copper smelter, but the difference is that arsenic exposure was generalized in * * * these other plants and is highly localized in [the Globe] plant (Tr. 6/7/90, p. 105).

Thun's evaluation of the entry level and long-term jobs, and their associated arsenic exposures, was indirectly confirmed by Mr. Robbins, of the Globe ASARCO plant. The areas of the plant where the highest exposures to cadmium occurred were in the retort furnace and pre-melt areas (Tr. 6/12/90, p. 55).

As Mr. Robbins indicated:

* * * the area of the retort * * * [primarily cadmium exposures] * * * is one of the areas that we're very concerned about product quality. So it's important to have experienced people * * * working in that job. And it's my sense that the turnover rate is fairly low * * * (Tr. 6/12/90, p. 47).

The highest arsenic exposures would have occurred in the solution charging area, which was in the "front-end" of the process. Workers in these areas, as well as the solution area, would historically, have been considered to be in entry level jobs according to Mr. Robbins (Tr. 6/12/90, p. 51). The area in which the "quality" of the cadmium compound was of most importance would not have been entry-level positions, with some arsenic exposures.

Furthermore, when the Globe plant had the Godfrey roasting and calcine operations, those were the highest areas for arsenic exposure and would have been entry level positions as well, although there would have been some cadmium exposures in these areas. Mr. Robbins stated:

Thun was looking at historical exposures at the Globe plant and there was a time when Globe had Godfrey roasters * * * that are no longer there * * * [T]here would have been job categories that aren't here that would have been here 20 years ago * * * (Tr. 6/12/90, p. 47).

In response to questions, Mr. Robbins indicated that in all areas that workers had exposures to high levels of arsenic, the workers would also have some exposure to cadmium. However, the high cadmium exposure operations, which require long-term, skilled professionals, generally do not have arsenic exposures. Thus, there clearly were work areas which were predominantly cadmium exposure areas where there was no arsenic exposure (the retort furnace and pre-melt sections). In addition, there were work areas with high arsenic exposure and some cadmium exposure (currently the solution charging areas and historically both the solution charging and high purity production areas.)

This would mean that while all the workers in the Thun et al., cohort could have had some exposure to arsenic in entry level job positions, the arsenic exposures would tend to be equal among the workers and across exposure categories as Dr. Thun indicated. In each of the cumulative cadmium exposure dose groups, the arsenic exposure per worker would not increase as cadmium exposures increased.

When questioned about whether arsenic and cadmium exposures were truly independent, Dr. Thun responded:

They're not completely independent. There is some independence because when workers would move to other departments like retort and foundry in which cadmium exposures were substantial, they would be exposed to cadmium but no arsenic. (Tr. 6/7/90, pp. 167–168).

If all the jobs with cadmium exposure were the same ones that had arsenic exposures, the finding of a dose-response relationship between lung cancer and cumulative doses of cadmium would be more likely to be confounded by arsenic. However, there does not appear to be a perfect correlation between cadmium and arsenic exposure. Thus, the finding of a dose-response relationship between lung cancer and cadmium exposure should not be attributed to arsenic exposure, either in part or in total. (Tr. 6/8/92, p. 147). Thun et al. conducted an analysis of the potential magnitude of the effect of arsenic and concluded that no more than 0.77 cancer cases could be attributed to arsenic (Ex. 4–68) (See Section VI–QRA).

OSHA received the comment that as late as 1979, this plant received an OSHA citation for levels of arsenic exceeding 100 μ/m^3 (Ex. 12–41). As Dr. Thun indicated:

Only six industrial hygiene measurements were made in these (arsenic) areas before 1975. In 1950, airborne arsenic concentrations ranged from 300 to 700 μ/m^3 near the roasting and calcine furnaces, the areas of highest exposure. Measurements * * * in 1979 * * * show that arsenic exposures in these areas had decreased to about 100 μ/m^3 (Ex. 4–68).

It was therefore argued that arsenic should be considered as the major factor affecting the observed elevated lung cancer deaths in the Thun study (L–19–59). The main issue was that Dr. Thun's assumptions for calculating cumulative exposure contained a number of errors that would tend to underestimate the

risk due to arsenic and overestimate cadmium's risk per unit of dose.

In Thun's analysis, the estimated number of cancer deaths that would result from the arsenic exposures in this cohort by was calculated by assuming:

(1) An average arsenic exposure of 500 μ/m^3 in the "high arsenic" areas;

(2) A respirator protection factor of 75%, similar for both cadmium and arsenic;

(3) An estimated 20% of person-years of exposure spent in high-arsenic jobs; and,

(4) An average employment duration of 576 post-1926 workers of 3 years for 1,728 person-years of exposure.

As described in section VI–QRA, Dr. Thun concluded that no more than 0.77 lung cancer cases could be attributed to arsenic exposures, based on estimated arsenic exposures and using the risk assessment model developed by OSHA.

Dr. Lamm (Ex. L–19–59) proposed the following alternative assumptions and arguments regarding exposures:

(1) The appropriate mid-range of arsenic exposure levels is 2,650 μ/m^3;

(2) The respirator protection factor should be 1.00, based on observations of respirator use at various smelters (Globe, Tacoma, and Anaconda);

(3) Employees spent 67% of their cadmium exposure time in high cadmium exposure areas and 47% of that time was spent concurrently in high arsenic exposure areas, meaning that an estimated 32% of person-years of exposure were spent in high-arsenic jobs; and,

(4) A total of 3,941 person-years of cadmium exposure.

When these factors are taken together, the estimate of arsenic-induced lung cancer is high. Dr. Lamm stated,

* * * we conclude that the NIOSH [Thun] estimate of 0.77 cases * * * was based on a vast underestimate * * * (Ex. L–19–59)

Dr. Thun indicated that Dr. Lamm's analysis included several misconceptions and faulty statistical procedures which caused an overestimation of arsenic exposure at the Globe plant (Ex. L–140–23). First, the exposure data from the 1940's to which Dr. Lamm refers come from a survey by the University of Colorado, Division of Industrial Hygiene, dated 1945. According to Dr. Thun, Dr. Lamm incorrectly reported the mid-range of these exposure data as being 8,700 μ/m^3 rather than 500 μ/m^3 used by NIOSH. Dr. Lamm reduced this level as a "midrange" value of exposures by eliminating the highest level and then taking the midrange, resulting in his estimate of 2,650 μ/m^3. Dr. Thun, on the other hand, indicated that the median of these exposure measurements is 205 μ/m^3; the geometric mean is 213.6 μ/m^3; and, the arithmetic mean is 392.2 μ/m^3.

Dr. Thun recommended that perhaps the best measure of the midpoint of these samples would be the geometric mean, weighted for the number of workers in each operation. This value equals 156.9 μ/m^3 without taking respiratory protection into account.

An unspecified "midrange value", used in Dr. Lamm's report, is less useful than the mean and median values given by Dr. Thun, and mathematically is meaningless. It would appear that the usual level of exposure to arsenic in areas with potential exposure to arsenic was considerably less than Dr. Lamm estimated.

Furthermore, according to the same survey, cited above, by the University of Colorado, the departments where arsenic exposure potentially occurred were only operational for four months of the year. The intermittent nature of these exposures should have been taken into consideration by Dr. Lamm, according to Dr. Thun. If the intermittent nature of these exposures had been taken into consideration, it would have resulted in further lowering of cumulative arsenic exposures.

Dr. Lamm claimed that the respirator usage and exposure data on arsenic exposures in three plants (the Anaconda, ASARCO Tacoma, and the ASARCO Globe plants) should be used to represent the respirator use and the arsenic exposures at the Globe plant. In this way, according to Dr. Lamm, a resulting protection factor of 1.00 for respiratory protection should be used instead of 0.26 used by Thun. This, however, ignores the fact that Smith's study of respirator usage, cadmium exposures, and arsenic exposures, was conducted at the Globe plant. The respirator protection factor used by Thun is thus more appropriate for use in studies of workers from the Globe plant.

Dr. Thun indicated that Dr. Lamm's assertion that the controls in his case-control study spent 68% of their time in high cadmium areas does not contradict Thun's estimate that an estimated 20% of person-years of exposure were spent in high-arsenic jobs. Dr. Thun's estimate is an estimate of time spent in high arsenic areas, not high cadmium areas. The high arsenic areas were sampling, mixing, roasting, and calcine. Furthermore, Thun's estimate was based on the entire cohort, covering the entire post-1926 period, while Dr. Lamm's estimate was based on a small sample of workers in his case-control study (N=75, or 12% of the cohort) who did not die of lung cancer. Thus, the estimate of time spent in arsenic exposure areas in the Thun study is more likely to be an accurate estimate in that it was based on a larger sample, utilized more complete employment records than were available to Dr. Lamm, was confirmed by several sources, and did not exclude workers who died of lung cancer.

Dr. Thun indicated that the major problem encountered by Dr. Lamm in his analysis was that he lacked sufficient work history data to identify departments with potential arsenic exposure in adequate detail to analyze these data by duration of employment; Thun used person-years of employment in high arsenic areas instead.

For several reasons, Dr. Thun believed that the estimate of 0.77 cancers may have been an overestimate rather than an underestimate. These included: (1) The high arsenic exposure jobs were frequently staffed with short-term employees who were not in the study cohort, thereby excluding workers with less than six months employment; and, (2) urinary arsenic levels of workers in the high areas from 1960–80 averaged only 46 μ/L, which would equal an inhaled arsenic of 14 μ/m^3, far lower than the estimated average arsenic exposure of 125 μ/m^3, cited by Thun (Ex. L 140–23).

As Dr. Thun indicated, it is clear that Dr. Lamm's model overestimates the number of deaths attributable to arsenic:

On the basis of Dr. Lamm's risk assessment mode, 143 deaths from lung cancer were expected based on arsenic exposure. Since only 24 lung cancer deaths were observed, it is apparent that Dr. Lamm's model greatly overestimates the number of deaths. On the other hand, Dr. Thun's model predicted 0.77 deaths, which is more consistent with the observed deaths (Ex. L–140–23).

However, according to Dr. Thun:

If we took our worst case scenario and the estimated exposure to arsenic was twice what we said it was (representing a two-fold improvement in respiratory efficiency over time), then in the cohort over their entire life time, one would expect twice 0.77 cases of lung cancer attributable to arsenic. A very small number, less than two, which would by no means explain the excess that's observed. So the two fold underestimation that may have occurred due to differences in respirator efficiency does not account for the excess of lung cancer.(Tr. 6/7/90, p. 172).

Furthermore, Dr. Thun stated that if arsenic was causing the excess of lung cancers in this cohort, one would have seen a higher SMR for lung cancer in the low dose exposure group (Tr. 6/7/90, p. 177).

OSHA has recalculated the estimated number of arsenic lung cancer deaths that may have resulted from arsenic

exposures, in the quantitative risk assessment section. (See Section VI–QRA.) OSHA is of the opinion that the original analysis by Dr. Thun was adequately justified. It is fair to state, as did Dr. Thun, that while arsenic may have contributed to the excess lung cancers observed in this plant, it would not totally account for the excess lung cancer.

iv. *Lamm's Period-of-Hire Argument.* One primary objective of Dr. Lamm's case-control study was to examine the role of cadmium exposure when controlling for period-of-hire (Ex. 144–7–b). Relative cadmium exposure was expressed as a ratio of the mean cadmium exposure of the cases to that of the controls. Based on the case-control study, Dr. Lamm observed that the relative case-to-control cadmium exposure (mg-yrs/m^3) was 1.0, with a range from 0.9–1.1 (Exs. 12–33–e; 19–43–e; 144–7). Dr. Lamm concluded that the lung cancer risk in this workplace was:

> * * * more related to the period of hire, not to the cumulative cadmium exposure. The period of hire appears to be a surrogate for arsenic exposure as related to feedstock. The measures used here seem to indicate that exposure to arsenic and cigarette particulates, rather than cadmium particulates, may have caused the lung cancer increase of these workers. (Ex. 144–7–b)

OSHA has reanalyzed Dr. Lamm's results in the quantitative risk assessment section. In summary, the results of Dr. Lamm's case-control analysis could be explained by methodological errors in the study design or by random statistical fluctuations. (See Section VI–QRA). One example of methodological errors, Dr. Thun pointed out, would be the use of the case-control design in Dr. Lamm's study which is at variance with the common use of this method. Typically, "nested" case-control studies are conducted when there is an opportunity to classify *exposure* more accurately than is possible in a cohort study in which all workers are considered exposed to some degree. However, in the case-control study, the original cadmium exposure data from the Thun study was used for a subset of workers, and no additional information was collected and/or used for the whole cohort. Thus, the choice of a case-control study design introduced a major disadvantage in that the controls were not representative of the study population. That is, only a portion of the total information was used as opposed to a cohort study where all information on all workers is used. At the same time, this case-control study design applied to these data offered few of the advantages of the case-control design, (i.e., the addition of new data on the total cohort) (Ex. 8–645).

Random statistical fluctuations, which were perhaps exacerbated by "overmatching", could explain the results. Overmatching occurs when controls are matched to cases on a variable that is related to exposure but is not a risk factor for disease independent of exposure. Such overmatching can actually reduce study precision. (See Section VI–QRA overmatching.)

In general, when rules are developed for selecting controls, factors known or strongly suspected of being related to disease occurrence should be taken into consideration. Once a factor is matched, it is eliminated as an independent study variable and the control group can only be used for the study of other factors. This suggests that caution is required regarding the amount of matching attempted in any study. If the effect of a factor is in doubt, the preferable strategy is not to match for that factor but to control for it in the statistical analysis. If in a case-control study, for example, one matches cases to controls on exposure, no information on the association between exposure and disease will be obtained.

In general, several criteria should be met if one is to consider designing a "matched" study: the purpose of the study design should not pertain to the factor matched; if the factor is not "matched", one should be reasonably certain that the factor will be confounding; such confounding should be expected to be more than just trivial; and, there is no possibility that the factor is part of the causal pathway linking the exposure and disease under study.

According to Dr. Thun, in the case-control study by Lamm controls were inappropriately matched, or "overmatched", to cases on the variable of "date of hire" (Ex. 8–645). While OSHA agrees that cadmium exposure is very likely to be correlated with year-of-hire, OSHA believes the correlation is not perfect. (See Section VI–QRA). However, in terms of the Lamm case control study, overmatching is a potential flow that would lead to the finding of no difference in cadmium exposures between cases and controls. According to Dr. Thun:

> Overmatching is most severe for the eight cases and 24 controls hired before 1940. Workers hired before 1940 were only enrolled in the study if they continued to work in cadmium production for at least six months after 1940. Thus, cases and their controls hired in 1930 typically remained in cadmium production for 10.5 years (until July 1, 1940) to be enrolled in the study (Ex. 8–645).

The approach used by Lamm, according to Dr. Thun, almost guarantees that there will be little difference between cadmium exposures among cases and controls. Dr. Thun continued:

> Still another problem is that the investigators overestimate the relevant cadmium exposure of the controls. In the Lamm analysis, controls are allowed to accumulate exposure after death of the case. Thus, the cases' potential exposure ends at death, but the controls' exposure is not similarly truncated. This approach inappropriately inflates the exposure of the controls and obscures the potential ill effects of exposure. A less biased method of analysis would exclude the experience of controls following the death of the case (Ex. 8–645).

Thus, the main difference between cases and controls, if overmatching on controls for arsenic and cadmium occurred, would be, as Dr. Lamm noted, that there could be differences in smoking, but no differences in exposures to either cadmium or to arsenic.

6. *Thun's exposure assessment.* In general, for epidemiological purposes, exposure data should contain information on other substances in the workplace to which workers may have been exposed. For a given work area, records should be kept on the substances used, the quantity used, and the period of their use. The work area should be some identifiable area that is small enough to have relatively uniform usage and exposure to industrial substances but large enough to have a reasonable number of workers. Further, a work area should be convertible to some personnel code, so that data on work areas can be linked to data on individual workers.

Dr. Thun's exposure assessment for the members of his cohort was the subject of comments in the cadmium rulemaking. Several commentators agreed with the Environ study in its comments on the Thun study:

> A further strength of this study for the purpose of risk assessment is that quantified ranges of cadmium exposure were estimated. From plant and personal hygiene measures, exposure assessments for individual workers have been made * * * for many of the other epidemiological studies exposure data are limited to the identification of an average exposure level for the plant. Dose-response relationships cannot be postulated for these other studies. (Environ, Ex. 12–41).

The exposure estimates provided to Thun were developed by Smith after extensive communication with plant personnel who were familiar with the operation of the plant. Thun computed

individual cumulative cadmium exposures for each worker included in the cohort. Smith (Ex. 4–64) described the plant and the work areas in great detail:

> Cadmium production was performed in a complex of ten buildings, with each phase in a physically isolated building or section of a building * * * Cadmium enters the process principally as cadmium oxide dust, recovered as a by-product of air pollution control at nonferrous smelters, especially zinc smelter * * * Each shipment of raw material is assayed for cadmium when received. The cadmium-bearing materials are roasted, mixed with sulfuric acid, calcined, and dissolved in a sulfuric acid solution that is purified by precipitation and filtration. Highly purified cadmium metal is plated out of the solution in an electrolytic refinery (tankhouse) and melted and cast into shapes at the foundry. Some of the metal is reoxidized in gas-heated retorts to make high purity oxide, and some is redissolved in sulfuric acid and treated with hydrogen sulfide to make yellow cadmium sulfide pigment. Dry materials are transported between buildings and process and then pumped to the electrolytic refinery.
>
> Substantial levels of airborne cadmium have been observed over a long period in several areas of the plant * * * Exposures to cadmium oxide (CdO) dust occurred during sampling, loading, transporting of dust between roasting, mixing, and calcine operations, and during the loading of the purified oxide. Exposures to CdO fume occurred during the roaster, calcine, retort, and foundry operations. Exposures to cadmium sulfate occurred during the solution and tankhouse operations (mist). Job designations are associated with the operating departments * * * with little overlap between them. The plant also has facilities to produce small amounts of lead, arsenic, thallium, and indium. These operations are performed sporadically by a few individuals in three isolated buildings. High purity arsenic, thallium, and indium are produced in facilities on a laboratory scale.
>
> The cadmium production process has not changed during the past 40 years; however, over this period the company has added a number of emission control systems to reduce exposures in the work areas. Ventilation controls have been added to the roasting, mixing, calcine, foundry, and retort areas * * *.
>
> Plant offices and laboratories are located in separate buildings outside the production area. However, they have some cadmium contamination from dust carried in on the footwear and clothes of supervisory personnel and from general air contamination from the plant's activities."(Ex.4–64)

From his description, Smith provided information on areas in the workplace where cadmium exposures existed, the relative cadmium exposure levels in these areas, the length of employment of workers in each area, and workers' exposures to other chemicals. When used with existing historical exposure measurements, individual worker's personnel records, and information provided by plant personnel, Dr. Smith was able to quantify exposures for individual workers in the cohort. The true advantage of this study over other epidemiological studies is the estimate of dose for each member of the cohort.

In using the exposure data to assess the risk of cancer from exposure to cadmium, a major assumption underlying Dr. Thun's analysis is that one year of exposure to cadmium at 10 μ/m^3 is equivalent to 10 years of exposure at 1 μ/m^3. This assumption was questioned during the rulemaking process (Ex. 19–13). Epidemiological data upon which to make such an evaluation are usually lacking. Analyses performed in the quantitative risk assessment section (section VI) of this preamble indicate virtually the same potency estimate for cancer in animals exposed to CdO dust regardless of whether exposure was continuous of intermittent. Thus, dose rate effects in relation to cadmium exposure and lung cancer were not observed. This observation supports the use of a cumulative dose concept for occupational exposure to cadmium and lung cancer.

In addition to the above issue, comments were submitted to OSHA on other assumptions in Thun's study (Ex. 12–41). Cumulative exposure was estimated using length of employment, jobs within the plant, and an estimate of each worker's time-weighted-average inhalation exposure to cadmium calculated from personal sampling data (1973–1976) and area sampling data (1943–1976). These estimates were originally made by Dr. White (Ex. 4–64).

Because many of the personnel records specified general work areas rather than single departments, Thun categorized each period of a worker's employment into one of seven broad job categories. The average exposure to airborne cadmium for each of these composite categories was calculated on the basis of the industrial hygiene data reported by Smith (Ex. 4–64), with each department contributing to a weighted average according to the proportion of workers usually employed there. Each worker's cumulative exposure over time was computed as the sum of the number of days worked in a given job category for the relevant time period. Cumulative exposure was expressed in milligrams per cubic meter-days (mg-days/m^3).

In the Environ report, the authors summarized the main questions about the method by which Drs. Thun and White estimated exposure. The Environ report called into question: (1) The ratio used between area and personal exposure geometric means for six of the eight general plant areas; (2) the weighting factor; and, (3) the factor used to calculate the effects of respirator usage. Regarding the ratio between area and personal exposure geometric means, area sampling data were available for the time period between 1943 and 1976. Personal exposure measurements were also available for the time period 1973–1976. Dr. Smith calculated a multiplier, or ratio of personal exposure data to area exposure data, based upon data collected in six of eight work areas in the Globe plant between 1973–76. This ratio was then used to adjust the remainder of the historical area exposure data to reflect personal exposures.

The Environ report indicated that there was the possibility that the ratios might not have been the same in the earlier years before the introduction of many of the industrial hygiene controls. If, as the Environ report pointed out, the personal measures in 1973–76 were in fact unrepresentative of the other time periods for which actual personal monitoring data were not available, the ratio between the air concentrations and the personal measures could be different from those calculated and used by Smith. The end result of this assumption could be that the Thun data underestimated dose and thus overestimated the risks associated with cadmium exposure.

Smith acknowledged that:

> * * * the accuracy of the estimates may change with increasing time into the past because conditions have changed in some of the work areas * * * [and] as a result * * * the precision was probably not as good for the older exposures as for the more recent ones (Ex. 4–64).

Smith stated that:

> * * * we could not construct personal exposure histories based on each individual's own sampling * * * [W]e are uncertain about the degree of error introduced by the use of group data. In spite of these difficulties, our estimates were reasonable attempts to consider all of the factors that affect inhalation exposures and have produced exposure-effect relationships that are consistent with the known toxicological behavior of cadmium (Ex. 4–64).

OSHA agrees with Dr. Smith that the true direction of the bias in the exposure assessments can only be guessed. Despite the concerns raised, even the Environ report concluded that of all the assumptions that could operate in the misclassification of exposures, the use of the ratio measure was the "exception" (Ex. 12–41).

Dr. Smith clearly indicated that he was basing his assessments of earlier

exposures on area data. The calculation of personal exposures from area measurements was based on the assumption that the ratio between them was approximately constant. He stated that this assumption was reasonable because:

(1) The same sampling locations had been used for area samples for the past 20 years;

(2) The ratios were calculated from the averages of several measurements for both area and personal data (individual samples can vary quite widely); and

(3) The jobs were routine, well-defined, limited by area, and had not changed significantly during the past 40 years, all of which would tend to make the ratios extremely stable (Ex. 4–64).

The ratio calculated by Dr. Smith between the 1973–76 personal and area sampling data is neither unexpected nor implausible, and would not necessarily change for historical area data regardless of ambient airborne levels, particularly for heavy metal exposures.

In general, in epidemiological studies, even though personal data are preferred for heavy metals and best reflects the worker's environment if sampling is conducted closer than 30 cm from nose (8–668), exposure data of any kind are often lacking. The exposure information is rarely of adequate quality or based upon individual workers personal sampling. Thus, it is plausible that area data could be used to approximate the personal exposures. Since area data were available to Drs. Thun and Smith, it is appropriate that they should have been used.

Regarding the use of area data, the Environ report raised one additional recommendation which was that Smith use the area sampling measures that existed for the time period 1943–54, with or without the ratio multiplier, to calculate the exposures for those periods. If cadmium levels at the smelter were in fact much higher during this period, as the report indicated, then assigning measures taken from 1955 to 1959 to earlier years would underestimate the actual exposure conditions, perhaps considerably, and thus overestimate risk.

In his original report, Smith addressed this issue, stating that he did not use these data for several reasons:

> Although sampling data were available for most of the work areas before 1955, these data were not used because (1) different sampling techniques were used-impingers and electrostatic precipitators instead of filters-and (2) a different sampling strategy was used-breathing zone sampling with hand-held collectors instead of fixed-location samplers * * * Therefore, 1955–59 conditions were used to estimate pre-1955 conditions * * * (Ex. 4–64).

However, during questioning at the cadmium hearings, Dr. Thun further clarified this issue. Dr. Smith had data for the five year period from 1945–50, and these data were used by NIOSH for estimating exposures per worker. Prior to 1945, exposure data were estimated based upon existing data and the knowledge that major engineering controls or changes in the process during those earlier years were absent (Tr. 6/7/90, p. 128).

A second objection raised in the Environ report was that each period of a worker's history was categorized into one of seven broad job categories whose weighted average exposure was based upon the departmental measures from the Smith estimates. The weight used for this average was the number of workers usually employed in the department.

As Dr. Thun indicated, in order to link the personnel records to the industrial hygiene data, it was assumed that the average exposure in the high exposure category, (category 1 which included sampling, roasting/baghouse, mixing, calcine, foundry, and retort areas) and in the low exposure areas (category 7 which included solution, tankhouse, and pigment areas) would be a weighted average of the various departments within these two categories. The average exposure in the high exposure category was assumed to be a weighted average based on the average number of worker-shifts per week in each department.

Environ stated that this was "peculiar" since the number of workers is not an inherent part of the estimate of exposure. Thus, use of the number of measures as a weight had the possibility that the exposure would be overestimated because more measures may have existed for an area where a problem existed. Further, the area of high exposure might not be one where many workers were employed (Ex. 12–41).

The weighting system, or number of eight-hour shifts completed in each department per week, used by Drs. Smith and Thun was based upon telephone conversations with Dr. Lowell White, an ASARCO hygienist, and with Mr. Ernie Lovato, the former president of the local union and a long time employee. The estimates were generally consistent with a listing of job titles in each department at the Globe plant in a 1980 doctoral thesis by Dr. Jeffrey Lee (Ref. in Ex. 33; Smith, 1976).

Thun divided his cohort into homogeneous exposure subgroups on the basis of each individual's occupation, place of work, and shift, and the basic sampling unit was the "worker-shift." The weighted effort was allocated to certain "worker-shifts" based on several factors: the standard deviation in exposure for that particular homogeneous group, the labor turnover of the group, and the number of men belonging to the group. An underlying assumption of this strategy was that exposure to an individual worker is supposed to be indistinguishable from the shift average of the whole group.

It is clear that the measure of the exposure that is applied to any individual in a group should be the mean exposure level. An individual's cumulative exposure should be derived as the mean exposure level times the duration of each individual's employment in that part of the plant.

OSHA agrees with the Environ assessment that Thun's use of average exposures would stabilize the estimates and make the assessments relevant even without a weighted scheme based on the number of measures. However, OSHA did further evaluate the magnitude of the effects of such assumptions relative to arsenic exposure and substantially verified the Thun results for weighted averages (see Section VI–QRA). Thus OSHA concluded weighted averages are more appropriate than unweighted averages.

The last major issue raised by Environ about assumptions in Smith's study was the reduction of the calculated personal exposure by using a factor of 3.9 (approximately 75%). This factor was judged by Smith to be the degree of protection afforded by respirator use. In a series of papers (Exs. 4–64; 8–281), Smith evaluated the average reduction in inhalation exposures produced by the intermittent use of filter cartridge respirators by cadmium workers in the Globe plant.

Questions were raised about the actual degree of protection afforded by respirator use when applied to correcting for arsenic exposures (Exs. 12–41; L–19–59). The main problem was the application of Smith's factor of 3.9 to correct for respirator use as it pertained to arsenic exposures. It was noted that respirators were not routinely worn, which would, in turn, affect the cadmium exposure assessment, as well.

According to Environ and others (Exs. 12–41; 19–43) exposures were underestimated due to the use of the respirator protection factor. Respirator use before 1940, it was stated, was likely to have been minimal at best and the respirators available were not very protective (Ex. 19–43). In the case of arsenic, the dose was underestimated

thus understating the risk; more lung cancer risk should have been attributed to arsenic. In the case of cadmium, the exposure was underestimated, and the risk overstated.

According to Mr. Bidstrup, Counsel for SCM Chemicals, Inc., who cited Dr. Lowell White, formerly of ASARCO, it was not until barrier cream was developed that workers wore respirators in arsenic areas because workers who used respirators before that were afflicted with " * * * a 'horrible face rash' or dermatitis" (Ex. 19–42–b–3, pp. 10–11)." Workers often did not wear respirators for this reason. In addition, Dr. White noted that a different type of respirator (a Jesse James respirator) was worn until the 1940's—not the style of respirator used when the protection factor for cadmium was calculated. Furthermore, if respirators were worn at all, they were often improperly fitted. These considerations make it:

* * * very difficult to accept Thun's assumption that the same respirator protection factor of 3.9 which was purportedly operative for cadmium exposures was similarly protecting against arsenic exposures. These and other reservations exist as to whether arsenic has been adequately controlled for as a potential confounder ((Ex.19–42–b–3, pp. 10–11).

Dr. Smith described respirator use in this plant as follows:

The company has had a policy since the 1930's that requires the use of filter cartridge respirators in work areas with the potential for fume and dust exposures. This policy has been tightly enforced in recent times, but the level of enforcement in the past is unknown, although workers and management have been well aware of the hazard of acute cadmium exposures (Ex. 4–64).

Thus, both Dr. Smith and the commentors were aware of the same issues. However, as Dr. Thun indicated at the hearing:

* * * I think that the impression that has been communicated that there was a major arsenic problem historically in the calcine and roaster area of this plant * * * has been constructed rather recently * * * when I have spoken about this with Professor Smith * * * he says that Globe was not recognized to have an arsenic problem, that the symptoms of arsenic skin irritation were not being brought forth to the environmental group, and that the speculation about what past exposures may have been is based to a large extent on speculation (Tr. 6/7/90, pp. 149–150).

However, Dr. Thun did agree that Dr. Smith's impression of the respirator usage among arsenic exposed workers at this plant did differ from that of Dr. White. And while Dr. Thun is of the opinion that Dr. Smith is probably more accurate, OSHA acknowledges that the true degree of respirator use may not be known. An error in estimates of respirator protection leads to uncertainty in exposure assessments which could result in either overestimates or underestimates of exposure. OSHA developed three sets of exposure data for arsenic exposures, one one of which was respirator adjusted. The original respirator-adjusted estimates were within the range of the two estimates thereby supporting the respirator adjustment further (see section VI–QRA).

The protection factor that Dr. Smith calculated was based on intermittent usage measurements that included times when the respirator was both worn and when the respirator was hanging around the neck of the worker during the workday shift. This would cover those situations in which workers were unable to wear respirators due to facial rashes. Dr. Smith estimated the inhalation exposures for nine workers by measuring the cadmium concentration inside the respirator while it was worn or hanging around the worker's neck. Air concentrations of cadmium were measured simultaneously inside the respirator and at the worker's lapel using a dual sampling system, and workers were sampled for three consecutive days over a full days' workshift. On the average the inhalation exposure was 26% of the lapel concentration, i.e., the average effective protection factor, or the ratio of personal exposure to inhalation exposure, was found to be a geometric mean factor of 3.9. This factor was then used to calculate the inhaled cadmium exposure per worker. Personal exposures were divided by 3.9 to estimate the median inhalation exposures of workers in those department where respirators were worn, and these values were used in the development of each workers' cumulative exposure assessment.

Thus, Smith made three corrections to the existing area exposure level data base. The first correction was to adjust the historical area sampling data by a correction factor to reflect personal sampling. The second correction was the weighting of high exposure areas by number of worker-shifts, and the third was the division of the estimated personal exposures, in those departments and calendar periods in which workers wore respirators, by 3.9—the geometric mean respirator protection factor measured in the Globe plant.

OSHA has substantially verified the latter two adjustments (see section VI–QRA), and believes that the ratio adjustment for area samples did not operate towards misclassification of exposure (Ex. 12–14). OSHA agrees with Dr. Smith's conclusions that he attempted to address all of the factors that could affect the exposures to which workers were exposures. It was obvious, for instance, that the effects of emission control systems and improved ventilation were taken into consideration in each of Smith's estimated exposures for each department as a function of time. (See pg. 323, Table I, Ex 4–64.) Through his study design, Dr. Smith tried to estimate the actual inhalation exposures for individual workers, i.e., the actual dose of cadmium that a worker received to the lung, rather than the ambient cadmium levels, taking into consideration variations in respirator use.

Further, according to Dr. Roth:

* * * regarding the exposure estimates * * * we have no reason to believe that any of the measurements are biased in either one direction or the other and from a statistical standpoint, that's the key issue. (Tr. 6/6/90, pp. 55–56).

It is OSHA's opinion that despite the issues raised regarding the exposure assessment, the forethought by Smith and Thun in applying this exposure assessment to the individual's in the cohort, taking into consideration the use of available data and using advice from the representatives of the workplace, would tend to minimize the errors in the exposure assessments. The underlying strength of the Thun study was the availability of unusually good industrial hygiene records that allowed for the computation of cumulative individual exposures, and from that, some quantitative dose response data. OSHA agrees with the Environ report which stated that despite questions, the quantified exposure estimates were: "* * * a further strength of this study for the purpose of risk assessment * * * (Ex. 19–42b)." Furthermore, the validity of these assessments has been determined, to some extent, by comparison of Thun's results with those of other independent researchers and in other studies.

Regarding this last point, Dr. Thun stated that:

The calculations of cumulative exposure have been validated, to some extent, by comparing them to *in-vivo* data collected by the Brookhaven National Laboratory in 1979 (Ex. 4–27). A strong correlation was found between the calculated cumulative exposure, using these data, and the Brookhaven measurements of liver cadmium * * *. The strength of this approach is that it considers both the intensity and duration of exposure * * * this gives you an actual estimate of cumulative exposure * * * our

analysis grouped individuals into categories * * * to correspond to the level of detail that was available in the personnel records. (Ex. 33).

Dr. Thun was referring to a study by Ellis et al (Ex. 4–64). For Dr. Ellis' analysis, cumulative exposures for individual workers were estimated in the same way as for Thun's analysis, on the basis of the same plant personnel records. A chronological record of each worker's job assignments was obtained. The time-weighted inhalation exposure (TWE) was calculated by multiplying the length of time (t_i) in a given work area by the estimated inhalation exposure for that area and year (E_i) and then summing these values for the total exposure history, or

$$TWE = \Sigma E_i t_i,$$

where E_i was obtained from the original estimates reported by Smith (Ex. 4–64).

Another partial validation of the exposure assessments of these workers was done by Smith who calculated the quantity of cadmium that would be retained in the kidneys of the workers in his study, based on his calculated time-weighted exposure measurement of cumulative cadmium exposure per individual worker, and compared this with the "critical concentration" of cadmium that would result in kidney dysfunction, indicated by a number of other researchers (Ref. in Ex. 4–68). Smith found that:

> The quantity 41 mg per kidney is somewhat higher than the 15–30 mg per kidney reported as the critical value for cadmium-by several investigators (WHO Task Group, 1975; Nomiyama *et al*, 1979: Ellis *et al*, 1980); however, it is quite close, considering the assumptions and the errors in the exposure estimates. These findings provide further support for the quality of the exposure estimates. (Ex. 4–64).

To the extent that levels of cadmium in urine reflect cumulative cadmium exposures in air, and are not influenced by the presence of kidney damage, these results by Dr. Smith appear to confirm Dr. Thun's exposure assessments.

Thus, the cumulative exposures in Thun's study were somewhat validated by two independent researchers who further evaluated the health status of a subset of the same workers included in Thun's study. Using *in-vivo* measurements of cadmium in liver and kidney tissues and kidney cadmium content, the two researchers, Smith (Ex. 4–64) and Ellis (Ex. 4–64), found associations between cumulative cadmium exposures and effects of cadmium that were both similar to those of other researchers and were plausible, given the available medical data on cadmium's effects. These "validity checks," of the exposure assessment provides another important advantage of the Thun study over other studies. The confidence that can be placed in the results obtained from the use of such exposure assessments, for both cadmium and arsenic exposures, is increased.

As Dr. Thun stated:

> * * * all of the cohorts have potential exposure to other occupational lung carcinogens besides cadmium. For the metallurgical groups * * * there is potential exposure to arsenic and for the nickel-cadmium battery plants, there is potential exposure to nickel * * * but the exposure data on this study are really exemplary. There are few occupational cohorts for which historical exposures are as well documented. (Tr 6/7/90, p. 87).

f. *OSHA's conclusions regarding the Thun study.* The major issues regarding the Thun study include potential confounding from arsenic exposure and from cigarette smoking. (See also Exs. 19–43; 66.)

Regarding the multiplicative or synergistic effects of smoking together with occupational cadmium exposures suggested by some commenters (Ex. 66), OSHA is aware of no evidence that supports the hypothesis of such synergistic effects. Of far greater concern to the Agency is the contamination of cigarettes by cadmium in the workplace (Ex. 29). Both cadmium and smoking are associated with lung cancer. Arsenic does not appear to have played a major role in the excess risk of lung cancer observed in the study. With data indicating that confounding from arsenic and cigarette smoking did not play a major role in the lung cancer excess, it would be imprudent to overlook the epidemiological data showing that cadmium appears to have been responsible for the excess lung cancer risk.

The obvious strength of the Thun study comes from the finding of a dose-response relationship. Dr. Kazantzis acknowledged that the study "* * * has shown evidence of the carcinogenicity of cadmium with a dose-response relationship" (Tr. 6/11/90, p. 142), and Dr. Rodericks stated that he would still point to the dose-response information from the Thun study "as a most important set of data." (Tr. 7/18/90, p. 26).

It is OSHA's opinion that the findings of the Thun study demonstrate a significant dose-response between cadmium exposure and lung cancer that could not be explained by confounding from cigarette smoking and arsenic exposure.

9. Summary and Conclusions

Complete in-depth review of the rulemaking record and careful analyses of the available epidemiologic data have led OSHA to conclude that a significant association has been demonstrated between occupational cadmium exposure and lung cancer. Evidence for this association is further strengthened by studies demonstrating the induction of lung cancer in experimental animals exposed by inhalation to several different cadmium compounds. The data also have revealed a significant association between cadmium exposure and prostate cancer, though recent studies show less of an association than earlier study results. IARC (Ex. 8–656) concluded that cadmium is probably a human carcinogen. The data presented in this rulemaking record and the analyses conducted and presented in the quantitative risk assessment section of this standard rule out any major potential confounding in the Thun *et al.* study from cigarette smoking and arsenic exposure on the excess risk of lung cancer observed among the cohort members. Thus, the association between cadmium exposure and lung cancer as noted by IARC is further strengthened by these new data and analyses. The epidemiologic findings demonstrating the carcinogenicity of cadmium establish cadmium as an occupational carcinogen.

Some commenters questioned the consistency of the epidemiologic data (Ex. 19–42b–3; The Environ Corporation, March 17, 1989). For example, Environ stated that "the results of lung cancer mortality studies in industrial settings where cadmium is present are mixed: The majority of reports do not show an excess lung cancer incidence in association with cadmium exposure and several provide strong evidence of alternative causes of the cancer excess observed." According to Environ, its conclusions are consistent with those reached by IARC, "* * * although our evaluation includes more recent studies than those reviewed by this agency (IARC)" (Ex. 19–42b-3). Environ continued:

> On the basis of the commonly-applied criteria for causation based on epidemiological evidence that: (1) a positive dose-response relationship be observed, (2) the association is not explicable by bias in recording, detection, confounding or chance; and (3) the association is observed repeatedly in different circumstances, it appears evident that the epidemiologic data on the potential lung carcinogenicity of cadmium are insufficient to establish causality for humans (Exs. 12–41 and Ex. 19–42b, p. 19).

SCM Chemicals, citing a review of epidemiologic studies relating to cadmium by a 12-member panel of expert epidemiologists, criticized the epidemiologic studies relating to cancer for failing to consider the effects of confounding factors in drawing their conclusions (Ex. 19–42A).

OSHA noted earlier that for all five major cohorts of cadmium-exposed workers, the lung cancer SMRs are elevated, and in updated studies of four of the cohorts, the SMRs for lung cancer are statistically significantly elevated (Ex. L–140–50). These four cohorts were U.S. cadmium recovery workers with two or more years of employment (Thun et al., Ex. 8–658a); nickel-cadmium battery workers in the U.K. (Sorahan, Ex. 12–12–A); nickel-cadmium battery workers in Sweden (Jarup et al., L–140–50); and workers in 17 British plants (Kazantzis et al., Ex. 8–684). Not only were the SMRs elevated for four of the five cohorts, but according to Drs. Thun, Elinder, and Friberg, in three of the five cohort studies, (Exs. 8–658a, 12–12–A and 8–684), a dose-response relationship was evident (Ex. L–140–50). Regarding the other commonly applied criterion cited by Environ, bias in recording, detection and chance confounding, analyses by Thun et al. and by Stayner show that arsenic contamination and confounding from cigarette smoking could not have accounted for the excess lung cancer risk in the Thun study. Furthermore, the study demonstrated a dose-response for lung cancer in relation to cadmium exposure.

Thus, contrary to the opinion stated by Environ, all three of the commonly applied criteria for causation are satisfied by the existing epidemiological data for occupational cadmium exposure and lung cancer:

(1) A positive dose-response relationship has been demonstrated;

(2) The association does not appear to be explicable by chance, bias in selection of subjects for study or by confounding from other exposures; (3) the association has been observed repeatedly in different occupational settings.

A large number of epidemiologic studies demonstrate an association between occupational exposure to cadmium and kidney dysfunction. Exposure data were of high quality from six epidemiologic studies that allowed estimates of a dose response between cadmium and kidney dysfunction. No participant in the rulemaking challenged the etiologic basis for cadmium and its role in kidney dysfunction.

Commenters have testified that in contrast to toxins such as Cr VI and lead, the correspondence between human and animal data for all adverse health effects of cadmium is "very good" (Tr. 6/7/90; pp. 3–71). Human studies indicate acute and chronic cadmium toxicity in the form of renal, liver, and pulmonary effects, and animal studies have demonstrated similar effects. Chronic animal studies by inhalation show cadmium-induced lung cancers in rats and some cases of prostatic cancers; the same effects have been observed in human studies. Both renal damage and lung disease (bronchitis) have been observed in chronically exposed humans and animals. There is also good correlation between ITAI-ITAI disease in humans and demineralization of the bone in animals. Liver damage is also seen both in humans and animals. However, it is noted that some effects have been seen only in animals (6/7/90; Tr. 3–3 to 3–71).

OSHA has received information indicating that additional epidemiologic studies are being conducted and some participants feel that the final standard should be delayed until these studies are completed. (Caza, Ex. 19–29; Kazantzis, L–140–50, pp. 701–701; DCMA, Ex. 19–40). OSHA believes, however, that delaying the final standard is not warranted and that the record supports this conclusion. OSHA agrees that the human-animal correlation for cadmium:

> * * * is probably one of the best sets of correlations that one sees between experimental animals and humans for a toxic agent. (M. Costa, Tr. 6/7/90, p. 8)

VI. Quantitative Risk Assessment

In February, 1990, OSHA proposed two alternative permissible exposure limits (PELs) of 1 $\mu g/m^3$ and 5 $\mu g/m^3$ as an 8-hour time-weighted average (TWA) and a 5 $\mu g/m^3$ and a 25 $\mu g/m^3$ ceiling limit for cadmium. These new exposure limits were based on an evaluation of carcinogenic and renal effects observed in workers or experimental animals following exposure to cadmium.

Summary of Quantitative Risk Assessment for Lung Cancer From Proposed Rule

To evaluate the potential carcinogenicity of cadmium, quantitative estimates of risk were made by OSHA based on the Takenaka et al. (Ex. 4–67) study in rats and the Thun et al. (Ex. 4–68) study in humans. These studies provide the strongest evidence of carcinogenicity of cadmium in animals and humans, as well as the most appropriate data for a quantitative assessment.

Experimental Data

Cadmium has been shown to be a carcinogen in animals following administration via inhalation. At the time of the proposed rule, the strongest evidence of carcinogenicity in animals came from a rat bioassay conducted by Takenaka et al. (Ex. 4–67). In this bioassay, Takenaka exposed three groups of 40 male rats 23 hours/day for 18 months to cadmium chloride aerosol at nominal cadmium concentrations of 12.5, 25, and 50 $\mu g/m^3$. An additional group of 41 male rats served as controls. The animals were observed for 13 months following exposure, at which time all surviving rats were sacrificed. A statistically significant increase in the incidence of malignant lung tumors was observed in treated animals and a statistically significant dose response relationship was observed. The incidence of lung carcinomas was 0/38 (0%) in the controls, 6/39 (15.4%) in the low-dose group, 20/38 (52.6%) in the mid-dose group, and 25/35 (71.4%) in the high-dose group. Table VI–1 contains a summary of the lung tumor data from this study.

OSHA concluded that the Takenaka study was particularly suitable for quantitative risk assessment for several reasons. First, the exposures were well documented. The study was run with concurrent controls, and a statistically significant excess of malignant neoplasms in the exposed rats and a statistically significant dose-response relationship were observed. Finally, the route of exposure used in this study (inhalation) is the primary exposure route in most occupational settings.

TABLE VI–1.—INCIDENCE OF LUNG CARCINOMAS IN MALE WISTAR RATS EXPOSED TO CADMIUM CHLORIDE AEROSOLS [a]

Tumor type	Controls (percent)	12.5 $\mu g/m^3$ (percent)	25 $\mu g/m^3$ (percent)	50 $\mu g/m^3$ (percent)
Adenocarcinoma	0/38 (0)	4/39 (10)	15/38 (39)	14/35 (40)
Epidermoid carcinoma	0/38 (0)	2/39 (5)	4/38 (11)	7/35 (20)
Mucoepidermoid carcinoma	0/38 (0)	0/39 (0)	0/38 (0)	3/35 (9)

TABLE VI–1.—INCIDENCE OF LUNG CARCINOMAS IN MALE WISTAR RATS EXPOSED TO CADMIUM CHLORIDE AEROSOLS [a]—Continued

Tumor type	Controls (percent)	12.5 μg/m³ (percent)	25 μg/m³ (percent)	50 μg/m³ (percent)
Combined epidermoid carcinoma and adenocarcinoma	0/38 (0)	0/39 (0)	1/38 (3)	1/35 (3)
Total carcinomas	0/38 (0)	6/39 (15)	20/38 (53)	25/35 (71)

Source: Ex. 18.
[a] Number of animals with lung carcinoma from Takenaka et al. (Ex. 4–67).

Quantitative Risk Assessment Using Animal Data

The extrapolation of carcinogenic risk across species rests on the assumption that when dose is measured in equivalent units for both species, then the risk associated with lifetime exposure to a substance, such as cadmium, is the same for each species at each dose. Exposure levels in rats were scaled to equivalent doses for rats and humans by expressing dose in units of micrograms per kilogram of body weight per day (μg/kg/day). No adjustments were made for particle size due to a lack of precise data available on the size of cadmium particles to which workers are exposed. Without specific human absorption data on various cadmium compounds, no adjustment was made for the solubility of cadmium chloride used in the experiment.

The probit, logit, Weibull, multistage, and one-hit models were all fit to the data. As indicated in the OSHA proposal, the preliminary Maximum Likelihood Estimates (MLEs) of excess cancer deaths following 45 years of occupational exposure to 5 μg Cd/m³ were estimated to be 11 (multistage), 15 (one-hit), 0 (probit), 0.7 (logit), and 4 (Weibull) per 1,000 workers (Table VI–2). MLEs of excess cancer deaths following 45 years of occupational exposure to 100 μg Cd/m³, the current time-weighted average PEL for cadmium fume, were estimated to be 221 (multistage), 266 (one-hit), 186 (probit), 190 (logit), and 210 (Weibull) per 1,000 workers. OSHA concluded that regardless of which model would be considered the "best," each model indicates that a reduction of the PEL to 5 μg/m³ will lead to a significant reduction in risk. However, OSHA relied primarily upon the multistage model of carcinogenesis. OSHA agreed with the position of the Office of Science and Technology Policy (OSTP) (Ex. 8–693) in that when data and information are limited, and when much uncertainty exists regarding the mechanisms of carcinogenic action, models or procedures which incorporate low-dose linearity are preferred when compatible with limited information. The multistage model and the one-hit model, a special case of the multistage model, are linear at low doses. The multistage model incorporates the biological assumption that there are a number of stages that cell lines go through to produce a tumor, and a carcinogen exerts its effect by increasing the rate at which cell lines pass through one or more of these stages. In the form in which it was used by OSHA, the multistage model assumes there is no threshold of exposure below which a carcinogen cannot induce cancer. Upper confidence limits on the excess risk from low exposures determined using the multistage model are proportional to the amount of exposure, i.e., the dose response relationship is linear at low doses.

TABLE VI–2.—OSHA PRELIMINARY ESTIMATES OF EXCESS CANCER DEATHS PER 1,000 WORKERS WITH 45 YEARS OCCUPATIONAL EXPOSURE TO CADMIUM [a,b]

Dose (μg/m³)	Multistage model	One-hit model	Probit model	Logit model	Weibull model [a]
200	485 (528)	481 (541)	468 (552)	469 (557)	445 (526)
100	221 (312)	266 (322)	186 (278)	190 (280)	210 (299)
50	109 (171)	143 (177)	44 (99)	56 (114)	90 (157)
40	87 (139)	116 (144)	25 (64)	39 (82)	68 (126)
20	43 (72)	60 (75)	2 (11)	11 (28)	28 (60)
10	21 (37)	30 (38)	0.2 (1)	3 (9)	11 (28)
5	11 (18)	15 (19)	0 (0)	0.7 (3)	4 (13)
1	2 (3.7)	3 (4)	0 (0)	0 (0.2)	0.5 (2)
X^2	3.00	3.63	1.52	1.59	2.56
Degrees of freedom	2	3	1	1	1
P-value	>0.25	<0.50	0.22	0.21	0.11

Source: Ex. 18.
[a] Estimates derived using data from the Takenaka rat bioassay.
[b] Numbers in parentheses are the 95% upper confidence limits.

Epidemiological Data

Human data for quantifying lung cancer risk associated with cadmium exposure was found in a mortality study conducted by Thun et al. (Ex. 4–68). This study is a historical prospective study of 602 white men employed in a production area of a cadmium smelter for at least six months between 1940 and 1969. Follow up was through 1978. Sufficient exposure data existed to determine exposure levels for workers and a dose-response relationship between cadmium exposure and lung cancer mortality was reported.

Prior to 1926, the cadmium smelter functioned as an arsenic smelter. Because arsenic is a known carcinogen resulting in lung cancer, the cohort was divided into two subcohorts for analysis: a sub-cohort of 26 men hired prior to 1926 and a sub-cohort or 576 workers hired after 1926. A statistically significantly elevated incidence of death due to lung cancer (4 observed versus 0.56 expected) was found in the sub-cohort of workers hired prior to 1926. Among the workers hired after 1926, 16 lung cancers were observed (versus 10.87 expected). Table VI–3 contains a summary of the lung cancer data from Thun et al. (Ex. 4–68).

TABLE VI-3.—DATA USED FOR ESTIMATING RISKS FROM A MORTALITY STUDY OF CADMIUM SMELTER WORKERS BY THUN ET AL.

Cumulative exposure (mg/m³-days)	Person years at risk	No. lung cancers observed	No. lung cancers expected [a]	SMR
<584	7005	2	3.77	53
585–2920	5825	7	4.61	152
>2921	2214	7	2.50	280

Cumulative exposure (mg/m³-days)	TWA equivalent (μg/m³)		Median dose [d] (mg/m³-days)	Continuous dose [e] (μg/m³ years)
	40-year [b]	45-year [c]		
<584	>40	>36	280	168
585–2920	40–200	36–178	1210	727
>2921	>200	>178	4200	2522

Source: Ex. 18.
[a] Expected incidence based on calendar time, age-specific death rates for U.S. white males.
[b] Calculated as (cumulative dose×1000)/(385×40).
[c] Calculated as (cumulative dose×1000)/(385×45).
[d] As provided by Thun to EPA.
[e] Calculated as median dose×1000×(8/24)×(1/365)×(240/365).

Airborne cadmium concentrations were measured by Smith et al. (Ex. 4–64) as 8-hour TWA for nine departments in the smelter and for office and laboratories combined (nonproduction work areas). Exposure for each of these areas was classified as high exposure or low exposure. Estimates of individual cumulative cadmium exposure were based on the period of time a worker was employed in a high or low exposure dose area.

Using this exposure information, Thun et al. divided the post-1926 cohort into three exposure groups: A low-dose group with a cumulative exposure of less than 584 mg/m³-days, a mid-dose group with cumulative exposures of 585–2920 mg/m³-days, and a high-dose group with cumulative exposures of greater than 2921 mg/m³-days. Based on this division, a dose-response relationship between cadmium and death from lung cancer was observed. For the low-dose group, two deaths due to lung cancer were observed while 3.77 were expected (RR=0.53). For the mid-dose group, seven deaths due to lung cancer were observed while 4.61 were expected (RR=1.52). For the high-dose group, seven deaths due to lung cancer were observed while 2.50 were expected (RR=2.80).

Quantitative Risk Assessment Based on Epidemiological Data

OSHA quantified risks from the Thun data using an absolute risk model and a relative risk model. Both are linear models; however, the two models are based on different assumptions which lead to different estimates of risk. The absolute risk model is based on the assumption that the increased lung cancer mortality rate from cadmium exposure depends only upon cadmium exposure and not upon age. The relative risk model rests on the assumption that the ratio of the lung cancer mortality risk in an individual exposed to cadmium to what his mortality risk would be if he had not been exposed to cadmium depends only upon cadmium exposure and not upon age. Thus, an absolute risk model would predict the same lung cancer mortality rate from cadmium exposure in 20-year olds as in 50-year olds, given equal cadmium exposures, whereas the relative risk model would predict a higher rate from cadmium exposure in 50-year olds because 50-year olds have a higher background rate of lung cancer than 20-year olds.

The estimates of excess lung cancer death from the relative risk model were approximately twice as large as those from the absolute risk model, but both models predicted significant risk at the current OSHA PEL of 100 μg/m³. As published in the proposal, at 100 μg/m³, these models predicted between 16 and 30 excess lung cancer deaths per 1000 exposed workers. At exposure levels as low as 5 μg/m³, the excess risk of lung cancer death estimated by these models was 0.8 per 1000 exposed workers for the absolute risk model and 1.6 per 1000 exposed workers for the relative risk model. At exposure levels of 1 μg/m³ the excess risk of lung cancer death estimated by these models was 0.2 per 1000 exposed workers for the absolute risk model and 0.3 per 1000 exposed workers for the relative risk model. (See Table VI-4.)

TABLE VI-4.—OSHA PRELIMINARY ESTIMATES OF EXCESS LUNG CANCER DEATHS PER 1,000 WORKERS WITH 45 YEARS OCCUPATIONAL EXPOSURE TO CADMIUM [a,b]

Dose (μg/m³)		Number of excess deaths	
TWA	Continuous [c]	Absolute risk model	Relative risk model
200	4.384	32.3 (4,60)	60.2 (8,109)
100	2.192	16.3 (2,30)	30.7 (4,57)
50	1.096	8.2 (1,15)	15.5 (2,29)
40	0.877	6.6 (0.7,12)	12.5 (2,23)
20	0.438	3.3 (0.4,6)	6.3 (0.8,12)
10	0.219	1.6 (0.2,3)	3.1 (0.4,6)
5	0.110	0.8 (0.1,2)	1.6 (0.2,3)
1	0.022	0.2 (0,0.3)	0.3 (0,0.6)

Source: Ex. 18.
[a] Estimates derived using data from the Thun mortality study of cadmium smelter workers.
[b] Numbers in parentheses are 5% lower and 95% upper confidence limits.
[c] Assumes exposure occurs for 8/24 hours and 240/365 days.

OSHA proposed a PEL of 1 $\mu g/m^3$ based on the risk assessment using the Takenaka rat bioassay. However, there is support for the use of the Thun et al. data for establishing an exposure level because no extrapolation across species is required. Estimates of risk based on the Thun data are lower than those from the Takenaka data, and support a PEL of 5 $\mu g/m^3$. OSHA therefore proposed alternated PELs of 1 $\mu g/m^3$ and 5 $\mu g/m^3$ based in part on the estimates of risk from Takenaka et al. (Ex. 4–67) and Thun et al. (Ex. 4–68) and in part upon the concerns for the technological feasibility of achieving a PEL of 1 $\mu g/m^3$.

Summary of Quantitative Risk Assessment for Kidney Dysfunction From Proposed Rule

In its proposal, OSHA quantified the risk of kidney dysfunction associated with cadmium exposure using two studies of cadmium workers that contained adequate data for such an assessment. One of the studies was a study of cadmium smelter workers conducted by Ellis et al. (Ex. 4–27). The other study was of workers at a refrigeration compressor production plant conducted by Falck et al. (Ex. 4–28). Kidney dysfunction was defined in both studies as an excess of urine protein, specifically β_2-microglobulin, a low molecular weight protein that, when found in the urine, indicates that damage has occurred to the proximal tubules and/or glomerulus. Because this damage may be irreversible and can lead to more serious health effects, OSHA considers this dysfunction to represent material impairment of health.

Ellis et al. studied 82 workers at the same smelter that was investigated by Thun et al. (Ex. 4–68; see discussion above in summary of cancer QRA). Air concentrations of cadmium in a given work area were estimated using industrial hygiene data provided by Smith (Ex. 4–64). A cumulative exposure was estimated for each worker based on these air concentrations and duration of work in a given work area. Twenty-four hour urine samples were obtained from each worker and used to determine whether a worker had abnormal kidney function. Kidney function was judged to be abnormal if urinary levels of β_2-microglobulin exceeded 200 $\mu g/g$ creatinine or if total urinary protein levels exceeded 250 mg/g creatinine. Eighteen out of 51 active workers and 23 out of 31 retired workers were classified as having abnormal kidney function. The mean time-weighted inhalation exposure estimate for active workers with abnormal kidney function was 1690 $\mu g/m^3$-years and for retired workers with abnormal kidney function was 3143 $\mu g/m^3$-years.

Falck et al. studied 33 male workers at a plant which produces refrigeration compressors with silver brazed copper fittings. The silver brazing consisted of 18–24% cadmium. Estimates of cumulative exposure were made for each worker based on data from air monitoring done by the Michigan Department of Industrial Health. The mean estimated cadmium exposures were 39 $\mu g/m^3$ for 11 years of operation for the automated brazing line and 110 $\mu g/m^3$ for 21 years of operation for the manual line. A time-weighted exposure was estimated for each worker based on the length of time in each brazing line. Twenty-four hour urine samples were obtained for eight of the 33 workers who were found to have elevated protein levels in spot urine samples. Seven of these eight workers were found to have urinary protein levels in excess of the 95% tolerance limit, based on urinary protein levels in 41 unexposed workers who served as controls. Based on this increase in urinary protein in exposed workers compared to unexposed controls, these seven workers were judged to have abnormal kidney function.

Using the logistic regression model and data provided by Ellis et al. and Falck et al., OSHA estimated the risk of kidney dysfunction from 45 years of exposure to a variety of occupational doses of cadmium. Estimates of kidney dysfunction per 1,000 workers with 45 years of occupational exposure to 5 $\mu g/m^3$ were 164.6 using the Ellis et al. data and 9.0 using the Falck et al. data. (See Table VI–5.)

TABLE VI–5.—OSHA PRELIMINARY ESTIMATES OF KIDNEY DYSFUNCTION PER 1,000 WORKERS WITH 45 YEARS OF OCCUPATIONAL EXPOSURE TO CADMIUM

8–Hour TWA dose ($\mu g/m^3$)	Cumulative dose ($\mu g/m^3$-yrs)	Incidence of kidney dysfunction	
		Ellis model	Falck model
1	4.5	26.1	0.1
5	22.5	164.6	9.0
10	45.0	317.7	58.9
20	90.0	523.7	300.5
40	180.0	722.0	746.7
50	225.0	774.0	845.7
100	450.0	890.0	974.1

Source: Ex. 16.

New Evidence and Issues Arising Since Publication to OSHA's Proposed Rule

Since the quantitative risk assessment was conducted for the proposed rule for cadmium, new information has become available which prompted a re-evaluation of the risk assessment conducted by OSHA. Additional animal studies have been conducted that demonstrate an increased risk of lung cancer in animals following exposure to cadmium (Exs. 8–694B, 8–694D, L–140–29F). The only animal study available for the risk assessment in the proposed rule which provided quantitative information concerning the carcinogenicity of cadmium was the study conducted by Takenaka et al. (Ex. 4–67). This study was conducted in male rats only and exposure was to cadmium chloride. Preliminary results from a study conducted by Oldiges et al. (Exs. 12–10i, 12–10h, and 12–35) were available and provided qualitative evidence that supported the carcinogenicity of cadmium. However, because these were preliminary results, they were not evaluated quantitatively. Since the proposed rule, the final results of the Oldiges et al. study (Ex. 8–694D) have been published, as well as a later report of this same study (Glaser et al. Ex. 8–694B). In Oldiges et al. and Glaser et al., groups of male and female Wistar rats were exposed to various cadmium compounds. These studies demonstrated that various cadmium compounds caused lung tumors in male and female rats.

The followup of the major epidemiological study available at the time of the proposed rule has been extended (Ex. 4–68). The Thun et al. cohort reported in the proposed rule was followed up through 1978. Since that time the cohort has been followed through 1984.

Since the proposed rule was issued, Stayner et al. (Ex. L–140–20) have completed a risk assessment based on the Thun cohort that differs in several respects from the one reported in the proposed rule. The Stayner et al. risk assessment is based on a followup of the Thun cohort through 1984, whereas the risk assessment reported in the proposed rule was based on followup only through 1978. Stayner et al. had access to the unprocessed data from the Thun cohort and consequently was able to conduct a wider range of analyses in its risk assessment than was possible based on just the data reported in the published Thun report (Ex. 4–68). In

addition, Lamm et al. (Ex. 144–7–b) have conducted a case control analysis of lung cancer cases from the same cohort as that studied by Thun et al.

Several studies concerning the kidney effects observed in workers following exposure to cadmium were not evaluated quantitatively in the proposed rule, and these studies provide quantitative information that would be useful in evaluating the risk of kidney effects following exposure to cadmium. In its proposed rule, OSHA quantified the risk of kidney dysfunction due to cadmium exposure using only the studies by Falck et al. (Ex. 4–28) and Ellis et al. (Ex. 4–27). OSHA has since identified four additional studies that may contain useful quantitative information. These include a study by Elinder et al. (Ex. L–140–45) of a cohort of 60 workers who had previously been exposed to cadmium through welder fume and dust associated with the use of cadmium soldiers, a study by Jarup et al. (Ex. 8–661) of 440 workers exposed to cadmium at a Swedish battery plant, a study by Mason et al. (Ex. 8–669A) of 75 workers exposed to copper-cadmium alloy in a factory in the United Kingdom, and a study by Thun et al., which is based on the same population of smelter workers studied earlier by Ellis et al. (Ex. 4–27).

Several issues concerning the quantitative risk assessment for cancer in the proposed rule have been raised that also prompted a reevaluation of OSHA's risk assessment. Concerns were raised over the appropriateness of the Takenaka et al. study for quantitative risk assessment by the Office of Management and Budget (OMB) (Ex. 17), Dr. Oberdörster (Ex. 31), Richard Bidstrup, Counsel for SCM Chemicals, Inc. (Ex. 19–42A), as well as others. The main issue was that in the Takenaka et al. study the rats were exposed continuously to cadmium chloride, while in the workplace exposure is not continuous and is mostly to cadmium oxide (Ex. 19–43). Therefore, the Takenaka et al. study was reevaluated to determine its relevance for the quantitative risk assessment of cadmium.

Mr. Leonard Ulicny (Ex. 144–17) and the Dry Color Manufacturers Association (Ex. 144–20) have requested that cadmium sulfide should have a separate PEL from other cadmium compounds. This request is based on the view that cadmium sulfide is less soluble in the human body, and therefore less toxic, than other cadmium compounds. Both commenters noted that the preparation of cadmium sulfide in the studies conducted by Glaser et al. (Ex. 8–694B) and Oldiges et al. (Ex. 8–694D) consisted of cadmium sulfide particles in suspension and subjected to light. The commenters concluded that this reaction could be responsible for the effects observed in animals following exposure to cadmium sulfide which they believe should be attributed to another cadmium compound, namely cadmium sulfate. Analyses have been conducted and reported by Dr. Oberdörster (Ex. 141) and Dr. Heinrich (Ex. 142) which need to be evaluated to determine if cadmium sulfide should have a separate PEL.

OMB (Ex. 17) questioned the impact of the Heinrich et al. (Ex. L–140–29F) study on the relevance of the quantitative risk assessment. The Heinrich et al. study was conducted in mice and hamsters. OMB thought that this study provided negative data and could possibly show that the carcinogenic effect of cadmium may be species-specific, because this study provided the only relevant data in species other than rat. This study was reevaluated to determine if the study could actually be considered negative and its impact on the quantitative risk assessment of cadmium.

In the quantitative risk assessment for cancer using animal bioassay data, OSHA performed its interspecies extrapolation assuming the risks were equal across species when dose across species was equal on a body weight basis. Dr. Oberdörster (Ex. 31) has recommended the use of lung dosimetry instead of equivalency based on body weight. The methodology recommended by Dr. Oberdörster will be considered in the reevaluation of OSHA's risk assessment.

The appropriateness of the Thun et al. cohort for quantitative risk assessment was questioned by many commenters (Exs. 38, 19–43, L–140(23), 144–8a, 144–8b, 144–8c, 144–170). The Globe plant from which the cohort was taken was formerly an arsenic smelter and many commenters, including George M. Obelodobel, Vice-President and General Manager of Big River Zinc Corporation (Ex. 19–30), Richard Bidstrup, Counsel for SCM Chemicals, Inc. (Ex. 19–42A), OMB (Ex. 17) and The Cadmium Council (Ex. 119), thought that arsenic, a known human carcinogen, may have been a contributing factor to the lung cancer observed in this cohort. Thun et al. had conducted an analysis of the contribution of arsenic to the risk of lung cancer observed in their study. However, this analysis was questioned (Ex. 17). Cigarette smoking was also mentioned by several of these reviewers as a possible confounding factor. These issues were considered in the reevaluation of the Thun et al. cohort.

The appropriateness of the mathematical dose-response models used in the quantitative risk assessments was raised as an issue by several commenters. In particular, the use of the linearized multistage model as the most appropriate model for the animal cancer quantitative risk assessment was raised by OMB (Ex. 17), as well as the use of the absolute and relative risk models for the quantitative risk assessment based on human epidemiological data (Exs. 17, 38). The risks from the animal and human quantitative risk assessments for cancer were also compared when these risk assessments were reevaluated. For the quantitative risk assessment of the kidney effects of cadmium, several commentors, including The Cadmium Council (Exs. 119, 19–43) recommended the use of the probit model for evaluating the kidney effects of cadmium rather than the logistic model used by OSHA.

In view of the new evidence that has become available since the proposed rule and the comments that have been received concerning the proposed rule, OSHA has decided to reevaluate the quantitative risk assessments for cadmium. The reevaluation of these quantitative risk assessments, as well as a discussion of the major issues are included below.

Risk Assessment for Lung Cancer

Assessment of Lung Cancer Risk Using Animal Data

The inhalation study conducted by Takenaka et al. (Ex. 4–67) exposed male rats to cadmium chloride, while Oldiges et al. (Ex. 8–694D) compared the results following exposure to cadmium chloride, cadmium oxide (dust or fume), cadmium sulfate, and cadmium sulfide in both male and female rats. In the Takenaka study, groups of 40 (41 in the control) male Wistar rats were exposed to a cadmium chloride aerosol continuously (23 hr/d, 7 d/wk) for 18 months at nominal concentrations of 0, 12.5, 25, or 50 $\mu g/m^3$ of cadmium. Rats were observed up to 31 months; necropsy was performed only on animals that had survived at least 18 months. In the Oldiges et al. study (Ex. 8–694D), groups of 20 male and female Wistar rats were exposed to cadmium chloride (30 or 90 $\mu g/m^3$), cadmium oxide dust (30 or 90 $\mu g/m^3$), cadmium oxide fumes (10 or 30 $\mu g/m^3$), cadmium sulfate (90 $\mu g/m^3$), or cadmium sulfide (90, 270, 810, or 2430 $\mu g/m^3$) for approximately 18 months and

followed for up to approximately 31 months.

In its reassessment of cancer risk based on animal data contained in the Takenaka et al. (Ex. 4–67) and Oldiges et al. (Ex. 4–694D) studies, OSHA has utilized three dose response models, all of which are different versions of the multistage model of cancer: The Armitage-Doll multistage model, the multistage model, and the multistage-Weibull model. The Armitage-Doll multistage model of cancer assumes that individual cell lines go through a series of stages in order to initiate a tumor, and different cell lines compete independently to be the first to produce a tumor. The rate at which cell lines go through a particular stage is assumed to be increased by exposure to the carcinogen by an amount that is proportional to the instantaneous dose of the carcinogen. This implementation of the Armitage-Doll theory was proposed for risk assessment by Crump and Howe (1984). This model is fit to time-to-tumor data. It does not require a TWA measure of dose as input, but instead utilizes the full time-varying pattern of dose in assessing risk.

The multistage model (Crump, 1984) is a generalization of the Armitage-Doll model that provides a dose-response that is flexible enough to model both linear and non-linear responses. However, upper statistical confidence limits on risk computed using this model will vary linearly with dose (hence, this model is sometimes called the linearized multistage model). This model is applied to quantal data on the number of animals with tumors; it does not use information on the time required for tumors to appear.

The multistage-Weibull model (Krewski et al., 1983) is an extension of the linearized multistage model that is applicable to time-to-tumor data. This model assumes that the probability of a tumor as a function of dose, for a fixed age, has the same form as the (linearized) multistage model, and the probability of tumor as a function of age, for a fixed dose, has a Weibull distribution.

Both the Armitage-Doll model and the multistage-Weibull model require information on the time at which tumors were discovered (time-to-tumor data), whereas the multistage model does not require this information. Since time-to-tumor data were not available from Takenaka et al., the Armitage-Doll and multistage-Weibull models were applied only to data from Oldiges et al. These time to tumor data were obtained by OSHA from an unpublished report from the Oldiges et al. study (Ex. 73). Both of the models that utilize time-to-tumor data require information on whether or not a tumor was fatal or incidental (i.e., observed incidentally at death from a different cause). OSHA did not have information regarding whether the lung tumors in the Takenaka et al. or Oldiges et al. studies were fatal or incidental, and consequently applied the models using both assumptions. These two approaches were found to give comparable results, and only results based on the assumption that all lung tumors were incidental are reported herein. These two approaches estimate different end points. When all tumors are assumed to be incidental, these models estimate the probability of having a tumor large enough to be observed in a histological examination by a given age; however, if all tumors are assumed to be fatal, the models estimate the probability of dying from a tumor by a given age.

Both the Armitage-Doll and multistage-Weibull require that an animal's age be specified to estimate risk. (These models estimate the probability of an animal acquiring a tumor by a particular age.) The age used to estimate risk from each study of a particular cadmium compound by Oldiges et al. is the duration of the study (days on test of the last animal to die).

The Oldiges et al. study involved groups in which animals were dosed for varying periods of time and the lifespans of the animals in some of the groups were reduced, apparently as a result of cadmium toxicity. Since the multistage model does not take into account reduced lifespans, this model was only fit to data from groups in which exposures lasted for at least 14 months (reduced survival appeared to be less of a problem in such groups.) With this method of fitting, the multistage model gave an acceptable fit (based on a chi-square goodness-of-fit test) to all of the data sets.

The Armitage-Doll and multistage-Weibull models were fit to all of the data on each cadmium compound. However, if these models did not adequately fit the data, data at the highest dose level was removed from the model fit. Data related to the highest dose level may be the least relevant to dose response modelling when there is a response at lower dose levels because of high or similar tumor responses at lower dose levels, reduced survival, or the possibility of altered metabolism including saturation of major or primary metabolic pathways at the highest dose levels. Removing data from the highest dose level resulted in reducing the number of dose groups for male rats exposed to CdO dust and for both male and female rats exposed to CdS when applying the multistage-Weibull model. However, the Armitage-Doll model gave an adequate fit to all of the data sets without any dose groups omitted.

The Armitage-Doll model makes use of the exact time-varying pattern of exposure. The dose of cadmium (in units of μg/kg/day) applied to this model during a period in which exposure was occurring was calculated as

$$DOSE = CC * IR * FD / W,$$

where

CC [μg/m³] = airborne cadmium concentration;
IR [m³/day] = volume of air inhaled per day (assumed to be 0.254 m³/day for male rats and 0.223 m³/day for female rats);
FD = fraction of day exposed;
W [kg] = average weight of rats at 18 months (assumed to be 0.43 kg for males and 0.35 kg for females).

A dose of zero was applied during a period in which the animals were not exposed.

The multistage and multistage-Weibull models require that a single summary dose be applied that represents the average daily dose, including periods in which animals were not exposed. This adjusted dose was calculated from the unadjusted dose as follows:

$$ADJDOSE = DOSE * ME / MO,$$

where

ME = number of months rats were exposed;
MO = number of months rats were observed (estimated as the number of days on test of the last rat to die in an experiment).

To estimate human risk from these models, a human exposure is calculated in units of μg/kg/day and applied to the dose response model estimated from the animal data. Human exposures were assumed to be occupational and to last from age 20 to age 65. For the Armitage-Doll model, the corresponding exposure period, expressed in terms of the life of a rat, was from [20/74*MO] to [65/74*MO] days, where MO is defined above. The average daily dose (in units of μg/kg/day) during the exposure period was calculated as

$$ADD = HCC * HIR / HW * [DW / 365],$$

where

HCC [μg/m³] = assumed human airborne cadmium concentration;
HIR = volume of air inhaled per 8 hour shift (assumed to be 10 m³/day);
HW [kg] = human body weight (assumed to be 70 kg);
DW = days worker per year (assumed to be 250).

To calculate the corresponding average daily human exposure, averaged over the entire lifespan, which is required to estimate human risk from the multistage

and multistage-Weibull models, ADD was adjusted as follows:

ADJADD=ADD*45/74,

where 45 is the number of years of work and 74 is the assumed human lifespan.

Table VI–6 contains the results of applying these three models to ten data sets from the Takenaka et al. and Oldiges et al. studies involving male or female rats exposed to five different types of cadmium. This table presents estimates of excess lung cancer deaths per 1000 workers having 45 years of occupational exposure to TWA cadmium exposures of 1, 5, 10, or 100 $\mu g/m^3$. Upper and lower 95% confidence limits for the expected number of excess deaths are presented for the multistage model, but only upper 95% confidence limits are presented for the other two models because of the lack of a computer program to calculate lower limits for these models.

TABLE VI–6.—ESTIMATES DERIVED FROM ANIMAL DATA OF EXCESS CANCER DEATHS PER 1000 WORKERS WITH 45 YEARS OF OCCUPATIONAL EXPOSURE TO CADMIUM

Reference	Type exposure	Sex	Multistage model			Armitage-Doll model		Multistage-Weibull Model	
			MLE*	95% upper bound	95% lower bound	MLE	95% upper bound	MLE	95% upper bound
Exposure to TWA of 1 $\mu g/m^3$									
Oldiges *et al.*	CdCl2	Male	5.7	8.9	3.4	7.3	10	0.046	16
Takenaka *et al.*	CdCl2	Male	3.0	5.1	0.78				
Oldiges *et al.*	CdO-Dust	Male	5.0	7.0	3.5	12	17	4.4	6.2
Oldiges *et al.*	CdO-Fume	Male	0.0025	0.66	0.00079	0.068	0.16	0.0037	1.2
Oldiges *et al.*	CdS	Male	1.1	1.5	0.74	4.0	5.3	1.1	1.5
Oldiges *et al.*	CdSO4	Male	1.5	2.6	0.83	0.50	0.90	5.3	11
Oldiges *et al.*	CdCl2	Female	3.7	6.2	2.0	4.7	7.4	5.7	10
Oldiges *et al.*	CdO-Dust	Female	4.9	7.7	2.9	13	18	4.9	7.3
Oldiges *et al.*	CdS	Female	1.4	1.9	0.95	4.9	6.5	1.5	2.2
Oldiges *et al.*	CdSO4	Female	2.0	3.1	1.2	11	19	7.2	20
Exposure to TWA of 5 $\mu g/m^3$									
Oldiges *et al.*	CdCl2	Male	28	44	17	36	51	1.2	76
Takenaka *et al.*	CdCl2	Male	15	25	4.3				
Oldiges *et al.*	CdO-Dust	Male	25	35	17	61	81	22	31
Oldiges *et al.*	CdO-Fume	Male	0.061	3.3	0.020	0.34	0.78	0.095	6.0
Oldiges *et al.*	CdS	Male	5.5	7.6	3.7	20	26	5.5	7.6
Oldiges *et al.*	CdSO4	Male	7.6	13	4.2	2.5	4.5	26	54
Oldiges *et al.*	CdCl2	Female	18	31	10	23	36	28	49
Oldiges *et al.*	CdO-Dust	Female	24	38	14	63	87	24	36
Oldiges *et al.*	CdS	Female	6.6	9.5	4.7	24	32	7.4	11
Oldiges *et al.*	CdSO4	Female	10	16	6.1	55	80	35	94
Exposure to TWA of 10 $\mu g/m^3$									
Oldiges *et al.*	CdCl2	Male	55	85	33	71	100	4.7	146
Takenaka *et al.*	CdCl2	Male	30	49	9.3				
Oldiges *et al.*	CdO-Dust	Male	49	68	34	117	155	43	61
Oldiges *et al.*	CdO-Fume	Male	0.25	6.6	0.079	0.68	1.6	0.38	12
Oldiges *et al.*	CdS	Male	11	15	7.4	40	52	11	15
Oldiges *et al.*	CdSO4	Male	15	25	8.3	5.0	9.0	51	105
Oldiges *et al.*	CdCl2	Female	36	60	20	46	71	56	96
Oldiges *et al.*	CdO-Dust	Female	48	76	29	121	166	48	71
Oldiges *et al.*	CdS	Female	14	19	9.6	48	63	15	22
Oldiges *et al.*	CdSO4	Female	20	31	12	108	171	69	179
Exposure to TWA of 100 $\mu g/m^3$									
Oldiges *et al.*	CdCl2	Male	433	589	289	521	650	374	793
Takenaka *et al.*	CdCl2	Male	302	398	211				
Oldiges *et al.*	CdO-Dust	Male	396	507	293	713	813	357	465
Oldiges *et al.*	CdO-Fume	Male	24	64	7.9	6.8	15	37	113
Oldiges *et al.*	CdS	Male	104	142	72	333	412	104	141
Oldiges *et al.*	CdSO4	Male	142	226	60	49	87	409	669
Oldiges *et al.*	CdCl2	Female	310	463	182	376	523	436	634
Oldiges *et al.*	CdO-Dust	Female	388	541	251	726	838	388	521
Oldiges *et al.*	CdS	Female	128	173	91	386	478	138	197
Oldiges *et al.*	CdSO4	Female	183	269	116	681	847	512	862

*MLE = Maximum likelihood estimate.

The maximum likelihood estimates (MLEs) based on the Takenaka et al. (Ex. 4–67) from OSHA's reassessment are slightly different than the estimates reported in the proposed rule. The estimates of excess cancer risk based on the Takenaka et al. data were 10.6 per 1,000 workers following 45 years of occupational exposure to 5 $\mu g/m^3$ in the proposed rule, but in the new assessment, this risk has changed slightly to 15 per 1,000 workers. This difference is due to a change in the method used to convert the animal dose in $\mu g/m^3$ to $\mu g/kg/day$ in the Takenaka et al. rat bioassay. In the proposed rule, it was assumed that the average survival for the animals in the study was two years; therefore, rats were exposed 23 hours/day for 75% of their lifespan (18 months). To adjust the experimental dose for less than lifetime exposure, the experimental dose was multiplied by 0.75 to produce an equivalent lifetime

dose. However, in the Takenaka et al. study, animals were observed for up to 31 months, with 50% of the animals in the control group surviving 30 months. Normally, to adjust for less than lifetime exposure, the average daily exposure is prorated over the lifetime of the animal (51 FR 33992; Sept. 24, 1986). This is done by taking a ratio of the number of months an animal is exposed to the number of months in the lifespan of the animal. For the Takenaka et al. study the lifespan is assumed to be 31 months. Therefore, in the reassessment based on this study a factor of 18 months/31 months (58%) rather than 18 months/24 months (75%) was used, resulting in slightly different estimates of dose and of risk.

The multistage model and Armitage-Doll models gave an acceptable fit to all of the data sets (e.g., $p > 0.05$, based on a chi-square goodness-of-fit test). (However, recall that the multistage model was only fit to data in which exposures lasted 14 months or longer, whereas the other two models were fit to all of the data.) The multistage-Weibull model also gave an acceptable fit to all of the data sets; however, to achieve an acceptable fit with this model, the data from the highest dose was deleted in the analyses involving exposure of males and females to CdS and exposure of males to CdO dust. (Also, in the multistage model to the data on exposure of male rats to CdO dust, the average exposures in the two experimental groups differed by only about 5%, and these two groups were therefore combined into a single exposure group for model fitting.)

The estimates of excess risk obtained from these models were consistently lower based on exposure to CdO fume than to other forms of cadmium. Dr. Oberdörster also noted the lower response of lung tumors in the Oldiges et al. study after exposure to CdO fume and concluded that this observation could most likely be explained by a lower lung burden of cadmium that resulted from a lower deposition fraction of the inhaled fume particles (Ex. 31). Estimates of risk resulting from other types of exposure agree much more closely. With the exception of CdO fume exposures, the ranges of estimates for the excess lung cancer risk from 45 years of occupational exposure to 5 $\mu g/m^3$ lifetime are as follows: multistage model, 5.5–28 excess deaths per 1000 workers; Armitage-Doll model, 2.5–63 excess deaths per 1000 workers; multistage-Weibull model, 1.2–35 excess deaths per 1000 workers. If exposure is to a TWA of 100 $\mu g/m^3$, the corresponding ranges are: Multistage model, 104–433 excess deaths per 1000 workers; Armitage-Doll model, 49–726 excess deaths per 1000 workers; multistage-Weibull model, 104–512 excess deaths per 1000 workers.

Discussion of Issues Related to the Risk Assessment for Lung Cancer Using Animal Data

Weight-of-Evidence Provided by the Takenaka Study

A weight-of-evidence evaluation is the first step in determining the likelihood that a chemical is a human carcinogen. According to EPA's methodology, the evidence is characterized separately for human studies and animal studies as sufficient, limited, inadequate, no data, or evidence of no effect. The characterizations of the animal and human data are combined, and based on the extent to which the chemical has been shown to be a carcinogen, the chemical is given a provisional weight-of-evidence classification. This classification can then be adjusted up or down based on other supporting evidence such as mutagenicity data (USEPA, 1989).

In EPA's Guidelines for Carcinogen Risk Assessment (51 FR 33992; Sept. 24, 1986), it is stated:

> The weight of evidence that an agent is potentially carcinogenic for humans increases (1) with the increase in number of tissue sites affected by the agent; (2) with the increase in number of animal species, strains, sexes, and number of experiments and doses showing a carcinogenic response; (3) with the occurrence of clear-cut dose-response relationships as well as a high level of statistical significance of the increased tumor incidence in treated compared to control groups; (4) when there is a dose-related shortening of the time-to-tumor occurrence or time to death from tumor; and (5) when there is a dose-related increase in the proportion of tumors that are malignant.

OSHA believes that these guidelines for a weight-of-evidence are not meant to be used in a pass-fail approach, since EPA refers to increases in the weight of evidence. Thus, all five conditions or a majority of conditions need not be satisfied for a chemical to be considered carcinogenic. Most especially all five do not have to be satisfied in any single study. Rather, these guidelines, and other sets of evaluation criteria, such as the EPA or IARC classification schemes, are meant to apply in a weight-of-evidence evaluation using the overall experimental and epidemiological data.

When the data base for cadmium is evaluated, the overall weight-of-evidence for the carcinogenicity in animals is strong, based on the above mentioned conditions. Statistically significant increases in the incidence of lung tumors were noted in male rats (Ex. 4–67, 8–694D) and female rats (Ex. 8–694D), exposed to cadmium compounds by the inhalation route, and when an adjustment for survival was made by life-table analysis a significant increase in lung tumors was also observed in female mice (Ex. L–140–29F) (see discussion below). Significant increases were noted in mammary fibroadenomas in rats given cadmium intratracheal instillation (Sanders and Mahaffey, Ex. 4–61) and in sarcomas (injection site) in rats injected with cadmium (Levy et al., Ex. 8–194; Kazantis, Ex. 8–576; Haddow et al., Ex. 4–34; Health et al., Ex. 8–117). In the Takenaka et al. and Oldiges et al. studies, statistically significant dose-response relationships were evident, and the proportion of malignant tumors increased and the latency time decreased with increased dose. (The controls did not have any lung tumors in either the Takenaka et al. or Oldiges et al. studies.)

The National Toxicology Program (NTP) (1984) in its Guidelines on Chemical Carcinogenesis Testing and Evaluation, has reported:

> Clear Evidence of Carcinogenicity is demonstrated in studies that are interpreted as showing a chemically related increased incidence of malignant neoplasms, studies that exhibit a substantially increased incidence of benign neoplasms, or studies that exhibit an increased incidence of a combination of malignant and benign neoplasms where each increases with dose.

Based on NTP's definition of clear evidence of carcinogenicity, the Takenaka et al. and Oldiges et al. studies provide clear evidence of the carcinogenicity of cadmium in animals.

Evidence of Carcinogenicity of Cadmium in Other Species

Cadmium, when administered by intratracheal instillation or injection, produced statistically significant increases in certain tumors but not lung tumors (Exs. 4–34, 8–576, and 8–117). Cadmium when given by the oral route, either in drinking water (Exs. 8–308, 8–121, 8–196), by gastric instillation (Levy et al., Exs. 8–034, 8–117), or in the diet (Loser, Ex. 8–643) did not produce an increase in either the total number of tumors or an increase in any specific type of tumor. The data show that cadmium, which is carcinogenic by the inhalation route in rats, has not been demonstrated to be carcinogenic by the oral route. This is consistent with the route-specific patterns for other heavy metals, such as chromium or nickel, that are established human carcinogens by the inhalation route but not by the oral route. However, lung tumors in workers

occupationally exposed by the inhalation route is the major concern. Therefore, for the proposed rule, the inhalation studies are the most relevant when assessing the risk due to cadmium exposure.

According to the Risk Assessment Guidelines published by the Office of Science and Technology Policy (OSTP, 1985), negative data as well as positive data should be considered in a weight of evidence determination of the carcinogenicity of a compound. As importantly, the selection of data for analysis should maximize any correlations between animals and humans with regard to pharmacokinetic considerations and mechanism of action. Inhalation studies have been conducted in male and female rats, mice, and hamsters. The studies in rats have convincingly demonstrated inhalation exposure to cadmium results in the production of lung tumors. The study in mice was less convincing, while that conducted in hamsters was labelled as negative by some. However, the mouse and hamster studies conducted by Heinrich et al. (Ex. L-140-29F) had several limitations.

In the mouse study, many of the animals were treated for a short duration of time with treatment duration ranging from 6 to 69 weeks. Survival problems were also reported in treated animals versus controls. Nine out of fourteen of the cadmium oxide exposed groups had significant shortening of mean survival time, based on life-table analysis. This shortening of lifespan was attributed to toxic effects in the respiratory tract. Of the remaining five treatment groups, three had significantly increased incidences of lung tumors. Due to the shortened survival of many of the treated mice, animals may not have survived long enough for some tumors to be observed. When a life-table analysis was conducted, which adjusts for survival, the probability of an animal dying with a lung tumor was statistically significantly greater in treated groups versus controls in most of the CdO treated groups and one of the CdS groups (90 $\mu g/m^3$). No information was reported concerning the time to first tumor or the type of lung tumors observed. Therefore, the latency period for tumor development in mice following exposure to cadmium cannot be determined.

As in the mouse study, exposure of hamsters to cadmium compounds were for short durations, ranging from 13 to 65 weeks. Shortened survival was also observed in some treated groups resulting from toxic effects to the respiratory tract. Survival problems may have precluded the development of lung tumors. However, dose-dependent statistically significant increases in the incidence of bronchiolaralveolar hyperplasia and proliferation of connective tissue, which are considered preneoplastic lesions and may indicate progression to cancer, were found with all cadmium compounds tested. Heinrich et al. reported that a few of the animals developed respiratory tract tumors; however, no tumor incidence data were reported. Although the results appear to indicate a progression to carcinogenicity, no definitive conclusions can be drawn as to the carcinogenicity of cadmium in hamsters.

These studies conducted by Heinrich et al. (Ex. L-140-29F) should not be considered as negative. Histopathological changes in the respiratory tract of hamsters, as well as the observation of some lung tumors, indicate the progression to possible carcinogenic effects. In mice, cadmium compounds appeared to be carcinogenic when adjustments were made for decreased survival. Despite the flaws in the Heinrich et al. study, this study provides some evidence of the carcinogenic potential of cadmium in species other than rats. Therefore, when all of the data are considered in a weight-of-evidence evaluation, the conclusions remain unchanged as to the relevance of the Takenaka data for use in risk assessment, and the potential carcinogenicity of cadmium in the occupational setting.

Continuous Exposure in Animal Studies Versus Intermittent in Occupational Settings

When actual exposure situations of concern differ from continuous, constant lifetime exposure, the EPA's Guidelines for Carcinogen Risk Assessment (51 FR 33992; Sept. 24, 1986) recommend that unless there is evidence to the contrary, the appropriate measure of exposure is the total or cumulative dose of the chemical of concern averaged or prorated over a lifetime, resulting in an average lifetime daily exposure. This assumes that a high dose of a carcinogen received over a short period of time is equivalent to a corresponding low dose averaged over a lifetime in terms of extra cancer risk. The supporting rationale for this relies on the underlying assumptions of the carcinogenic process: Risk is linearly related to dose, particularly in the low-dose region (51 FR 33992, Sept. 24, 1986; 50 FR 10372, Mar. 14, 1985; NAS, 1983). Currently when conducting a risk assessment, the total amount of chemical exposure (intake or dose) resulting from less-than-lifetime or intermittent exposure patterns is adjusted (prorated) over the expected lifetime of the individual. The result is an average lifetime daily exposure that corresponds to the same cumulative or total amount of chemical.

The Guidelines state that as the exposures in question become more intense but less frequent, this approach becomes problematic, especially when the agent has demonstrated dose-rate effects. Dose-rate effects are defined as a different degree or type of response that may occur with different dose patterns even when the total dose is the same for these dosing patterns.

Criticisms have arisen that the continuous exposures of animals to cadmium in Takenaka et al. (Ex. 4-67) (23 hours/day; 7 days/week) do not reflect occupational exposures of humans to cadmium (8 hours/day; 5 days/week). However, the available pharmacokinetic information for cadmium does not provide supporting evidence that dose-rate effects would be observed following intermittent versus continuous exposure to cadmium. Cadmium has a long retention time in the rat lung of 60-80 days and it is ten times longer in the human lung; therefore, although exposure in the workplace may be intermittent, cadmium remains in the lung during periods when exposure is discontinued, such as at the end of an 8-hour shift or over a two day weekend (Ex. 31).

Animal studies conducted by Glaser et al. (Ex. 8-694B) also provide evidence that dose-rate effects may not be an issue with cadmium. To evaluate this, the cancer potency estimated from results in rats exposed continuously was compared to that estimated from rats exposed using an intermittent pattern to simulate a work week. In this study, one group of male rats was exposed to 30 $\mu g/m^3$ CdO dust for 22 hours/day, 7 days/week for 18 months, followed by 13 months of observation; another group was exposed to 90 $\mu g/m^3$ CdO dust for 40 hours/week for 6 months, followed by 24 months of observation. The doses, expressed as an average daily intake, were approximately 9.9 $\mu g/kg/day$ for the male rats exposed to 30 $\mu g/m^3$ for 18 months and 2.7 $\mu g/kg/day$ for male rats exposed to 90 $\mu g/m^3$ for 6 months. The doses were prorated using the following equation:

$$\mu g/m^3 \times \frac{0.254\ m^3/day}{0.43\ kg\ body\ weight} \times \frac{number\ of\ hours\ per\ week\ exposed}{160\ hours/week} \times \frac{number\ of\ months\ exposed}{total\ months\ on\ study}$$

The incidence of lung tumors in these two groups was 28/39 for the 30 $\mu g/m^3$ group and 4/20 for the 90 $\mu g/m^3$ group. No lung tumors were reported in controls.

When these two data sets were evaluated using the multistage model, the potency factors obtained for these two data sets were similar, with 0.176 $(\mu g/kg/day)^{-1}$ obtained for the 30 $\mu g/m^3$ data set and 0.170 $(\mu g/kg/day)^{-1}$ obtained for the 90 $\mu g/m^3$ data set. If a dose-rate effect existed, i.e., if longer, continuous exposure resulted in higher estimates of risk, then the potency factors for these two data sets would be different rather than comparable. Therefore, the empirical data reported by Glaser et al. (Ex. 8-694B) do not show evidence of a dose rate effect for the lung carcinogenicity of cadmium.

Extrapolation From the Animals to Humans

Dr. Oberdorster has recommended that for the extrapolation of results of animal studies to humans, OSHA should use a lung dosimetric approach, rather than equivalency based on body weight. A lung dosimetric approach assumes that equal accumulated doses of cadmium per gram of lung tissues have the same carcinogenic potential in the peripheral lung of the rat and the human. Using a lung dosimetry methodology, the dose delivered to the lung can be expressed based on lung specific parameters, such as lung weight or lung airway surface area, rather than on body weight or body surface area.

Because the histopathology is not available to identify a specific cell line or area of the lung from which the tumors resulting from cadmium exposure arise in humans, if lung dosimetry is to be used, with surface area of the lung as a lung specific parameter, the total surface area of the lung must be used. If the histopathology were available to identify these areas, ideally the surface area of a specific region of the lung would be used.

Dr. Oberdorster compared the body weight equivalency approach used by OSHA and other regulatory agencies and the lung dosimetric approach and it appears that these two approaches give very similar risk estimates for cadmium. He concluded that the similarity in risk assessment in the case of cadmium is coincidental and does not mean that the choice of a dosimetric method is unimportant. However, it has recently been determined that total lung surface area, which would have to be used in this case, scales allometrically as body weight raised to the 0.66 power ($BW^{0.66}$) (USEPA, 1991). Therefore, the body weight equivalency method used by OSHA would be a close approximation of the lung dosimetric method, based on total surface area of the lung, and the similarity in the risk estimates derived by Dr. Oberdorster may not be a coincidence.

Regulation of Cadmium Sulfide

Several commenters (Exs. 31; 144-20; 19-42b) recommended that a higher occupational standard should be developed for cadmium sulfide (CdS) than OSHA's proposed standards of 1 or 5 $\mu g/m^3$ based primarily on the difference in solubility between CdS and $CdCl_2$ or CdO. To consider the validity of distinguishing CdS from other cadmium compounds several factors must be considered. There is sufficient evidence in animals for the carcinogenicity of cadmium. Studies conducted by Glaser et al. (Ex. 8-694B) and Oldiges et al. (Ex. 8-694D) appear to provide evidence that CdS is carcinogenic to animals exposed by the inhalation route. However, SCM Chemicals (Ex. 19-42b) suggested that the carcinogenic response observed in Glaser et al. (Ex. 8-694B) may be a result of exposure to $CdSO_4$ formed during the preparation of CdS. Two studies investigated the aerosol preparation technique of CdS used in the Glaser et al. (Ex. 694B) inhalation study (Glaser et al., 1991; Konig et al. 1991, refs. in Ex. 141). Both studies demonstrated that under the preparation technique used CdS may be solubilized under the influence of light and that, at low aerosol concentrations equivalent to 90 $\mu g/m^3$, 50% to 63% of the CdS solubilized. This indicates that the aerosol to which the rats were exposed contained both CdS and the more soluble $CdSO_4$. If it is assumed that only the more soluble $CdSO_4$ contributed to the carcinogenicity observed, then in the study by Glaser et al. (Ex. 8-694B), it would be expected that the tumor incidence of the CdS/$CdSO_4$ exposed rats to be approximately half that for the rats exposed to $CdSO_4$ since approximately 50% of the inhaled Cd was in the form of $CdSO_4$ (Ex. 142). However the tumor response in animals exposed to 90 $\mu g/m^3$ CdS was greater than 50% of that in animals exposed to 90 $\mu g/m^3$ $CdSO_4$, and in fact, the response was comparable in animals exposed to the two compounds. In males the lung tumor incidence among CdS exposed rats was 17/20 and only 11/20 among $CdSO_4$ exposed rats (although the CdS group was exposed for 18 months versus 14 months for the $CdSO_4$ group). In females the incidence was 15/20 in the CdS group and 18/20 in the $CdSO_4$ group. Thus, even if it is assumed that the 50% of the CdS had been converted to $CdSO_4$, these data suggest that the carcinogenic response was not due to the $CdSO_4$ alone and the data are, in fact, consistent with the CdS being just as potent a carcinogen as $CdSO_4$.

Intratracheal instillation studies provide further support that CdS is carcinogenic. Intratracheal instillation studies conducted by Pott et al. (Ex. 8-757) were aimed at investigating the pulmonary carcinogenicity of different cadmium compounds, including CdS. A statistically significant increase in the incidence of lung tumors was observed in rats exposed to 10 weekly instillations of 250 μg cadmium via CdS. Although it is possible that a small portion of the CdS could have dissociated, based on information from Konig et al. (Ex. L-140 27b), this could only have resulted in the formation of approximately 3% $CdSO_4$ from CdS in the group administered 250 μg cadmium. Therefore, the formation of $CdSO_4$ cannot account for the excess tumors observed following exposure to CdS. According to Oberdörster (Ex. 141) and Heinrich (Ex. 142) the results of the instillation study along with the inhalation study indicate that CdS is a pulmonary carcinogen; however, inhaled CdS may have a lower potency than other cadmium compounds.

If, as is generally assumed, only the solubilized Cd ion is responsible for the observed carcinogenicity, the potential carcinogenicity of any cadmium compound theoretically should be related to the cumulative amount of cadmium ion released in close proximity to target lung cells, averaged over a specific period of time. The release of cadmium is governed by the rate of

dissolution of the cadmium ion from the cadmium compound, the biological halftime in the lung, and the mechanism of clearance from the lung. These are interdependent and each contributes to the estimate of lung burden. Since lung dosimetry is extremely complex, the relative solubility of CdS compared to that of CdO or $CdCl_2$ is only one of the determining factors. While the dissolution rate of the Cd ion from CdS or other cadmium compound may be a function of that specific compound in a physiological environment, biological half-time and mechanism of clearance are dependent on a number of factors that include the nature of the inhaled material, i.e., gas, vapor, aerosol, particle; the characteristics of the respiratory tract; and breathing pattern. The mechanism of clearance is directly related to the deposition within the respiratory tract, which is a function of the particle size. In the upper respiratory tract, clearance by the mucociliary escalator is operative, while in the lower part of the respiratory tract or in the alveoli, clearance can occur by dissolution and direct uptake by macrophages, which are also cleared by the mucociliary escalator. Biological half-time is influenced by the competence and efficiency of these clearance processes. Removal of particles from the lung by mucociliary action, rather than by dissolution and diffusion, may allow for a longer retention time. However, any cytotoxicity that slows ciliary movement or creates an overburden on macrophage capability would increase that retention time, thus allowing for more dissolution and formation of the free cadmium ion, resulting in a higher carcinogenic potency than may be expected based on solubility alone. This would also be of concern because the biological halftime of particles with low solubility is about ten time longer in the human lung than in the rat lung (Ex. 142).

To differentiate risk associated with CdS from that for other cadmium compounds is not feasible at this time. In the workplace, exposure typically does not occur to CdS alone, but rather to a mixture of cadmium compounds. CdS appears to have carcinogen potential, and the contribution to risk from CdS would be additive to that of the other cadmium compounds (Ex. 142). Factors other than the solubility of CdS affect the retention in the lung, and hence the availability of cadmium ions. Factors in the work place that influence lung dosimetry, such as the size of cadmium particles or the total lung burden from all particulates, may also be important. A better understanding of the molecular and cellular mechanisms of cadmium carcinogenicity is required to determine if the carcinogenic potential of CdS is different from that of other cadmium compounds (Ex. 142).

Assessment of Lung Cancer Risk Using Human Data

The Risk Assessment by NIOSH (Stayner et al., Ex. L–140–20)

Since the publication of OSHA's proposed rule, Stayner et al. have completed a risk assessment based on the Thun cohort. There are several differences between this risk assessment and the one reported in the proposed rule (Ex. 18). The Stayner et al. risk assessment is based on recent additional followup of the Thun cohort through 1984, whereas the risk assessment reported in the proposed rule was based on followup only through 1978. Stayner et al. had access to the unprocessed data from the Thun cohort and, consequently, was able to conduct a wider range of analyses in their risk assessment than was possible based on just the data reported in the published Thun report (Ex. 4–68).

The cohort studied by Stayner et al. contained 606 white males and was defined the same way as in the earlier study of Thun et al. (Ex. 4–68). As in the earlier study, workers with employment prior to January 1, 1926 were excluded from the analysis in order to minimize the potential for confounding by arsenic exposure.

A life-table analysis was used to study the lung cancer mortality of the cohort. Person-years were accumulated beginning with the time an individual had been employed for six months at the facility or with January 1, 1940, whichever came later. Because Hispanics are reported to have lower lung cancer rates than non-Hispanics, the cohort was separated into Hispanic and non-Hispanic based on surname, and results were reported separately for these two groups; however, U.S. white males were still used as the comparison population for each group. Stayner et al. categorized the person-years in four ways: Cumulative exposure, latency (elapsed years since first exposure), year of observation, and age. Results from this analysis are reported in Table VI–7.

TABLE VI–7.—RESULTS OF LIFE TABLE ANALYSIS OF DATA FROM NIOSH UPDATE THROUGH 1984 OF CADMIUM SMELTER COHORT

Category	Non-Hispanic			Hispanic [a]			Combined		
	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR
Overall	21	9.95	**211	3	6.12	49	24	16.07	149
Exposure: [b]									
<584	1	3.35	29	1	2.38	42	2	5.73	34
585–1460	7	2.64	*265	0	1.64	0	7	4.28	163
1461–2920	6	1.55	*386	0	1.20	0	6	2.75	217
>2921	7	2.41	*290	2	0.90	223	9	3.30	*272
Latency [c] (Years):									
<10	0	0.41	0	1	0.28	363	1	0.69	145
10–19	2	1.41	142	0	1.00	0	2	2.41	83
>20	19	8.13	**233	2	4.84	41	21	12.97	*161
Year:									
1940–1959	2	0.89	225	0	0.38	0	2	1.26	158
1960–1969	5	2.24	223	1	1.27	78	6	3.51	171
1970–1979	10	4.43	*226	2	2.89	69	12	7.30	164
>1980	4	2.39	167	0	1.59	0	4	3.98	101
Age (Years):									
<50	0	0.78	0	1	0.50	201	1	1.28	78
50–54	2	1.01	198	0	0.67	0	2	1.68	118
55–59	1	1.61	62	2	1.00	200	3	2.60	115
60–64	5	2.20	227	0	1.20	0	5	3.40	146
65–69	4	2.12	188	0	1.13	0	4	3.25	123

TABLE VI-7.—RESULTS OF LIFE TABLE ANALYSIS OF DATA FROM NIOSH UPDATE THROUGH 1984 OF CADMIUM SMELTER COHORT

Category	Non-Hispanic			Hispanic [a]			Combined		
	OBS	EXP	SMR	OBS	EXP	SMR	OBS	EXP	SMR
70–74	5	1.37	*366	0	0.84	0	5	2.20	227
>75	4	0.87	*547	0	0.79	0	4	1.66	241

[a] U.S. rates for white males were used as the referent group for hispanic and non-hispanic males in this analysis.
[b] Milligrams cadmium per cubic meter of air-days.
[c] Time since first exposure.
* $p < 0.05$ (two-tails).
** $p < 0.01$ (two-tails).

Overall, there was an excess of lung cancer (OBS=24; EXP=16.07; SMR=149) that is statistically significant (p=0.035) by a one-tailed test for higher lung cancer rates in the cohort. Moreover, there is a clear dose-response trend of higher SMRs for lung cancer in groups with higher cumulative cadmium exposures. Lung cancer was significantly elevated among non-Hispanics [SMR=221, 95% Confidence Intervals (CI)=131, 323], but reduced among Hispanics (SMR=49, 95% CI=10, 143). This latter finding is consistent with the fact that Hispanics are reported to have lower lung cancer rates in general than non-Hispanics (Ex. 33) and that reference rates used were for U.S. white males.

There is a deficit in lung cancer deaths in the lowest exposure group [584 mg-days/m^3) relative to the control population, among both non-Hispanics (OBS=1, EXP=3.35) and Hispanics (OBS=1, EXP=2.38). However, neither of these deficits is statistically significant (p=0.15 among non-Hispanics and p=0.31 among Hispanics, one-tailed tests). Neither is the deficit statistically significant in the combined cohort (OBS=2, EXP=5.73, p=0.075) despite the fact that a deficit among Hispanics is expected because control rates were for white males. Thus, these deficits are not inconsistent with ordinary random fluctuation.

Excesses of lung cancer are observed in the remaining three exposure groups for both non-Hispanic and combined Hispanic and non-Hispanic. These excesses are statistically significant (using U.S. white males as the referent population) in all three groups for non-Hispanics and in the highest exposure group for combined Hispanics and non-Hispanics.

When person-years are categorized according to latency, significant responses occur only in the group with a latency of ±20 years, which is consistent with the latency of other agents that cause lung cancer. Table VI-7 also indicates that the excess of lung cancer was greatest among older members of the cohort (>70 years of age).

Stayner et al. used both Poisson regression and Cox regression to model the relationship between cumulative cadmium exposure and risk. Both Poisson regression and Cox regression involve a regression model that expresses the lung cancer rate per person-year (i.e., per person per year) in the cohort in terms of various potential explanatory variables for lung cancer such as age, calendar year, and cadmium exposure.

In Poisson regression, the person-years of observation are categorized according to values of the explanatory variables. The model is fit to the data using the assumption that the number of observed cases in each cell determined by the categorization has approximately a Poisson distribution with expected value equal to the number of cases predicted by the regression model. Poisson regression can either utilize background lung cancer rates from an external control population in defining the regression model, or else can estimate all of the parameters necessary to define the lung cancer rate directly from the cohort data without resort to an external control population. OSHA used Poisson regression of the former type in its risk assessment that was presented in the proposed rule (Ex. 18), whereas Stayner et al. utilized Poisson regression of the latter type. In addition to a measure of prior cadmium exposure, Stayner et al. included age, calendar year, and Hispanic ethnicity as covariates (explanatory variables) in the Poisson regression analyses.

Stayner et al. utilized the following functional forms for the lung cancer mortality rate per person-year in Poisson regression analyses:

Exponential (log-linear):
$h = \exp(\alpha + E_j(\Theta_j W_j) + \Gamma\chi + \delta Y + \beta X)$
Linear:
$h = \alpha + E_j(\Theta_j W_j) + \Gamma\chi + \delta Y + \beta$
Power:
$h = \exp(\alpha + E_j(\Theta_j W_j) + \Gamma\chi + \delta Y) * ([X+1]^{\beta})$
Additive relative rate:
$h = \exp(\alpha + E_j(\Theta_j W_j) + \Gamma\chi + \delta Y) * [1 + \beta X]$
where
h is the lung cancer mortality rate per person-year hazard rate,
α is the intercept,
W_j represents the calendar-year groups (W_j is a category variable that equals 1 if the observation is from the j-th calendar year group and equals 0 otherwise)
Θ_j is the regression coefficient for the j-th calendar-year group,
$E(\Theta_j W_j)$ represents the effect of the calendar-year group
[$E_j(\Theta_j W_j) = \Theta_j$, where j is the particular calendar year group associated with the observation]
χ represents Hispanic ethnicity ($1\chi = 1$ if the observation is from a person of Hispanic ethnicity and zero otherwise)
Γ is the regression coefficient for Hispanic ethnicity,
Y is age,
δ is the regression coefficient for age,
X is a measure of prior cadmium exposure,
β is the regression coefficient for cadmium exposure.

Each of these functional forms, except the linear form, was also fit using Cox regression. Both cumulative exposure and cumulative exposure lagged 5 years were used as the measure of exposure in the Poisson regression analyses.

Stayner et al. utilized the following functional forms for the lung cancer mortality rate per person-year in Cox regression analyses:

Exponential (log-linear):
$h = h_o(t) * \exp(E_j(\Theta_j W_j) + \Gamma\chi + \beta X)$
Power:
$h = h_o(t) * \exp(E_j(\Theta_j W_j) + \Gamma\chi) * ([X+1]^{\beta})$
Additive relative rate:
$h = h_o(t) * \exp(E_j(\Theta_j W_j) + \Gamma\chi) * [1 + \beta X]$
where
t is age,
$h_o(t)$ is a base-line mortality rate.

Otherwise, the variables have the same meanings as in the Poisson regression models.

In Cox regression the baseline mortality rate, $h_o(t)$, is not estimated, but is left unspecified. Consequently, the method can only estimate the mortality rate relative to this baseline rate. Since the linear model applied in Poisson regression cannot be represented as the product of a baseline mortality rate and a function of the explanatory variables (as is required in Cox regression) no counterpart to this model could be applied in Cox regression. Cox regression does not involve

categorization and grouping of data into cells, as is required in Poisson regression. Stayner et al. applied several measures of prior cadmium exposure in the Poisson regression analyses: cumulative cadmium exposure (i.e., the integral of cadmium exposure over time, expressed in units of mg-days/m^3) and measures formed by "lagging" cumulative exposures by 5, 10, 15, or 20 years. In the lagged analyses, the exposure variable was cumulative exposure achieved up to 5, 10, 15, or 20 years prior to the observation time. This technique was used to discount the most recent exposures that may be etiologically irrelevant to cancer risk because of an apparent minimum delay between exposure and the effect of that exposure upon cancer risk for many chemical carcinogens. Stayner et al. found that lagging exposures 5 years slightly increased the magnitude of the cadmium parameter exposure estimates in the Poisson regression analyses, which is to be expected since the lagged exposure variables are smaller than the unlagged variables. However, lagging the exposures for 10, 15, or 20 years reduced the magnitude of the exposure parameters. This means that the association between lung cancer and cadmium exposure was reduced if exposures were lagged more than 5 years. Stayner et al. consequently concluded that 5 years was the most appropriate lag period. Only results derived from analyses involving a 5-year lag will be discussed further.

The results of the Poisson regression analyses involving cumulative cadmium exposures lagged 5 years are summarized in Table VI–8. Table VI–8 indicates that the deviance associated with the linear model was much larger than that associated with the remaining three models fit by Poisson regression. This means that the linear model fit the data much more poorly than the other models that were applied to the data using Poisson regression. (The deviance differs by a constant from the negative of twice the log-likelihood, and thus, like the log-likelihood, can be used to assess the significance of parameters and assess improvements in fit (BEIR IV, 1988). The power model produced the smallest deviance; however, it predicted unrealistically low background lung cancer rates (e.g., about a factor of 100 lower than that observed for U.S. white males aged 70 during 1970-1979) and for this reason was considered to be inappropriate for assessing risk from cadmium exposure.[1] Of the remaining two models, the additive relative rate (Additive RR) model yielded a better fit (i.e., lower deviance) than the exponential model.

TABLE VI–8.—RESULTS FROM POISSON REGRESSION MODELS AND COX REGRESSION MODEL FITTED TO 5-YEAR LAGGED DATA BY STAYNER ET AL. (EX. L–140–20)

Model	Degrees of freedom	Deviance	Exposure parameter estimate (β) ([μg/years/m^3]$^{-1}$)
Poisson Regression:[a]			
Linear	213	97.71	0.00000008
Exponential	213	82.29	[c] 0.00012
Power function	213	79.28	[d] 0.58
Additive RR	213	80.70	[c] 0.00061
Cox Regression:[b]			
Additive RR			[c] 0.00026

[a] All models include categorical variables to control for calendar year and Hispanic ethnicity, and a continuous variable to control for age.
[b] Model included categorical variables to control for calendar year and Hispanic ethnicity. Age was controlled by matching on survival to the same age.
[c] $p<0.05$.
[d] $p<0.01$.

The same qualitative results were obtained by Stayner et al. using Cox regression. The additive relative rate model fit the data better than the exponential model, but not as well as the power model; however, the power model predicted unrealistically low background lung cancer rates.

Based on these results, Stayner et al. selected the additive relative rate model as the best model to represent the dose response for cadmium and lung cancer. Table VI–8 also contains the results of applying this model using Cox regression.

As indicated in Table VI–8, except for the linear model (which fit the data very poorly), all of the models fit using Poisson regression indicated a statistically significant effect of cadmium exposure upon lung cancer (i.e., the estimate of β, the cadmium exposure parameter, was statistically significantly greater than zero in each of the three analyses.) Similarly, the additive relative rate model fit using Cox regression also indicated a statistically significant effect of cadmium exposure upon lung cancer.

Stayner et al. used the results from the relative rate model to estimate the excess lifetime risk of lung cancer based on the method described by Gail (Ex. 8–561), which was also used by OSHA in the proposed rule (Ex. 18). The formula for the excess lung cancer risk is

Where:

$$\sum_{i=20}^{100} (RR_i - 1)\, q_1(i) \exp\left[- \sum_{j=20}^{i} \{ (RR_j - 1)\, q_1(j) + q_a(j) \} \right]$$

RR_i is the risk ratio for lung cancer predicted by the model based on the exposure scenario assumed,

q_1 is the background age-specific lung cancer mortality rate at age i,

$q_a(i)$ is the background age-specific mortality rate for all causes of death at age i,

and I is the oldest age through which excess risk is accumulated.

For this calculation it was assumed that persons were exposed occupationally to a constant cadmium concentration for 45 years beginning at age 20. The $q_1(i)$ and $q_a(i)$ were based on mortality rates for lung cancer and all causes, respectively, from 1984 for U.S. males (all races). The risk ratio used in the calculation is $RR_i = 1 + \beta X_i$, where β is the lung cancer potency derived from the additive relative rate model obtained either by Poisson regression or Cox regression, and X_i is the measure of exposure associated with age i. For each year, the cadmium exposure is calculated for the midpoint of the year. For example, if cadmium exposure is lagged 5 years and risk is estimated from exposure to an 8-hour time weighted exposure level, Z, beginning at age 20, then $X_i = 0$ for $i < 25$, $X_{25} = 0.5 * Z$, $X_{29} = 4.5 * Z$, and for $i > 70$ (i.e., after age 70) $X_i = 45 * X$.

In their original work, Stayner et al. (Ex. L140–20) accumulated risk through age 74 (i.e., set I=74), which is the same as the approach used by OSHA in the proposed rule. However, in an

[1] If the power model had been used for risk assessment it would have predicted a much higher risk than the other models. Since this model predicts a very low background, it predicts a very large differential in lung cancer mortality between unexposed and exposed. However, when estimating lifetime risk the background lung cancer is estimated from general mortality rates and is hence the same no matter which model is applied. Consequently, the very large differential predicted by the power model would result in a very large risk if used to estimate lifetime risk.

addendum (Ex. L-163), Dr. Stayner noted that accumulating excess risk only through age 74 will result in an underestimate of the cadmium-induced risk of lung cancer because any increased risk that occurs after 75 years of age is not included. Dr. Stayner corrected this oversight in the addendum by accumulating the excess risk up through age 100 (i.e., set I=100), an age that exceeds the vast majority of human lifespans. OSHA believes that this approach provides a better estimate of the total risk from cadmium than truncating the risk calculation at age 74. This approach has been followed in all calculations of risk derived from human data presented herein.[2]

Dr. Stayner also noted that their original estimates (Ex. L-140-20) had been based on respiratory cancer rates rather than rates for lung cancer, and rates for lung cancer only were used in calculations reported in the addendum.

Dr. Stayner also reported in the addendum on the results of extending their analyses to include applying the multistage model of cancer to the data on the Thun et al. cohort with follow up through 1984. The multistage model was proposed for risk assessment by Crump and Howe [1984] and is based on a multistage theory of carcinogenesis that assumes that a single cell line has to go through a number of discrete stages in order to produce a tumor. Dr. Stayner assumed a five-stage model for lung cancer, explaining that "this is the number of stages that has generally been observed in other multistage analyses of lung cancer." He also assumed that cadmium affected one of the five stages. He fit the multistage model to the Thun et al. data varying the stage affected by cadmium and found that the model fit best when it was assumed that cadmium affected the third stage. Dr. Stayner fit the model to the data using a Cox regression approach. He then calculated estimates of excess using the same approach based on Gail's formula that he applied to the results from the additive relative rate model. These estimates were based on a multistage model with five stages with cadmium exposure affecting the third stage.

Table VI-9 presents estimates of the excess risk of lung cancer from 45 years of occupational exposure at various TWA exposures that were reported by Stayner in his addendum. The relative rate model obtained from Cox regression provides estimates of risk that are about twice as large as those obtained from the same model using Poisson regression. The estimates obtained from the multistage model fall in between the estimates derived from the other two approaches. The expected number of excess lung cancer deaths from 45 years of occupational exposure at a TWA of 5 $\mu g/m^3$ cadmium is estimated as being between 3.9 and 9.0 per 1000 workers. If the TWA is 100 $\mu g/m^3$ cadmium, the corresponding number of excess lung cancer deaths is estimated as being between 73 and 157 per 1000 workers.

TABLE VI-9.—ESTIMATES OF EXCESS LUNG CANCER DEATHS PER 1000 WORKERS FROM 45 YEARS OF OCCUPATIONAL EXPOSURE TO CADMIUM OBTAINED BY STAYNER ET AL. BASED ON THE ADDITIVE RELATIVE RATE MODEL APPLIED USING BOTH POISSON REGRESSION AND COX REGRESSION WITH A 5-YEAR LAG FOR CADMIUM EXPOSURE, AND ON THE MULTISTAGE MODEL

Exposure (μgm^3)	Excess deaths (per 1000 workers)		
	Relative Rate Model		
TWA	Poisson regression [a]	Cox regression [b]	Multistage model [c]
1	1.8	0.8	1.1
3	5.4	2.3	3.3
5	9.0	3.9	5.5
7	12.5	5.4	7.7
10	17.8	7.7	11.0
20	35.1	15.3	21.8
40	68.2	30.3	42.9
50	84.1	37.7	53.2
100	157.0	73.0	102.2
200	275.7	137.6	189.1

[a] = 0.00061 (μg-years/m^3)$^{-1}$.
[b] = 0.00026 (μg-years/m^3)$^{-1}$.
[c] The multistage model was fitted assuming five stages. Results presented assume the third stage affected by cadmium exposure, which maximized the likelihood.

Update of OSHA's Risk Assessment Based on the Thun Cohort

OSHA has also updated its risk estimates presented in the Proposed Rule (Ex. 18), based on the additional followup presented in the Stayner et al. risk assessment. OSHA's earlier risk assessment was based on the result of the life-table analysis conducted by Thun et al. (Ex. 4-68) on the followup of the cohort through 1978. The data set studied by Stayner et al. contained the results of additional followup through 1984.

The results of the life-table analysis conducted by Stayner et al. are contained in Table VI-7. The information from this table that will be used to update the risk assessment is contained in the section of the table labeled "EXPOSURE." This information consists of observed and expected numbers of lung cancer deaths in the cohort categorized by cumulative cadmium exposure and by Hispanic versus non-Hispanic. Expected numbers of deaths were calculated based on the mortality experience of U.S. white males.

In its earlier risk assessment OSHA applied both an absolute risk model and a relative risk model to the data from the Thun et al. study. However, the number of person-years in each category in Table VI-7, which is needed for the application of the absolute risk model, was not reported by Stayner et al. Consequently, only the relative risk model will be applied to the update. (It should also be noted that the linear model used by Stayner et al. (Ex. L-140-20), which is similar in functional form to the absolute risk model, provided a poor fit to the data.)

The relative risk model assumes that the lung cancer mortality (hazard) rate at age t is given by

$$h(t) = h_0(t) * (1 + \beta * X) = h_0(t) + [h_0(t) * \beta * X],$$

where $h_0(t)$ represents the hazard rate in the absence of cadmium exposure, X is a measure of cadmium exposure, and β is the slope of the dose response (i.e., β is the carcinogenic potency of cadmium). The measure of cadmium exposure available from the Stayner et al. paper was cumulative exposure, which was the same measure used by OSHA earlier. The specific measure used in the fitting was the median exposures in units of mg/m^3-days derived from the life-table analyses and converted into units of $\mu g/m^3$-years by Stayner et al. by multiplying by 1000 and dividing by 365; the resulting exposures as reported by Stayner et al. are 795, 2466, 5699 and 10,636 $\mu g/m^3$-days corresponding to the four cumulative exposure groups displayed in Table VI-7. (It was necessary for Stayner et al. to divide by 365 instead of 240, the number of work days in a year, because in calculating the exposures used to obtain the

[2] Each term in the sum used to calculate the excess risk is the product of the probability that a person lives to the given age, times the excess risk of dying of cadmium-induced cancer given that he lived to that age. Thus, the method adjusts for risk of death from non-cadmium causes and does not assume that a person will live to be 100 years old. However, truncating the sum at 100 is equivalent to assuming that a person will not live past 100 years of age. Although there is a small probability that a person will live past 100 years of age, there is a much larger probability (on the order of 0.5) that a person will live past age 74. Consequently, accumulating excess risk through 100 years of age provides a much better approximation to the total excess risk than accumulating risk only through age 74, which is equivalent to assuming that no one lives past age 75. A similar accounting for total excess risk was made in the risk assessments used by OSHA to support its standards for arsenic and for benzene.

categorization shown in Table VI–7 it was assumed that one-month exposure in a work category meant 30 days of exposure.).

The background rates used in the life-table analysis in Table VI–7 were for U.S. white males (which includes Hispanics). Since the cohort involves a sizable fraction of Hispanics (a larger fraction than in the U.S. in general), additional parameters were included in the model to control for the possibility that the background rates in the population differed between Hispanics and non-Hispanics and between either of these groups and U.S. white males in general. Since Thun et al. did not report their data separately for Hispanic and non-Hispanic, it was not possible for OSHA to conduct analyses similar to those in the risk assessment reported in the Proposed Rule.

The resulting model for the expected number of lung cancer deaths in a group with a cumulative cadmium dose of X is

$$E_0 * \exp(a_i) * (1 + \beta * X),$$

where

E_0 is the expected number of cancers (obtained from Table VI–7) in the group based on rates for U.S. white males,

a_i is a category variable with i=H applying to Hispanics and i=NH applying to non-Hispanics.

The model was fit both with the restriction a_{NH} 0 (corresponding to applying the U.S. white male rates to the non-Hispanic cohort) and without this restriction. The observed deaths in a group were assumed to have a Poisson distribution whose expectation is given by the above expression. Thus, this analysis is a form of Poisson regression, with the principal difference between this analysis and the Poisson regression conducted by Stayner being that this analysis utilizes mortality rates from an external population to define background mortality rates, whereas Stayner et al. did not utilize an external population in their Poisson regression model. The parameters of the model were estimated by maximizing the likelihood (e.g., by Poisson regression), utilizing the computer program AMFIT (BEIR V, 1990).

A summary of the results of fitting this model to two different cases is presented in Table VI–10. In Case I, lung cancer mortality rates for U.S. white males are used as background rates for non-Hispanic white males in the cohort. In Case II, background rates for non-Hispanic white males in the cohort are assumed to differ from rates for U.S. white males by the multiplicative constant exp (a_{NH}), which is estimated from the data. In both analyses, background rates for non-Hispanic white males in the cohort are assumed to differ from rates for U.S. white males by the multiplicative constant exp (a_H).

TABLE VI–10.—RESULTS OF APPLYING OSHA'S MODIFIED RELATIVE RISK MODEL TO THE 1984 FOLLOWUP OF THE THUN COHORT

	Case I [a] ($a^{NH}=0$)	Case II [a] (a^{NH} estimated)
a_H (s.e.)	−1.4 (0.60)	−1.8 (0.91)
a_{NH}	0	−0.48 (0.77)
β_0	0.00027 (0.000098)	0.00054 (0.00057)
Deviance	10.29	9.88

[a] Case I assumes lung cancer mortality rates for U.S. white males are appropriate background rates for non-Hispanic white males in this cohort. Case II permits background rates for non-Hispanic white males to differ from rates for U.S. white males by the multiplicative constant, exp (a_{NH}).
[b] Units are $(\mu g\text{-years}/m_3)^{-1}$.

This analysis does not indicate that mortality rates for U.S. white males are inappropriate for the non-Hispanics in this cohort. The reduction in the deviance when a_{NH} is estimated is only 10.29–9.88=0.41, which is not significant (p=0.52) based on the chi-square distribution with one degree of freedom. On the other hand, a_H is significantly less than zero in both cases, implying that the Hispanics in this cohort had a lower background mortality rate from lung cancer than U.S. white males.

TABLE VI–11.—Observed and Predicted Lung Cancer Deaths from the Relative Risk Model Applied to the 1984 UPDATE TO THE THUN COHORT

Exposure (μg-years/m_3)	Number of lung cancers observed	Number of lung cancers predicted	
		Case I, ($a_{NH}=0$)	Case II, (a_{NH} estimated)
Non-Hispanics			
795	1	4.1	3.0
2466	7	4.4	3.8
5699	6	4.0	3.9
10836	7	9.5	10.3
Hispanics			
795	1	0.71	0.50
2466	0	0.67	0.63
5699	0	0.75	0.80
10836	2	0.87	1.0
		$X_2=8.5$ (NS) 6 df	$X_2=8.8$ (NS) 5 df

NS=nonsignificant lack of fit.
df=degrees of freedom.
[a] Case I assumes lung cancer mortality rates for U.S. white males are appropriate background rates for non-Hispanic white males in this cohort. Case II permits background rates for non-Hispanic white males to differ from rates for U.S. white males by the multiplicative constant, exp (a_{NH}).

Table VI–11 indicates that both of these cases provide an adequate fit to the data from the 1984 update of the Thun cohort. For Case I($a_{NH}=0$), the chi-square is 8.56 [6 degrees of freedom (d.f.),p=0.20], and for Case II (a_{NH} estimated) the chi-square is 8.82 (5 d.f., p=0.12). The lung cancer potency estimates obtained from these analyses

were $\beta=0.00027$ [μg-years/m^3]$^{-1}$ (Case I) and $\beta=0.00054$ [μg-years/m^3]$^{-1}$ (Case II). Both of these estimates are within the range of the corresponding estimates obtained by Stayner et al. when fitting the additive relative rate model, which was their preferred model, by Cox regression ($\beta=0.00026$ [μg-years/m^3]$^{-1}$) or Poisson regression ($\beta=0.00061$ [μg-years/m^3]$^{-1}$). (See Table VI–8.)

Thus, both Case I and Case II provide adequate descriptions of the data and both provide estimates of the carcinogenic potency of cadmium that are similar to estimates obtained by Stayner et al. using different modelling approaches. Case I is somewhat simpler than Case II since it requires one fewer parameters to be estimated.

Table VI–12 contains estimates, based upon Case I, of the number of excess lung deaths per 1000 workers exposed for 45 years to different TWA concentrations of cadmium. This table contains both MLEs and upper and lower statistical confidence limits. The MLEs were calculated in exactly the same way as the corresponding estimates in Table VI–8, which were made by Dr. Stayner, except that the potency estimate, $\beta=0.00027$ [μg-years/m^3]$^{-1}$, corresponding to Case I was used in the calculation. The 95% lower and upper confidence limits in Table VI–12 were calculated in this way also, except that the lower and upper confidence limits for β were used instead of the MLE. The 95% lower limit was $\beta=0.00013$ [μg-years/m^3]$^{-1}$ and the 95% upper limit was $\beta=0.00046$ [μg-years/m^3]$^{-1}$, both of which correspond to Case I. These confidence limits were calculated using the likelihood ratio approach.[3] MLEs based on Case II (with a_{NH} estimated) are about twice as large as those in Table VI–12 and the corresponding lower limits on risk calculated using the likelihood approach are zero.

TABLE VI–12.—OSHA FINAL ESTIMATES OF EXCESS LUNG CANCER DEATHS PER 1000 WORKERS WITH 45 YEARS OF OCCUPATIONAL EXPOSURE TO CADMIUM BASED ON THE RELATIVE RISK MODEL ASSUMING U.S. LUNG CANCER RATES ARE APPROPRIATE FOR NON-HISPANIC WHITE MALES IN COHORT [$a_{NH}=0$][a,b]

Exposure (μg/m^3) TWA	Risk per 1000
1	0.6 (0.3, 10)
3	1.8 (0.9, 3.0)
5	3.0 (1.5, 5.1)
7	4.2 (2.1, 7.1)
10	6.1 (2.9, 10.1)
20	12.1 (5.9, 20.1)
40	23.9 (11.7, 39.6)
50	29.8 (14.5, 49.1)
100	58.3 (28.8, 95.0)
200	112.1 (58.5, 177.9)

[a] Estimates derived using data from the 1984 update by Stayner *et al.* (Ex. L–140–20) of cadmium smelter workers.

[b] Numbers in parentheses are 95% upper and lower confidence limits.

As indicated by Tables VI–9 and VI–12, all of the estimates of excess risk of lung cancer obtained from the Thun cohort are similar despite the fact that the underlying analytic methods differed in several respects. Estimates of excess risk from 45 years of occupational exposure computed using the various approaches range from three excess deaths per 1000 workers to nine excess deaths per 1000 workers exposed to a TWA 5 μg/m^3 and from 58 to 157 excess deaths per 1000 workers exposed to a TWA of 100 μg/m^3. As Table VI–3 indicates, these estimates are somewhat higher than those obtained by OSHA in the proposed rule. OSHA believes that the differences between the new estimates and those in the proposed rule are most likely attributable to three factors: (1) The new estimates are based on additional followup of the Thun cohort; (2) the estimates appearing in the proposed rule were not adjusted for ethnicity (Hispanic versus non-Hispanic);[4] (3) the estimates were adjusted with the assumption that a person could live beyond age 74 years. Because the new estimates are based upon more complete data and more reliable quantitative methods, OSHA believes that the new estimates are more reliable than those that appeared in the proposed rule.

Discussion of Issues Related to Risk Assessment for Lung Cancer Based Upon Human Data

Potential for Confounding by Arsenic Exposure in Thun Cohort

Several commenters questioned whether there was an excess of lung cancers among workers hired in or after 1940, and whether an excess of lung cancer in persons hired prior to 1940 could have been due to arsenic rather than cadmium (Exs. 144–8B, 38). Dr. Schulte (Ex. 144–8c) addressed the lung cancer response among workers hired in 1940 or later as follows:

We have never felt that an analysis of the subcohort hired between 1940 and 1969 was scientifically justified. The analysis was only done because ASARCO desired it on the basis of their arsenic assumptions. We do not feel this analysis is justified for several reasons: (1) We do not see an important change in the arsenic content of the feedstock in 1940, (2) the subgroup hired after 1940 is too small to provide sufficient statistical power for a scientifically definitive analysis, and (3) the latency period for workers hired after 1940 was not long enough to scientifically justify analyzing this subcohort. said, we can interpret the post-1940 data with the aforementioned caveats. Clearly, there was an excess of lung cancer in the medium and high exposure groups combined (OBS=13, EXP=5.71, SMR=228, 95% CI=121–389) and no excess in the low group; these data are supportive of a dose-response pattern. The fact that the risk estimate for the high exposure group was lower than that for the medium group can be explained by the low number of workers in this group, and thus, the low statistical power to describe the effect* * *.

Thus, an analysis by NIOSH of workers first employed after 1940 did demonstrate an excess of cancer in the medium and high exposure groups and was supportive of a dose-response pattern.

Stayner et al. also addressed the issue of whether there was a lung cancer effect in workers first hired in 1940 or later by adding a category variable to their analysis representing whether or not year of first hire was in 1940 or later (Ex. L–140–20). When this variable was added, it was not significant, which indicates that there was no statistically significant difference between the lung cancer mortality rates among persons first hired before 1940 and those hired later that was not already being explained by the model. Moreover, if arsenic exposure was higher prior to 1940 and if this exposure was wholly or partially responsible for the excess in lung cancers observed in this cohort, then inclusion of the category variable for year of hire should reduce the magnitude of the coefficient for

[3] With this approach, a 95% lower (upper) limit is calculated as the value of β smaller (larger) than the maximum likelihood estimate that satisfies the equation $[2*(L_{MAX}-L(\beta))]^{0.5}=1.645$ where L_{MAX} is the maximum value of the log-likelihood and $L(\beta)$ is the log-likelihood expressed as a function of β (Cox and Hinkley, 1974).

[4] The data necessary for such an adjustment were not published in Thun et al. (Ex. 4–68) and consequently were not available to OSHA when preparing the proposed rule.

cadmium exposure. However, when the category variable representing year of hire was added, the magnitude of the cadmium coefficient increased, which is not consistent with the hypothesis that arsenic exposure prior to 1940 was largely responsible for the increased lung mortality seen in this cohort.

This analysis by Stayner et al. was commented on by Mr. Leonard Ulicny of SCM Chemicals as follows:

> This analysis is significantly flawed, as the year of hire variable and the cumulative exposure variable are not truly independent * * * For nearly any composite of work departments, the estimates of cadmium inhalation in workers hired before 1940 will be higher than estimates for those hired after 1940. Since the "independent" variables are in fact related, regression analysis cannot distinguish between them (Ex. 144–17).

OSHA agrees that cadmium exposure is very likely to be correlated with the year of hire variable used by Stayner et al. However, OSHA also believes that there were significant cadmium exposures after 1940 and there were considerable differences in cadmium exposures, both among men first hired prior to 1940 and among those first hired subsequently. Consequently, OSHA believes that the correlation between the two variables is far from perfect. Indeed, if it were perfect or nearly so, inclusion of the year of hire variable would have resulted in a decrease in the magnitude of the cadmium exposure variable. However, when the year of hire variable was included, the cadmium exposure variable actually increased in magnitude.

If there was a perfect correlation between cadmium exposure and arsenic exposure (or a surrogate for arsenic exposure such as year of hire), which OSHA does not believe is the case, then an internal analysis of the Thun cohort would be incapable of separating the effects of arsenic and cadmium. However, it would still be possible to address the potential magnitude of an effect of arsenic using the carcinogenic potency of arsenic estimated from other studies. Such an analysis has been conducted by Thun et al. (Ex. 4–68) and will be reviewed below. Thun et al. (Ex. 4–68) addressed the question of whether arsenic exposure may have been largely responsible for the excess lung cancer incidence observed in this cohort. This was done by estimating the potential number of arsenic-related cancers in their cohort using the carcinogenic potency of arsenic estimated by OSHA in its final rule on its most recent arsenic standard (48 FR 1864; Jan. 14, 1983). Thun et al. estimated that the average exposure to arsenic was 500 $\mu g/m^3$ in the areas of highest arsenic exposure (near the roasting and calcine furnaces), based on exposure measurements taken in 1950. After reducing this exposure by 75% to account for respirator use, exposure in the high arsenic areas was estimated as 125 $\mu g/m^3$. They further took into account that an estimated 20% of person-years were spent in high arsenic work areas, resulting in an average arsenic exposure of 25 $\mu g/m^3$ during work hours for the 576 workers hired in or after 1926. Thun et al. estimated that these workers worked an average of 3 years and consequently accumulated 1728 person-years of arsenic exposure. Thun et al. estimated, based on the OSHA risk assessment model for arsenic (48 FR 1864; Jan. 14, 1983), these arsenic exposures would account for only 0.77 lung cancers and consequently would not account for the excess lung cancer mortality in this cohort.

Thun et al. apparently based this estimate on OSHA's preferred estimate of lifetime risk of 40/1000 from a 45-year working lifetime of exposure to 50 $\mu g/m^3$ arsenic (48 FR 1890; Jan. 14, 1983), as follows:

$$[(1728\ PY) * (500\ \mu g/m^3) * (0.25) * (0.2)] / [(45\ PY) * (50\ \mu g/m^3)] * [40/1000] = 0.77\ \text{lung cancers.}$$

OSHA has updated this calculation to reflect the additional followup of the cohort through 1984. OSHA has also adjusted the estimate of the average person-years work, and has made some additional analyses to account for the fact that the Thun et al. estimate of the number of lung cancers attributable to arsenic exposure represents the ultimate number after complete followup rather than after the partial followup currently available, and to incorporate additional information on arsenic exposures in the cohort.

Addressing first the estimate of the average person-years of work, Lamm (Ex. 144–8) calculated an average of 6.94 years of work at the plant per cohort member which is more than double the value of 3 years estimated by Thun et al. To resolve this discrepancy, OSHA asked Dr. Stayner to calculate the average duration of work for the cohort of men first exposed in or after 1926 based on followup through 1984. Dr. Stayner obtained an arithmetic mean of 7.15 years and a geometric mean of 3.04 years (Stayner, personal communication). Since the former figure is very close to the figure reported by Lamm and the latter figure is very close to the value reported by Thun et al., OSHA concludes that Thun et al. must have used the geometric average, whereas Lamm reported the arithmetic average. Since the average is used to calculate the total person-years of exposure reported, OSHA concludes that the arithmetic average is appropriate for this application and the geometric average is inappropriate. (The total person-years is equal to the product of the number of persons in the cohort times the arithmetic average of person-years of exposure, not the geometric average of person-years of exposure.) The arithmetic average of 7.15 years of exposure corresponds to a total person-years of exposure of 7.15 * 606=4333 person-years in the cohort reported on by Stayner et al. (Ex. L–140–20), where 606 is the number of persons in Stayner et al.'s cohort.

We now consider the adjustments to Thun et al.'s methodology needed to account for the fact that followup of the cohort currently is only through 1984 and consequently is incomplete. Since Thun et al. used OSHA's lifetime risk estimate for arsenic in their calculation, the 0.77 cancers represent the ultimate number of cancers in the cohort after complete followup, rather than the number of cancers through 1984. Stayner et al. (Ex. L–140–20) reported that only 27% of the cohort of workers hired in or after 1926 had died after followup through 1984 (162 out of 606). Consequently, the estimate of the ultimate number of lung cancers attributable to arsenic exposure should be multiplied by 0.27 to estimate the number of lung cancers attributable to arsenic exposure after followup through 1984.

Considering next the estimates of arsenic exposures, the average arsenic exposure of 500 $\mu g/m^3$ in high arsenic exposure areas that was used by Thun et al. in their calculation was based on arsenic measurements made in 1950. Two additional sources of data on arsenic exposures are also available: a 1945 report by the University of Colorado, Division of Industrial Hygiene on plant dust and fumes, including arsenic measurements (cited in Ex. L–140(23) and Ex. 144–8c), and urinary arsenic level measured in the high arsenic areas from 1960 to 1980 (Ex. 4–68). OSHA has reviewed the data from each of these sources and used these data to quantify arsenic exposures in the cohort.

In 1991 Dr. Schulte of NIOSH (Ex. 144–8c) used the 1945 exposure data to estimate average arsenic exposures in high arsenic exposure areas. Data tables contained in the 1945 report provide estimated 8-hour arsenic exposure values for 18 sample groups that were collected in the high arsenic exposure operations of sampling, mixing, roasting

and calcine. Estimates of work shift exposure were calculated by combining the arsenic concentrations obtained from short-term samples that were collected while various tasks were being performed, or in the general areas where the worker was during the work shift. Based on these data, Dr. Schulte presented several summary measures of arsenic exposure, including both arithmetic and geometric averages. Both types of averages were calculated both unweighted and weighted by the number of workers in each operation. OSHA has substantially verified the NIOSH results for the weighted averages, which were 936 $\mu g/m^3$ for the weighted arithmetic mean and 157 for the weighted geometric mean. OSHA also concludes that the weighted means are more appropriate than the unweighted means since estimates of overall exposure should take into account the number of workers exposed to each level (e.g., if 100 workers are exposed to 100 $\mu g/m^3$ and one worker to 1000 $\mu g/m^3$, it is not reasonable to assume an average exposure of $[100+1000]/2=550$ $\mu g/m^3$ for the entire cohort). OSHA also concludes that the arithmetic weighted average is a more appropriate summary measure for assessing risk than the geometric average because the arithmetic average is more likely to be closely correlated with lung cancer risk than the geometric average. (To cite an extreme example of the unreasonableness of the geometric average in this context, if a single sample value is zero, then regardless of the values of the remaining samples, the overall geometric average is zero.) In summary, based on Schulte's data, OSHA concludes that the weighted average of 936 $\mu g/m^3$ is the most reasonable summary measure of arsenic exposure in the high arsenic exposure areas from the 1945 data for purposes of risk assessment. Using the respirator adjustment factor of 0.25 introduced by Thun et al. results in a average exposure of $0.25 * 936$ $\mu g/m^3=234$ $\mu g/m^3$.

Turning now to the urinary arsenic data, Thun et al. (Ex. 4–68) noted that the average urinary arsenic level measured in the high arsenic areas from 1960–1980 were consistent with an average inhaled arsenic concentration of 14 $\mu g/m^3$. If one assumes that the reduction in airborne arsenic levels paralleled the reduction in airborne cadmium levels over time in these areas (this does not require assuming that individual exposures to cadmium and arsenic were proportional since workers generally moved among several areas), then the urinary arsenic data can be used in conjunction with the cadmium exposure estimates (Ex. 4–68, Table 1) to estimate the arsenic exposures prior to 1960. Since the (respirator-adjusted) cadmium exposures at the calcine furnace are estimated to be 0.15 $\mu g/m^3$ after 1965, 0.4 $\mu g/m^3$ between 1960 and 1964, and 1.5 $\mu g/m^3$ in earlier years, the estimate of arsenic exposure previous to 1960 at the calcine furnace is estimated to be between $14 * 1.5/0.4=52.5$ $\mu g/m^3$ and $14 * 1.5/0.15=140$ $\mu g/m^3$. Similarly, since the estimated cadmium exposures in the roaster area were 0.6 $\mu g/m^3$ after 1950 and 1.0 $\mu g/m^3$ before 1950, arsenic exposures in the roaster area are estimated as 14 $\mu g/m^3$ between 1950 and 1960, and $14 * 1.0/0.6=23.3$ $\mu g/m^3$ prior to 1950. Since these estimates are based on urinary levels, they reflect what was actually inhaled and require no additional adjustment for respirator use.

In summary, OSHA has developed three sets of estimates of arsenic exposure in high arsenic exposure areas for the period prior to 1960. After adjusting for respirator use, these estimates are: 125 $\mu g/m^3$ based on 1950 monitoring data, which was used by Thun et al. to quantify arsenic exposure; 234 $\mu g/m^3$ based on 1945 monitoring data; and between 14 $\mu g/m^3$ and 140 $\mu g/m^3$ based on changes over time in cadmium exposures and urinary arsenic levels measured between 1960 and 1980.

We note that the original respirator-adjusted estimate of arsenic exposure of 125 $\mu g/m^3$ made by Thun et al. is within the range of the other estimates summarized in the previous paragraph. If this estimate of arsenic exposure is retained and the person-years of arsenic exposure are adjusted as explained earlier and the factor of 0.27 is added to account for the fact that most of the cohort members were still alive at the end of the most recent followup, the resulting estimate of the number of cancer deaths in the cohort by 1984 attributable to arsenic exposure becomes

$[(4333\ PY) * (125\ \mu g/m^3) * 0.2] / [(45\ PY) * (50\ \mu g/m^3)] * [40/1000] * 0.27 = 0.52$ lung cancer deaths.

Even if the highest OSHA estimate of average arsenic exposure (234 $\mu g/m^3$) is used, instead of 125 $\mu g/m^3$, the estimated number of lung cancer deaths attributable to arsenic exposure is 0.97. On the other hand, Stayner et al. observed 24 lung cancer deaths and an overall excess of eight (including an excess of 11 among non-Hispanics only). Therefore, even though OSHA's analysis differs from that of Thun et al. in several respects, the overall conclusion is the same: It is unlikely that arsenic accounts for the excess lung cancer deaths observed in this cohort, or even for a substantial proportion of that excess.

Any error in the estimate of respirator use will result in uncertainty in the estimate of arsenic exposure for those members of the cohort who were employed in high arsenic exposure areas. If the arsenic exposure is underestimated the contribution of arsenic to the excess lung cancer risk would be underestimated. If, on the other hand, the arsenic exposure was overestimated, the contribution of arsenic to the excess lung cancer risk would be overestimated. As discussed in Section V on health effects, OSHA is of the opinion that Drs. Thun and Smith made reasonable estimates of both arsenic and cadmium exposures, but realizes that the actual certainty of the estimates will never be known.

Dr. Schulte of NIOSH (Ex. 144–8C) pointed out three factors that indicate that the average concentrations derived from the 1945 monitoring data above may be substantial overestimates of actual arsenic exposure.

First, the 1945 report states that three of the departments with the highest arsenic concentrations (crusher, including unloading; Godfrey Roasters; and beghouse) "in recent years have operated about one month in every two or three." The TWA should be multiplied by 0.5 or 0.33 to estimate the actual average arsenic exposure to take this work pattern into account. Second, loading and unloading railroad cars are among the jobs with the highest exposure, but not only are these jobs done intermittently, they should not be equated with departmental averages throughout the departments where arsenic exposure potentially occurs. Third, particle size sampling was not done during the 1944 and 1945 surveys. Many of the samples taken were of dust, and thus a portion of the sample was of non-respirable size. This is especially true in the jobs involving loading and unloading, which included some of the highest arsenic values.

Dr. Thun (Ex. L–140–23) cites two additional reasons why the estimated average arsenic exposure of 500 $\mu g/m^3$ may be a substantial overestimate. One is that an estimate of the average exposure derived from the urinary arsenic data is so much lower. The other is the fact that high arsenic exposure jobs were frequently staffed with short-term employees who were not included in the study and whose arsenic exposures therefore did not affect its results.

Dr. Lamm (Ex. 144–8) disputed each of the factors used by Thun et al. to estimate arsenic exposures in this cohort. Lamm posits a mid-range value of 8,700 $\mu g/m^3$ (representing simply one-half of the highest recorded measurement), or 2,650 $\mu g/m^3$ (obtained

by "exclusion of the highest level and taking a mid-range of other high levels"). OSHA considers the weighted arithmetic average used in its analysis to estimate exposures from the 1945 data to be a more appropriate scientific approach than Lamm's use of a mid-range of certain selected "high levels." Since other data are available which indicate lower levels of arsenic and because of the potential for overestimation of arsenic exposure as described by Dr. Schulte and Dr. Thun, OSHA considers that, to the extent that its estimate of 936 $\mu g/m^3$ based on the 1945 data is in error, it is more likely to overestimate rather than underestimate arsenic exposures.

Dr. Lamm also questioned the estimate by Thun et al. that 20% of the person-years of exposure were spent in high arsenic exposure areas, citing that the controls in his case control study spent "more than two-thirds of their time (68%) in the high cadmium areas." However, Thun (Ex. L-140-23) explains that he and his co-investigators used several sources of information in making this estimate.

> The primary source of information was biomonitoring data which gave department numbers, and thus could be used to estimate the percent of time spent in high arsenic areas. We also used information provided in the doctoral thesis of Jeffrey Lee which included information on shift assignments. The 20% estimate was discussed with Dr. Lowell White of ASARCO and with Mr. Ernie Lovato, president of United Steelworkers Local 557, who confirmed the 20% estimate. Finally, personnel records showing two-week shift assignments were reviewed to see if they confirmed the 20% estimate.

Dr. Thun also points out that Lamm's 68% figure does not contradict this estimate because, first, Lamm's figure is for high cadmium areas, not high arsenic areas and, second, Lamm's figure is derived from a small sample of workers from his case control study (comprising only 12% of the cohort).

The Dry Color Manufacturers' Association (DCMA) commented that Thun et al. underestimated the percentage of the workforce exposed to "high arsenic" work areas by assuming only 20% were so exposed when in reality everyone was exposed because entry-level positions were in these high-exposure areas (Ex. 120). This comment appears to be based on a misconception regarding what the 20% figure is supposed to represent. It represents the percent of person-years spent in high-arsenic exposure areas, not the percent of workers that ever worked in these areas. Even if DCMA were to be correct in its claim that 100% of workers were exposed in high arsenic areas, this would in no way contradict the 20% estimate made by Thun et al.

Dr. Lamm contends that the "arsenic content of the fines used as feedstock prior to 1940 were considerably higher than those used after 1940" (Ex. 144-7B). Lamm presents a graph of mean arsenic in the feedstock from 1926 through 1958 (Ex. 144-7, Figure 5) that indicates levels were two to three times as high between 1926 and 1940 as between 1940 and 1958. However, Thun (Ex. 33) presents a graph of total pounds of arsenic processed by year from 1924 through 1958 that indicates no particular trend after 1926. In fact, the highest amount of arsenic processed between 1927 and 1958 appears to have occurred in 1953. The lack of a difference in amount of arsenic processed during the two time periods is corroborated by Table 8 in Lamm et al. (Ex. 144-7) that indicates the average arsenic produced was 5,150 kg/yr between 1928 and 1940 and 4,356 kg/yr between 1941 and 1958. OSHA believes that it is questionable as to whether the amount of arsenic processed or the arsenic concentration of the ore is a better indicator of worker exposures. It seems reasonable that the amount of fugitive dust present would be likely to be related to the total amount of ore processed and not to the arsenic content. If so, then the total amount of arsenic processed is likely to be a better predictor of the total amount of arsenic released into the air. At the outside, these data do not suggest a large difference between the arsenic air concentrations between 1926-1940 and post-1940. Thus, OSHA finds Dr. Lamm's argument to be less than compelling and concurs with Dr. Thun's conclusion that "[t]hese data [on amount of arsenic processed by year] do not support the hypothesis that arsenic contamination was markedly higher from 1926-1940 than thereafter" (Ex. 33).

Dr. Lamm indicates that he calculated, based on computerized work histories supplied by NIOSH, an average employment of members of the Thun cohort of 6.94 years as opposed to the 3 years used by Thun et al. in their arsenic calculation. As explained earlier, based on the followup through 1984, Dr. Stayner of NIOSH recently calculated an arithmetic average employment duration of 7.15 years which agrees substantially with the value calculated by Dr. Lamm. This figure of 7.15 years was incorporated by OSHA into its calculations as described earlier.

Finally, Dr. Lamm contends that Thun et al. were in error in reducing exposures by 75% to account for respirator use. Lamm argues that respirator use was not considered in OSHA's risk assessment of arsenic and therefore not using a respirator reduction factor would be equivalent to assuming that respirator protection in this cohort was comparable with that in the cohorts upon which OSHA's risk assessment for arsenic was based.

But OSHA relied mainly on data from the Anaconda, Montana and the Tacoma, Washington copper smelters in its risk assessment for arsenic. Arsenic exposures at the Tacoma smelter were estimated from urinary arsenic measurements and based on correlations of air measurements and urinary arsenic levels collected from workers who did not wear respirators during the time the data were being collected (48 FR 1878, Jan. 14, 1983.) Air levels estimated from such measurements thus would reflect actual inhaled doses and further correction for respirator use would not be appropriate. As stated by OSHA in connection with the final arsenic rule, "they [estimates of exposure in the Tacoma smelter based on urinary arsenic data] take into account the protection afforded by the respirators that were sometimes worn." (48 FR 1887, Jan. 14, 1983).

Respirator use was also accounted for in some analyses of data from the Anaconda smelter: "Because respirators generally were worn in the heavy exposure areas, Lubin et al. reduced the assigned exposure level to 1.13 mg/m^3 in the heavy exposure category for some of their multivariate analyses" (48 FR 1870, Jan. 14, 1983). Moreover, some of the risk assessments of data from the Anaconda smelter upon which OSHA relied omitted data from the heavy exposure category (Ex. 206 ref. in 48 FR 1864, Jan. 14, 1983). This constitutes a *de facto* correction for respirator use, because the group most likely to have used respirators were not included in the analysis.

On the other hand, the exposure estimates in the epidemiological study of the Anaconda smelter by Higgins et al. did not include adjustments for respirator use because the authors did not believe such adjustments were appropriate. Thus, some of the risk assessments cited by OSHA included adjustments for respirator use and at least one did not. The estimates of lifetime risk from arsenic exposure preferred by OSHA were consistent with estimates made from studies cited above in which adjustments for respiratory use were either made or judged not to be appropriate.

It should also be noted that, like the estimates of arsenic exposure made in the Tacoma arsenic smelter based on urinary data, estimates of arsenic exposure at the Colorado cadmium

smelter based on the urinary arsenic data (discussed earlier in this section) did not require nor employ any adjustment for respirator use. Nevertheless, estimates of arsenic exposure derived from these data were generally lower than estimates made from other types of data for which adjustment for respirator use was deemed necessary and therefore employed.

After review and modification of the Thun et al. analysis of the potential effect of arsenic and consideration of the above points, OSHA concludes that Dr. Lamm's contention that Thun et al. seriously underestimated the potential impact of arsenic upon lung cancer in this cohort is not convincing. OSHA's preferred estimate of the expected number of deaths from lung cancer due to arsenic in the cohort studies by Stayner et al., which were first exposed in 1926 or later, is 0.52 out of a total of 24 that have been observed. Further, based on its analysis described above, OSHA believes that it is unlikely that the number could be substantially larger than this preferred value.

Potential for Confounding by Smoking in the Thun Cohort

In addition to arsenic exposure, tobacco smoking is also a risk factor for lung cancer in the Thun cohort. As explained by Dr. Thun in his testimony on the proposed rule (Ex. 33), smoking information was available for 43% of the workers in the study. This information was collected by the company in 1982 using a questionnaire mailed to surviving workers or next of kin of deceased workers and using medical records. The questionnaire inquired about the ages of starting and stopping smoking and the usual amount smoked. Dr. Thun compared the smoking habits of the cadmium workers as of July 1, 1965 to smoking habits for U.S. white males in 1965 as determined by a Health Interview Survey (HIS) of the National Center for Health Statistics. Table VI–13 was used by Dr. Thun to summarize these data. This table compares smoking habits of Hispanic and non-Hispanic workers separately to smoking habits of U.S. white males.

TABLE VI–13.—SMOKING HABITS AMONG HISPANIC AND NON-HISPANIC WORKERS AND AMONG WHITE MALES IN U.S. GENERAL POPULATION

[In percent]

Group	Non- and former smokers	Current smokers		
		<15	15–24	>25
U.S. Males	48.5	13.3	24.1	14.1
Cadmium Workers:				
Hispanic	43.7	31.0	20.7	4.6
Non-Hispanic	50.9	13.5	21.5	14.1

Source: Thun (Ex. 33).

Although Dr. Thun cautioned that smoking information was collected differently from the cadmium workers than in the 1965 HIS and therefore may not be comparable, the smoking pattern for non-Hispanics is very similar to the smoking habits for U.S. white males in general. These data do not suggest that differences in smoking habits could have accounted for the 11 excess lung cancers (SMR=211, $p<0.01$) observed by Stayner et al. (Ex. L–140–20) among non-Hispanics. If anything, they suggest that smoking rates may have been slightly lower among non-Hispanics than in the referent group of U.S. white males used by Stayner et al. which could cause the effect of cadmium to be underestimated in the life-table analysis.

The smoking data on Hispanics in Table VI–13 indicate that the Hispanic workers were more likely to be current smokers, but smoked fewer cigarettes per day. Dr. Thun pointed out that this pattern is typical of Mexican-American men. Dr. Thun also pointed out that "[s]everal studies have shown low rates of lung cancer among Hispanics in the Southwest", and "[i]n Denver between 1969–1971, Hispanic males had less than half (0.41) the incidence of lung cancer compared to other whites." Thus the lower mortality from lung cancer among Hispanics found in this study is consistent with generally lower rates among Mexican-American men. These findings support the use of U.S. white males as the referent population for non-Hispanics in this study, as was used by Stayner et al. in their life-table analysis, but suggests that this referent population has a higher background rate of lung cancer than the population of Hispanics in this study. This could have caused Stayner et al. to underestimate the effect of cadmium among Hispanics in their life-table analysis.

As noted by Stayner et al. (Ex. L–140–20), the modelling procedures they used based on Poisson regression and Cox regression greatly reduced the potential for confounding by cigarette smoking. This is because these modelling procedures rely on internal comparisons within the cohort rather than upon comparisons with an external control population. Consequently, "[i]n order for smoking to confound this analysis, one would have to propose that smoking habits varied between the exposure categories used in the analysis, which seems unlikely." Moreover, Dr. Thun showed (Ex. 33) that the percent of Hispanics, which may be acting as a partial surrogate for cigarette smoke, was evenly represented in the low, medium and high cadmium exposure groups.

In summary, the smoking data that are available indicate that smoking patterns among non-Hispanics in this cohort were comparable with those of U.S. white males in general and therefore cannot explain the significant excess of lung cancers among non-Hispanics in this cohort. The smoking pattern among Hispanics in the cohort indicated that the Hispanic smokers tended to smoke less than U.S. white males. This pattern is consistent with generally lower smoking rates among Mexican-American men and may explain at least partially the lower lung cancer rates observed among Hispanics in this study. In neither Hispanics nor non-Hispanics did the smoking data indicate a higher than normal prevalence of smoking that could account for the observed increased lung cancer mortality rate in this cohort. Moreover, even if the rate of smoking in this population had been different from that expected among any comparable mixture of Hispanics and non-Hispanics, such differences would be unlikely to affect the statistical analysis conducted by Stayner et al. that did not make use of an external control population.

Summary of OSHA's Review of Potential Confounders in the Thun Cohort

OSHA has carefully considered the evidence regarding whether the excess lung cancers in the Thun cohort can be attributed to arsenic exposure, and particularly to arsenic exposure prior to 1940. The analysis presented by Dr. Schulte of NIOSH demonstrates that the increased lung cancer mortality in this cohort is not confined to workers first employed prior to 1940. Similarly, results obtained by Stayner et al. were not consistent with the increased lung cancer in the cohort being a result of arsenic exposure that occurred prior to 1940. Finally, even though there are several reasons stated by Dr. Schulte and Dr. Thun as to why the analyses conducted by Thun et al. and modified by OSHA could overestimate the effect of arsenic exposure, these estimates indicate that arsenic exposure does not explain the increased lung cancer mortality observed in this cohort. OSHA also finds no evidence of excess smoking in the population that could explain the excess of lung cancers. Thus, OSHA concludes that the excess in lung cancer among workers in the Thun cohort who were first employed in or after 1920 is unlikely to be due to arsenic exposure or to cigarette smoking and is more likely to be attributable to cadmium exposure. This conclusion is strengthened by the knowledge that lung cancer has unequivocally been related to inhalation of cadmium in animals.

Review of Other Issues

The Low SMR in the Low Exposure Group in the Thun Cohort

Several commenters (Exs. 38, 19–30), noted the low SMR (SMR=53, based on two lung cancer deaths) in the low exposure group (584 mg-days/m^3) of the Thun et al. study (Ex. 4–68) and suggested that this was evidence of a threshold for the carcinogenic effect of cadmium. Dr. Thun addressed this issue in his testimony at the OSHA hearing (Ex. 33) by presenting results for followup through 1984 and by calculating the expected number of lung cancers using both U.S. and Colorado rates. His findings with respect to the low exposure group [<584 mg-days/m^3] are summarized in Table VI–14. In none of the four cases is the deficit in lung cancers statistically significant. Moreover, the life-table analysis of this cohort by Stayner et al. (Ex. L–14020) demonstrates that the deficit is also not statistically significant when considering only non-Hispanics (1 case observed and 3.35 expected, p=0.15, see Table VI–7). Further, the deficit in the lung cancer rate in the low exposure group is smaller when Colorado mortality rates are used (Table VI–14). Moreover, as noted by Dr. Thun (Ex. 33), several studies have shown low rates of lung cancer among Hispanics in the Southwest (possibly as a result of reduced smoking among Hispanics) and 40% of the cohort are Hispanics whereas in 1980 only 6.5% of Colorado males were Hispanic (USDOC, 1980). OSHA also suggested that this could be due to a healthy worker effect. The healthy worker effect is seen in worker cohorts because the health status of people who are accepted for employment is better than the health status of the general population used for comparison (Ex. 50). Thus, OSHA concludes that the deficit in lung cancers in the low exposure group may be attributed to: (1) Random fluctuation, (2) the healthy worker effect, (3) differences between U.S. and Colorado lung cancer rates, and (4) an excess of Hispanics in the cohort, and does not indicate a threshold for the carcinogenic effect of cadmium. Similarly, Dr. Thun (Ex. 33) expressed the opinion that the apparent deficit of lung cancers among workers exposed to less than 584 mg-days/m^3 (the low exposure group) "is an artifact of the lower smoking habits of the cadmium workers and should not be interpreted as showing a 'safe' level of cadmium."

TABLE VI–14.—EXPECTED AND OBSERVED NUMBERS OF LUNG CANCERS IN THE LOWEST EXPOSURE GROUP (≤584 MG-DAYS/M^3) OF THE THUN COHORT (EX. 33) HIRED IN OR AFTER 1926

Followup period	Based on rates of U.S. white males		Based on rates of Colorado white males	
	O/E[a]	SMR	O/E[a]	SMR
Through 1978	[b]2/3.76 (p=0.28)	0.53	[b]2/2.64 (p=0.51)	0.76
Through 1984	[b]2/6.06 (p=0.06)	0.33	[b]2/4.37 (p=0.19)	0.46

[a] Observed/expected.
[b] Probability of observing two or fewer lung cancers assuming lung cancers are Poisson distributed with mean given by the respective expected number.

Lamm et al.'s Case Control Analysis

Lamm et al. (Ex.144–7B) conducted a case control analysis of 25 lung cancer cases in the Thun cohort. Three controls per case were selected from this cohort. Controls were matched to cases by date of hire and age at hire. Explanatory variables were cumulative cadmium exposure, cigarette smoking history, and "plant arsenic exposure status at time of hire."

Lamm et al. stratified his cadmium exposures by period of hire (pre–1926, 1926–1939, and 1940–1969). Within each period mean cumulative cadmium exposure was nearly equal among cases and controls (ratio of exposure—cases/controls—was 0.99, 1.05, and 0.91, for the three periods of hire, respectively). Among those for whom smoking histories were available (72% of the cases and 57% of the controls), the odds ratio for smoking was 8.2 (p=0.046). Lamm et al. interpreted these findings as suggesting "that the cumulative cadmium exposure * * * is not a major determinant of lung cancer within the study group."

Lamm et al. matched for both age and date of first hire in their case control study. It seems likely that date of hire could be significantly correlated with cadmium exposure in this analysis because higher cadmium exposures would be expected to occur in persons with earlier periods of employment, both because estimated airborne cadmium levels were higher in earlier years and because persons employed earlier had longer to accumulate exposure. Such a correlation could mask any effect of cadmium exposure in Lamm et al.'s analysis because they only compared the exposures of cases and controls for those that had similar dates of hire. Lamm et al. raised the possibility that such "overmatching" may have been the reason there was no difference in cadmium exposures between cases and controls. They point out that a considerable range of exposures exist "in this study, ranging from about 1 to 30 mg/m^3 for those hired prior to 1940 and from about 0.3 to 17 mg/m^3 for those hired subsequently." However, since each of the ranges are determined by the exposures of only two members of the

cohort (the most highly exposed and the least exposed in each group), presentation of these ranges does not adequately address the issue of whether or not the cadmium exposure and age at first hire are highly correlated.

Because of the potential flaw due to "overmatching" in the methodology used by Lamm et al., OSHA does not accept the conclusion from this study that "exposure to arsenic and cigarette particulates, rather than cadmium exposure, may have caused the lung cancer increase of these workers." NIOSH demonstrated a significant excess of lung cancer in medium and high cadmium exposure groups among workers first hired in 1940 and later, when Lamm et al. contend arsenic exposures were lower (Ex. 144–8c). Similarly, in Stayner et al.'s analysis (Ex. L–140–20) the magnitude of the cadmium variable increased rather than decreased when they controlled for first employment prior or subsequent to 1940. Finally, the Thun et al. analysis of the potential impact of arsenic, as reviewed and modified by OSHA earlier in this section, indicates that arsenic exposures would account only for a very small fraction of the total lung cancers observed in this cohort.

Disaggregation of Data and Use of Multistage Model

Dr. Thomas Starr commented that "OSHA should redo its analysis with the individual person-year information collected by Thun et al.," noting that the latter data provided just three data points, and they are only very crudely characterized by the median cumulative exposure for each category" (Ex. 38). He also recommended that "OSHA should reanalyze the Thun et al. (Ex. 4–68) data with the multistage dose-response approach model utilizing an approach similar to that described by Crump and Howe (1984)." The risk assessment by Dr. Stayner and his associates at NIOSH (Exs. L–140–20, L–163) incorporates both of these recommendations. The Poisson regression conducted by Stayner et al. divided the person-years into about 200 cells, defined by categorizations on age, calendar year, ethnicity (Hispanic versus non-Hispanic), and cumulative cadmium dose. The Cox regression conducted by Stayner et al. did not involve any grouping of person-years. Finally, Dr. Stayner et al. did reanalyze the Thun et al. data, using the followup through 1984 rather than that through 1978 that was reported in Thun et al. (Ex. 4–68), based upon the multistage dose response approach described by Crump and Howe (1984). These methods all gave very similar estimates of excess risk (Table VI–9), and are very similar to OSHA's estimates (Table VI–12) in its final risk assessment that were derived from more aggregated forms of the data.

Summary of Cancer Risk Assessment Based on Both Animal and Human Data

In its proposed rule, OSHA assessed cancer risk from occupational exposure to cadmium by applying several different risk assessment models to the animal data of Takenaka (Ex. 4–67) (results shown in Tables VI–1 and VI–2) and by applying relative and absolute risk models to the data on followup through 1978 of the Thun cohort (results shown in Tables VI–3 and VI–4).

Since writing the proposed rule, significant new data have become available that prompted OSHA to conduct additional risk calculations. Oldiges et al. (Ex. 8–694–D) showed that inhalation exposure to several types of cadmium caused lung tumors in male and female rats. Stayner et al. (Ex. L–140–20) reported on additional followup of the Thun cohort through 1984 and developed new estimates of risk from this update.

OSHA maintains that the animal carcinogenicity data on cadmium is relatively extensive and of high quality. It shows unequivocally that several different forms of cadmium induce lung tumors when inhaled by male or female rats. These data are satisfactory for establishing estimates of human risk according to toxicological methods generally employed by federal regulatory agencies, including OSHA.

OSHA has carefully evaluated the human data from the Thun cohort and the likelihood that the excess lung tumors were caused by either smoking or arsenic. It concludes that these tumors are unlikely to be explained by either of these factors, but are more likely attributable to cadmium. OSHA also determines that the data from this study satisfy the necessary requirements for obtaining quantitative estimates of excess risk. OSHA further concludes that the human data on cadmium from the Thun cohort are substantially strengthened and corroborated by the animal data. First, the animal data show unequivocally that inhalation of cadmium can induce lung tumors, the same type of tumors that are seen in excess in the Thun cohort. Second, estimates of excess risk of lung cancer obtained from the animal data and from the Thun cohort are in essential agreement.

In its new risk estimates based on the recently developed animal data (Table VI–6), OSHA utilized three dose-response models, all of which are different versions of the multistage model of cancer: the multistage model, the Armitage-Doll multistage model and the multistage-Weibull model. The Armitage Doll model makes more detailed biological assumptions regarding the effect of exposure and will always predict a linear response. The multistage and multistage-Weibull models are flexible dose response models that can assume a variety of curve shapes, both linear and non-linear. However, upper confidence limits calculated from these models will be linear. Furthermore, when applied to data with only two dose groups (a treated group and a group of control animals), the multistage and multistage-Weibull models become linear by default, because there is not enough information from only two doses to estimate the shape of the dose response. The multistage model is applied to the quantal data specifying whether an animal had a lung tumor response, and the Armitage-Doll and multistage-Weibull model also utilized the time at which the response was observed.

Regarding the cancer risk assessment models applied to epidemiological data, OSHA has reviewed the new risk assessment by Stayner et al. based on the updated followup through 1984 of the Thun cohort, and has also updated its own risk assessment utilizing this new information. Stayner et al. employed three dose response models: the power model, the exponential model, and the additive relative rate model. Although all three of these models are linear at the very lowest cadmium exposures, they have different amounts of non-linearity at higher doses, with the power model being the most nonlinear and the additive relative rate model being essentially linear. Although the power model gave the best fit to the data, this model predicted unrealistically low rates of lung cancer in unexposed subjects and consequently was discounted by Stayner et al. [This model would also predict much higher lung cancer risks than the other two models at exposures in the range OSHA is considering regulating (1 $\mu g/m^3$–100 $\mu g/m^3$).] Between the two remaining models, the additive relative rate model fit the data slightly better than the exponential model and was selected by Stayner et al. as the best model of the three for risk assessment. OSHA believes that this is a reasonable scientific conclusion from the results of the Stayner et al. analysis.

Dr. Stayner (Ex. L–163) also reported on results from applying the multistage model to the updated Thun cohort. Application of this model to the Thun cohort had been recommended by Dr. Starr (Ex. 38). This model assumes that

lung carcinogenesis is a five-stage process. Dr. Stayner estimated that cadmium affects the third stage in this process.

Dr. Starr also criticized OSHA's use of "purely linear models of absolute and relative risk." He stated that "Today, it is nearly universally accepted that the process of carcinogenesis, and chemical carcinogenesis in particular, is multistage in character with numerous distinct events required for the conversion of normal cells to malignant ones. Thus, the use of the one-hit model (or linear models derivable from it) for low-dose purposes are wholly inadequate."

OSHA agrees that there is good scientific evidence that carcinogenesis is generally a multistage process. However, OSHA disagrees with Dr. Starr's conclusion that a multistage process is incompatible with a linear dose response. It is plausible that a carcinogen affects a multistage process by increasing the rates at which the different stages occur by an amount that is proportional to the amount of the ultimate carcinogen present. If this is the case, then the dose response shape is determined mainly by two factors: the number of stages affected by the carcinogen (not the total number of stages as implied by Dr. Starr), and the interaction of the carcinogen with background carcinogenesis. If the carcinogen acts on a single stage, then the dose response will be linear. Even if the carcinogen affects multiple stages, if its effect is to increase the background rate at which these stages occur, then the process can still generate essentially a linear dose response (Crump, 1985).

Dr. Stayner's application of the multistage model to the data from the Thun cohort provides direct evidence that the multistage model is compatible with a linear dose response. He applied a multistage model assuming five stages and one of the stages was affected by cadmium. The excess risks he estimated from this model were intermediate between those he obtained with two versions of the relative rate model, which is a linear model (Table VI–9).

In its updated risk assessment based on followup through 1984 of the Thun cohort, OSHA applied a linear version of the relative risk model. OSHA determined using a goodness-of-fit test (Table VI–11) that this linear model was completely compatible with the dose response data from this cohort.

Three of the ten animal data sets analyzed by OSHA using the multistage model (Table VI–6), and seven of the nine animal data sets analyzed using the multistage-Weibull model, involved three or more treatment groups and therefore provided information on the shape of the dose response curve. In none of these ten model fits did a non-linear version of the model fit significantly better than a linear model. (Most significant of the ten p-values for a test of departure from linearity was $p=0.17$.) In all but two of these ten cases, the best-fitting model was linear. [Even if the true dose response is linear, the probability is only one-half that the best fitting model to a data set will be linear (Crump et al., 1977).] Moreover, the Armitage-Doll model, which is a linear model, provided an adequate fit to all seven data sets in which there were three or more treatment groups, based on a standard chi-square goodness of fit test.

OSHA concludes that a linear dose response model is compatible with both the animal and human data on lung cancer in cadmium-exposed cohorts, and that it is also compatible with multistage mechanisms of carcinogenesis.

OSHA believes that the theoretical understanding of cancer is not sufficient to unequivocally establish a single dose response function for cadmium-induced lung cancer. In view of this uncertainty, the fact that linear models are compatible with both the current theoretical understanding of cancer and the animal and human data on cadmium, and the fact that inappropriate application of a non-linear model could seriously underestimate human risk, OSHA maintains that in order to be compatible with current scientific understanding of carcinogenesis and cadmium dose response data, and to satisfy its mandate to protect worker health, OSHA should give particular consideration to estimates of cancer risk obtained from linear models.

Among the various linear models applied to either the animal and human data, OSHA is unable to select a single one as being most appropriate. However, OSHA does not believe that this is a serious problem because the different linear models generally provided similar estimates of risk when applied to the same data.

All of the risk estimates derived from the Thun cohort (Tables VI–9 and VI–12) are based upon linear models. All of the risk estimates derived from animal data (Table VI–6) are based upon linear dose responses except the fits of the multistage-Weibull model to the Oldiges et al. data on male rats exposed to $CdCl_2$ or to CdO fume.

Comparing the estimates of excess risk of lung cancer made from animal data (Table VI–6) with those made from human data, OSHA finds that they are in essential agreement. Estimates based upon human data of the excess risk from lung cancer from 45 years of exposure at a TWA of 5 $\mu g/m^3$ range from three excess deaths per 1000 workers to nine excess deaths per 1000 workers (Tables VI–9 and VI–12). The corresponding ranges in excess risk made from the three models applied to animal data are as follows: multistage model, 0.061–28 excess deaths; Armitage-Doll model, 3.3–38 excess deaths; multistage-Weibull model, 0.095–35 excess deaths. The corresponding ranges for numbers of excess deaths estimated per 1000 workers from 45 years of exposure to a TWA of 100 $\mu g/m^3$ are as follows: Human data, Thun cohort, 58–157 excess deaths; animal data, multistage model, 24–433 excess deaths, animal data, Armitage-doll model, 6.8–726 excess deaths, animal data, multistage Weibull model, 37–512 excess deaths. Although estimates made from animal data tend to be somewhat higher than those made from human data, the ranges of risk obtained from each of the three models applied to animal data overlap the range obtained from the human data. The excess risks from exposure to CdO-fume estimated using animal data are somewhat smaller than the risks estimated from the other forms of cadmium; Dr. Oberdörster hypothesized that this could be attributed to a lower uptake by the lung of the inhaled fume (Ex. 141). The ranges of risks from the animal data are much narrower if the CdO data are omitted. However, the resulting ranges still overlap the estimates obtained from the human data.

It may be that the estimates obtained from human data are somewhat more reliable than those obtained from the animal data because the former do not involve the uncertainty of cross-species extrapolation. However, the similarity of results from animal and human studies serves to strengthen OSHA confidence in estimates obtained from both types of data.

Based on human data, OSHA's preferred estimates of the excess lung cancer risk from 45 years of occupational exposure to cadmium are 58 to 157 excess deaths per 1000 workers from exposure to a TWA of 100 $\mu g/m^3$ and three to nine excess deaths per 1000 workers from exposure to a TWA of 5 $\mu g/m^3$. OHSA notes that estimates of excess deaths exceed one death per thousand workers even at a TWA exposure of 5 $\mu g/m^3$.

Risk Assessment for Kidney Dysfunction

In its proposed rule, OSHA quantified the risk of kidney dysfunction due to cadmium exposure using the study by Falck et al. (Ex. 4–28) of workers at a refrigeration compressor production plant and the study by Ellis et al. (Ex. 4–27) of workers at the cadmium smelter in Colorado. OSHA has since identified four additional studies that contain useful quantitative information on kidney effects from cadmium exposure. These are: (1) the study by Elinder et al. (Ex. L–140–45) of a cohort of 60 workers who had previously been exposed to cadmium through welder fume and dust associated with the use of cadmium soldiers; (2) the study by Jarup et al. (Ex. 8–661) of 440 workers exposed to cadmium at a Swedish battery plant; (3) the study by Mason et al. (Ex. 8–669) of 75 workers exposed to copper-cadmium alloy in a factory in the United Kingdom; (4) the study by Thun et al. (Ex. 19–43B), which is based on the same population of smelter workers studied earlier by Ellis et al. However, the data reported by Thun et al. (Ex. 19–43B) are not in a form that is suitable for quantitative modelling and consequently data from this study were not modelled by OSHA.

Table VI–15 summarizes some essential features of these studies. Many differences are noted in these studies, including size of study; type of cadmium; type, extent and quality of exposure data; type of urine sample; control of samples for pH; and definition of kidney dysfunction. Each of these differences could result in differences in quantitative estimates obtained from these studies.

TABLE VI–15.—FEATURES OF CADMIUM STUDIES OF KIDNEY EFFECT

	Falck (Ex. 4–28)	Ellis (Ex. 4–27)	Elinder (Ex. L–140–45)	Mason (Ex. 8–669A)	Jarup (Ex. 8–661)	Thun et al. (Ex. 19–43B)
Exposure site	(Michigan) Silver hazing wire in refrigerator compressors.	Smelter in Colorado	Swedish factory	U.K. copper-cadmium alloy factory.	Swedish battery factory.	Smelter in Colorado.
Type of exposure	Fume	Dust, fume	Welder fume, some dust.	CdO fume	CdO dust	Dust, fume.
Number exposed	33	82	60	75	440	45.
Non-cadmium controls.	41	None	None	75	None	32.
Matching	No			1:1 by age		No.
Sample type	Spot + 24 hr	24 hour	Spot	3-hr	No mention	Spot.
pH	Adjusted above 5.5	Adjusted	>5.6 (sodium bicarbonate).	Recorded	No control	No control.
Freezing of samples	Yes	Yes	No mention	Yes	No mention	No mention.
Effect definition	β_2>629 μg/creatinin	β_2>200 μg/g c. or total protein >250 mg/g creatinin.	β_2>300 μg/g creatinin.	RBP>89.9 μg/g creatinin.	β_2>310 μg/g creatinin.	β_2>486 μg/g creatinin.
Exposure	Earliest exposure data not stated (possibly 1961); automatic line opened in 1968; air sampled since 1961 by Michigan D.I.H.; 81 total samples; no time trends for either line; arithmetic average of all samples from each line used to calculate time-weighted exposures.	Occurred 1925–1983; 858 samples for years 1955–1976; 187 samples for years 1943–1954 not used (different measurement techniques); area sampling data adjusted to represent personal exposures using ratio (2:6) based on 1973–1976 data.	Occurred 1955–1978; 6 area and 27 personal measurements in 1976; 17 more in 1976–1977 after improvements; individual exposure assigned by a group of four.	Occurred 1926–1983; 482 samples (one-half area samples) for years 1964–1983; area samples adjusted upward by 20%; exposures estimated for years 1926–1963.	Measurements in air collected since 1947	Same as used by Ellis *et al.* except updated to cover 1979–1985.

In each of these studies, data were obtained on the cumulative cadmium exposure of each subject and on the concentration of a small molecular weight protein in urine [β2–microglobulin or retinol binding protein (RBP)], an excess of which is considered evidence of kidney dysfunction. Data on the protein levels in urine were available in two distinct forms. First, in each of the published reports of these studies, a cutoff level was specified that defined the boundary between normal individuals and those with proteinuria. The information available in these published reports was in terms of the "zero-one" variable that specified whether or not measured protein levels in a subject exceeded (coded as "one") or did not exceed (coded as "zero") the cutoff level. Such data are called quantal data. Second, the unpublished concentrations of marker proteins in urine from the Mason et al. study were made available to OSHA by Mr. Mason (Ex. 12–45). These type of data are called continuous data. Different types of statistical models are required for these two types of data.

The Office of Budget and Management (OMB) (Ex. 17–D) questioned OSHA's use of quantal data from the Falck et al. and Ellis et al. studies for risk modelling in the Proposed Rule. In both of these studies, data were only available in quantal form as presented in the published papers. Thus, OSHA had no choice over either whether to use quantal data in its modelling or the cutoff used to define kidney dysfunction in these studies. In the risk modelling to be presented below, OSHA reanalyzes the quantal data from the Falck et al. and Ellis et al. studies, and also analyzes data from the studies by Elinder et al., Jarup et al. and Mason et al. In all of these studies except Mason et al., data were available only in a quantal form derived from a cutoff selected by the original authors for defining kidney dysfunction. However,

since OSHA had access to the unpublished continuous data from the Mason et al. study, OSHA was able to explore the effect of different cutoffs for kidney dysfunction upon the analysis. (Such an analysis was suggested by OMB, Ex. 17–D). OSHA also applied models appropriate for continuous data to the continuous data of Mason et al.

Risk Assessment Based Upon Quantal Data

In the proposed rule, OSHA presented quantitative estimates based on the logistic model, which can be expressed as

$$\text{Ln}\{P(X)/[1-P(X)]\}=\alpha+\tau * \text{Ln}[X]$$

or, equivalently,

$$P(X)=e^{\alpha} * X^{\tau}/(1+e^{\alpha} * X^{\tau})$$

where

Ln indicates the natural logarithm,
X is cumulative occupational exposure in μg-years/m³,
P(X) is the probability of kidney dysfunction in a person with a cumulative cadmium exposure of X, and
α and τ are regression parameters estimated from the data.[5]

This logistic regression model is widely used to model quantal responses (in this case 0 = normal kidney function and 1 = abnormal kidney function) as a function of one or more explanatory variables (in this case cumulative exposure to cadmium). When used to define a dose response, as in the present situation, it provides a flexible model that is able to accommodate a wide range of dose response shapes ranging from threshold-like (when the parameter τ is large) to a shape that is linear (τ = 1) or even supralinear (τ < 1) at low doses.

The model as formulated above cannot accommodate any level of kidney dysfunction in persons without cadmium exposure (since the model definition implies the restriction P(0) = 0). However, kidney dysfunction is not restricted to persons with prior cadmium exposure. (In several studies the cutoff used to define proteinuria was either an upper quantile, or a statistical upper confidence limit, on the level of the marker protein in unexposed subjects, which implies that a quantifiable number of unexposed subjects would have urinary levels above the cutoff; e.g., Mason et al. defined their cutoff as the 95% upper quantile on the level of retinol binding protein in unexposed subjects; consequently, by definition, a background approaching 5% would be expected.)

The need for incorporating background response in the model was noted by several commenters. Dr. Starr pointed out this problem in his oral testimony, noting that "some adjustment must be made in the analysis procedure to account for that background response rate, which is not attributable to cadmium exposure" (Tr. 6/8/90). ENVIRON Corp. (Ex. 19–43G) indicated that, because of this (unexposed workers identified as having kidney disease), OSHA should use an independent background parameter that properly accounts for this false positive response rate. Mr. Edwin Seeger, representing the Cadmium Council, pointed out that (Ex. 19–43) the Council believes that OSHA's renal dysfunction risk estimate is biased high at low dose levels because it does not take account of the "normal incidence of elevated β2-microglobulin levels in the worker population even in the absence of cadmium exposure."

OSHA has therefore modified the logistic model in this revised quantitative risk assessment to include a background term. The modified model is

$$P(X)=(\delta+e^{\alpha *} X^{\tau}/(1+e^{\alpha *} X^{\tau}),$$

where δ is the probability of kidney dysfunction among persons not exposed to cadmium (δ = P(0)). Thus, this revised model is able to accommodate kidney dysfunction in persons unexposed to cadmium by estimating a positive value for δ.

This model has been applied to quantal data from five of the six of the studies described above. The Thun et al. study was excluded because the data were not reported in a form that is amenable to this type of analysis. The model was fit to the data from Elinder et al. (Elinder et al. Table II) and Jarup et al. (Jarup et al. Table 1), in which the subjects in the study were grouped according to their cumulative cadmium exposure. These data sets are listed in Table VI–16. Data for the Ellis et al. study used in the analysis were read from Figure 3 of the Ellis et al. study (Ex. 4–27) by OSHA and also an OSHA contractor (Ex. 16–B). Both data sets were analyzed and similar results were obtained. Results obtained from the OSHA reading are reported on herein (Ex. 4–27–A).

TABLE VI–16.—KIDNEY DYSFUNCTION VERSUS CUMULATIVE CADMIUM EXPOSURE FROM JARUP ET AL. (1988) AND ELINDER ET AL. (1985)

Cumulative cadmium exposure (μg-years/m³)		Number with kidney dysfunction/ number examined
Range	Midvalue	
Jarup et al. (1988)[a]		
< 359	131	3/264
359–<1710	691	7/76
1710–<4578	3460	10/43
4578–<9458	6581	10/31
9458–<15,000	12,156	5/16
15,000+	21,431	5/10
Elinder et al. (1985)[b]		
<1000	500	3/16
1000–<2000	1500	7/22
2000–<3000	2500	4/9
3000–<5000	4000	5/8
5000+	7500	5/5

[a] Definition of kidney dysfunction: β₂-microglobulin > 310 μg/g creatinin.
[b] Definition of kidney dysfunction: β₂-microglobulin > 300 μg/g creatinin.

Data from the Falck et al. (Ex. 4–28) study came from Table III of that paper. Falck et al. omitted three subjects, all of whom had elevated β₂-microglobulin in their spot kidney sample, from their statistical analysis because one (#14) was a controlled diabetic, one (#30) had a history of kidney infection, and one (#32) was hypertensive. OSHA, however, considers that it may not be appropriate to eliminate these subjects when estimating the effect of cadmium exposure in the general population because of the following statistical/study design concerns and biological reasons: (1) it is not clear from Falck et al. (Ex. 4–28) that the same exclusion rules were applied to subjects exposed to cadmium who had negative spot samples; (2) it is not clear from the report that the exclusion rules were applied to the controls; (3) these conditions also may occur among persons with occupational exposure to cadmium and these persons need to be protected from the adverse kidney effects of cadmium as well. OSHA therefore applied the modified logistic model to the complete data set of Falck et al. [N=33) as well as to the reduced data set obtained by omitting subjects #14, #30, and #32. OSHA also made a third analysis of the complete data set in which subject #4 (who had an elevated spot urine sample that was not confirmed by the 24-hour sample) was considered to be affected. OSHA notes that there are large differences between the β₂-microglobulin levels measured in spot samples and in 24-hour samples; β₂-microglobulin levels in the 24-hour

[5] In the proposed rule, β was used in place of τ in thed logistic regression model. However, both the proposed rule and the present document also used β as a potency parameter in the cancr models (i.e., β multiples cumulative cadmium dose, X, in the cancer models) whereas the parameter designated as β in the logistic regression model in the proposed rule is a shape parameter (i.e., cumulative dose, X, is raised to the power β). To avoid confusion, the symbol for this shape parameter has been chaned to τ.

samples are up to 200 times smaller than the levels in the spot samples. These differences are not explained by Falck et al. and no mention is made of controlling or testing for pH in the 24-hour samples. Thus, OSHA is of the opinion that the data from this study are less reliable for quantitative analysis as compared to the data from the remaining studies.

Mason et al. used elevated levels of RBP to define cadmium workers who were considered to have cadmium proteinuria. RBP was used instead of β_2-microglobulin because RBP appears to be less sensitive to urine pH than β_2-microglobulin, and because pH apparently was not adjusted or controlled in the Mason et al. study. However, since OSHA intends to base its regulations on urinary β_2-microglobulin levels, it was necessary for OSHA to relate the RBP levels in the Mason et al. study to corresponding levels of β_2-microglobulin, after adjusting for pH.

A regression of the logarithm of RBP level on the logarithm of urinary β_2-microglobulin concentration, restricted to the 114 samples for which the urine pH was 5.5 or greater, revealed a highly significant relationship ($p < 0.0001$) that explained a large proportion of the variation in the data ($R^2 = 0.84$). When the same analysis was performed on the 60 samples for which the pH was less than 5.5, although a highly significant relationship was also obtained ($p < 0.0001$), the R^2 was considerably smaller ($R^2 = 0.27$). OSHA concluded from this analysis that these data indicate that there is a relationship between RBP levels and β_2-microglobulin levels in urine samples in which the pH is 5.5 or greater that can be used to relate the level of 300 μg/g creatinine, or, equivalently, 33.8 μg/mmole creatinine, of β_2-microglobulin (used by OSHA to define proteinuria) to a corresponding level of RBP. The regression equation obtained, based on samples with pH of 5.5 or higher, was

$$\text{Ln}(R) = 0.032 + 0.88 * \text{Ln}(B2),$$

where R and B2 represent levels of RBP and β_2-microglobulin, respectively, in urine measured in units of μg/g creatinine. This equation indicates that an RBP level of 156 μg/g creatinine corresponds to a β_2-microglobulin level of 300 μg/g creatinine. Based on this cutoff, 15% of Mason et al.'s matched referents (11/72) would be defined as having proteinuria. On the other hand, Mason et al. indicate that they used the upper 95th percentile for urinary RBP calculated from their matched referent population to define cadmium workers who were considered to have proteinuria. Although Mason et al. do not specify this 95th percentile, based on the raw data from this study, OSHA has calculated this percentile as 338 μg of RBP per gram creatinine. OSHA has conducted analyses of the Mason et al. data using both of these cutoff levels, that is, considering subjects with urinary levels of RBP in excess of either 156 μg/g creatinine (Mason 1) or 338 μg/g creatinine (Mason 2) as having proteinuria.

Since there are questions regarding whether supralinear dose responses are reasonable for biological responses (see, e.g., Crump, 1985), whenever a $\tau < 1$ was estimated, the model was refit with τ fixed and equal to one. This occurred only with the data from the Jarup et al. study.

OSHA made a total of nine fits of the logistic model, modified to incorporate background response, to quantal data from five studies: the Elinder data; the Ellis data; three versions of the Falck data that involved minor changes in cohort definition and designation of subjects with proteinuria; two fits to the Jarup data, one with $\tau < 1$ (Jarup 1), and one with $\tau = 1$ (Jarup 2); and two versions of the Mason data using different cutoffs for defining subjects with proteinuria. The model was fit to data from the Elinder et al. and Jarup et al. studies that had been grouped by the authors into five and six exposure groups, respectively (Table VI-16). In the remaining studies the model was fit to the ungrouped data.

TABLE VI-17.—SUMMARY OF FIT OF MODIFIED LOGISTIC MODEL TO DATA ON KIDNEY DYSFUNCTION

Data set	Parameter estimate		
	δ	α	τ
Elinder	0.215	−23.74	2.92
Ellis	0.040	−11.1	1.60
Falck:			
1[a]	0.0663	−37.6	5.19
2[b]	0.139	−55.8	7.84
3[c]	0.0748	−56.4	7.93
Jarup:			
1[d]	0.0	−8.0	0.81
2[e]	0.0054	−9.6	1.0
Mason 1[f]	0.17	−26.1	3.7
Mason 2[g]	0.062	−18.6	2.51

[a] Includes all 33 subjects.
[b] Considers subject number 4 to have kidney dysfunction.
[c] Omits subjects 14, 30, 32.
[d] τ unrestricted.
[e] Restriction imposed of $\tau = 1$.
[f] Kidney dysfunction defined as RBP ≥ 18 μmoles/mg creatinine.
[g] Kidney dysfunction defined as RBP ≥ 38 μmoles/mg creatinine.

Table VI-17 records the estimates of the parameters δ, α, and τ of the logistic model for each of the nine fits to the five data sets, and Table VI-18 records the results of chi-square goodness-of-fit tests applied to each of the fits except those based on the Falck et al. data. (There were not enough affected subjects in this study to provide a valid goodness-of-fit test.) Although the logistic model was fit to the ungrouped data from Mason et al. and Ellis et al., the data were subsequently grouped into exposure groups as shown in Table VI-18 to obtain large enough expected numbers of affected subjects in each group to yield a valid goodness-of-fit test. As indicated by Table 18, the modified logistic model provided a good fit to each of the data sets. This indicates that there is no statistical evidence in these studies that the modified logistic regression model is not an appropriate model for modelling kidney dysfunction as a result of cadmium exposure.

TABLE VI-18.—FIT OF LOGISTIC MODEL TO DATA ON KIDNEY PROTEINUREA [a]

Cadmium exposure range (μg-year/m³)	Number of subjects	Number of cases		Chi-square (df) [b]	Lack of fit p-value
		Observed	Expected		
Elinder (Ex. L-140(45)):					
0–1000	16	3	3.5		
1000–2000	22	7	6.2		
2000–3000	8	4	4.0		
3000–5000	8	5	5.6		
5000+	5	5	4.7	0.63 (2)	0.66 (NS)
Ellis (Ex. 4-27):					
5–800	39	8	6.7		
820–1567	11	4	6.3		

TABLE VI–18.—FIT OF LOGISTIC MODEL TO DATA ON KIDNEY PROTEINUREA [a]—Continued

Cadmium exposure range (μg-year/m³)	Number of subjects	Number of cases		Chi-square (df) [c]	Lack of fit p-value
		Observed	Expected		
1600–2500	10	8	7.5		
3000–4900	8	7	7.2		
5000–6100	7	7	6.6		
6500–20,830	7	7	6.8		
				1.2 (3)	0.76 (NS)
Jarup 1 [b] (Ex. 8–661):					
0–359	264	3	4.7		
359–1710	76	7	5.0		
1710–4578	43	10	8.9		
4578–9458	31	10	9.4		
9458–15,000	16	5	6.7		
>15,000	10	5	5.3		
				2.5 (3)	0.48 (NS)
Jarup 2 [c] (Ex. 8–661):					
0–359	264	3	3.9		
359–1710	76	7	4.0		
1710–4578	43	10	8.7		
4578–9458	31	10	10.0		
9458–15,000	16	5	7.5		
<15,000	10	5	6.1		
				4.9 (4)	0.30 (NS)
Mason 1 [d] (Ex. 8–669A):					
0	96	15	16.8		
30–752	37	9	7.1		
810–1424	15	7	7.7		
1501–3219	8	8	7.0		
3752–5263	8	8	7.9		
6849–13,277	7	7	7.0		
				0.86 (2)	0.65 (NS)
Mason 2 [e] (Ex. 8–669A):					
0–192	109	7	6.8		
209–1414	38	7	7.0		
1424–3752	10	6	6.8		
3793–5263	7	7	6.5		
6849–13,277	7	7	6.9		
				0.15 (2)	0.93 (NS)

[a] df = degrees of freedom.
[b] Fitting was based on ungrouped data for Mason 1, Mason 2, and Ellis.
[c] β unrestricted.
[d] Restriction imposed of $\beta = 1$.
[e] Kidney dysfunction defined as RBP ≥ 18 μmoles/mg creatinine.
[f] Kidney dysfunction defined as RBP ≥ 38 μmoles/mg creatinine.

Table VI–19 provides estimates of the numbers of cases of proteinuria per 1000 workers exposed for a 45-year working lifetime at various 8-hour TWA exposures. Estimates in this table are based on extra risk {P(X)−P(0)/[1−P(0)]}, and confidence intervals were computed by the likelihood method. The results in Table VI–19 from the Ellis data and the Falck data differ from those contained in the proposed rule. The principle reason for this is that, unlike the model used to obtain the results in Table VI–18, the version of the logistic model used in the proposed rule did not allow for background response. OSHA considers the modified logistic model that incorporates background response to be more appropriate.

TABLE VI–19.—ESTIMATE OF KIDNEY PROTEINUREA PER 1000 WORKERS WITH 45 YEARS OF OCCUPATIONAL EXPOSURE TO CADMIUM DERIVED FROM MODIFIED LOGISTIC MODEL

8-Hour TWA exposure (μg/m³)	Elinder (Ex. L–140(45))	Ellis (Ex. 4–27)	Falck 1 [a] (Ex. 4–28)	Jarup 1 [b] (Ex. 8–661)	Jarup 2 [c] (Ex. 8–661)	Mason 1 [d] (Ex. 8–669A)	Mason 2 [e] (Ex. 8–669A)
1	3.3E–3 (0, 21) [f]	8.7 (0.27, 75)	1.8E–5 (0, 8.1).	7.6 (2.4, 16).	3.2 (1.3, 4.6).	5.2E–3 (0, 0.15).	0.12 (4.1E–4, 4.7).
5	0.37 (0, 99)	95 (14, 288)	7.5E–2 (0, 62).	27 (12, 45).	16 (8.3, 23).	1.9 (0, 12).	7.0 (0.29, 53).
10	2.8 (0, 180)	234 (69, 448)	2.7 (0, 145).	47 (25, 70).	31 (18, 44).	24 (0, 80).	39 (4.5, 142).
20	21 (0, 305)	472 (266, 636)	91 (4.4E–3, 362).	80 (49, 109).	60 (38, 85).	236 (0.17, 478).	166 (61, 354).
50	235 (3.4E–3, 555)	786 (652, 891)	921 (485, 1000).	155 (112, 197).	138 (96, 188).	899 (797, 1000).	696 (504, 860).
100	700 (266, 964)	915 (802, 975)	998 (709, 1000).	243 (187, 306).	242 (176, 316).	991 (969, 1000).	929 (784, 988).
200	946 (691, 1000)	969 (890, 995)	1000 (857, 1000).	360 (276, 452).	390 (299, 480).	999 (995, 1000).	987 (916, 999).

[a] Based on all 33 subjects.
[b] τ unrestricted (supralinear dose response).
[c] Restriction imposed of $\tau = 1$ (*linear dose response*).
[d] Kidney dysfunction defined as RBP ≥ 156 μg/g creatinine.
[e] Kidney dysfunction defined as RBP ≥ 338 μg/g creatinine.
[f] Numbers in parentheses are 95% lower and upper bounds.

Some of the confidence intervals in Table VI–19 are fairly wide, which reflects both the small size of some of the studies and the uncertainty in extrapolating results to low TWA exposures. Considering this and the differences among the underlying studies (see Table VI–15), these analyses yield reasonably consistent results. All of the analyses predict a high incidence (24%–99.8%) of proteinuria at exposures of 100 $\mu g/m^3$. Six of the seven analyses (all except the Mason 1 analysis), provide consistent estimates of the extra risk of proteinuria at TWA cadmium exposures of 1 $\mu g/m^3$ and 5 $\mu g/m^3$, in the sense that the 90% confidence intervals from all of the analyses contain a common range. That is, with the exception of the Mason 1 analysis, all of the 90% confidence intervals for the extra risk of proteinuria at a TWA exposure of 5 $\mu g/m^3$ contain the range between 14 cases per 1000 workers and 23 cases per 1000 workers.[6] Thus, within the limits of statistical variability, these six analyses are all consistent with an extra risk of proteinuria in this range, but are not all consistent with a risk of proteinuria outside this range. (The upper 95% confidence limit from the Mason 1 analysis is 12 cases per 1000 workers, which is just barely outside the range defined by the remaining six analyses.)

Some of the differences in the risk estimates from different studies is due to different definitions of kidney dysfunction used in the various studies. For example, considering the risk of kidney dysfunction from a TWA exposure of 5 $\mu g/m^3$ cadmium, the lowest risk was obtained from the Falck et al. study, which employed the most stringent definition of kidney dysfunction (β_2-microglobulin >629 μg/g creatinine [Table VI–15]), whereas the highest risk was obtained from the Ellis et al. study, which employed a much more liberal definition of kidney dysfunction (β_2-microglobulin >200 $\mu g/g$ creatinine [Table VI–15]). Other reasons for the differences in the risk estimates include different methods for controlling pH and differences in the quality and quantity of extent of exposure data and the methods used for estimating exposures from these data (Table VI–15). Considering these differences, and also the statistical uncertainty in the five studies due to small sample sizes, OSHA believes that the analyses summarized in Table VI–19 present a consistent picture of risks of kidney dysfunction from cadmium exposure. The best estimates from these analyses of the risk of kidney dysfunction from 45 years of occupational exposure to a TWA concentration of 5 $\mu g/m^3$ cadmium are in the range of 14 to 23 cases per 1000 workers.

Risk Assessment Based Upon Continuous Data from the Mason et al. Study

Since it had access to the raw data from the Mason et al. study (Ex. 8–669A), in addition to modelling, as discussed earlier, OSHA was able to model the continuous data from the Mason study on the actual level of RBP in the urine as a function of cumulative cadmium exposure. This approach does not require collapsing the urinary data into a yes-no response, and consequently may make more efficient use of the data.

OSHA applied two types of models to the continuous data from the Mason study: One that made use of the matching by Mason et al. of referents to exposed subjects, and one that did not make use of this matching. The matched analysis was applied to 72 matched pairs of exposed subjects and referents. (Although Mason et al. [Ex. 8–669A] reported 75 pairs in their analysis, in the data provided to OSHA, RBP values were missing for three of the matched referents.) The unmatched analysis was applied to all of the exposed subjects and referents recorded in the data furnished to OSHA by Mr. Mason for which there was both a cadmium exposure and a urinary value of RBP reported (the cadmium exposure was assumed to be zero for referents); this analysis included 75 exposed subjects and 96 referents.

In the model fitting that made use of the matching, the quantity $Log[R_e/R_r]$, where R_e is the urinary RBP of an exposed subject and R_r is the urinary RBP of the matched referent, was assumed to have a normal distribution with mean $\alpha * (X-X_0)^\tau$ and standard deviation, σ (independent of X), where

X is the cumulative cadmium exposure of the exposed subject in μg-yr/m^3,

X_0 is a posited potential threshold exposure to cadmium below which cadmium cannot adversely affect the kidney, and

α and τ are parameters estimated from the data. [Throughout this discussion, the expression $(X-X_0)^\tau$ is taken to be zero if $X \leq X_0$.]

In the model fitting that did not consider the matching, $Ln[R_e]$ is considered to have a normal distribution with mean $\delta+\alpha * (X-X_0)^\tau$ and standard deviation σ, where δ is a parameter representing the mean amount of urinary RBP in persons not exposed to cadmium. The remaining parameters have the same meaning as the model applied to the matched data.

Table VI–20 shows the results of fitting these models and various simpler submodels to the continuous data from the Mason et al. study. Considering the analyses applied to the unmatched data, in Case I the mean of the logarithm of urinary RBP $\{E[Ln(R_e)]\}$ is assumed to vary linearly with cumulative cadmium exposure; in Case II this mean is allowed to vary in a non-linear fashion with cumulative cadmium exposure (sub-linear if $\tau>1$, and supralinear if $\tau<1$). In Case III a threshold of X_0 μg-years/m^3 is assumed for the effect of cadmium; urinary RBP is assumed to be unaffected by cadmium exposure as long as the cumulative cadmium exposure is below X_0 μg-years/m^3 (the value of the threshold X_0 is estimated from the data). The mean of the logarithm of urinary RBP is assumed to increase linearly with increasing cumulative cadmium exposure for exposures higher than the threshold cadmium exposure of X_0. Case IV is a modification of Case III in which the mean of the logarithm of urinary RBP is allowed to increase non-linearly for exposures above the threshold cadmium concentration. Cases I–IV have similar meanings in the analyses applied to the matched data.

TABLE VI–20.—RESULTS OF FITTING MODELS TO CONTINUOUS DATA ON RETINAL BINDING PROTEIN (RBP)

	Log-likelihood
Analyses Based on Unmatched Data	
I. $E[Ln(R_e)]=\delta+\alpha X$ $\delta=2.14$; $\alpha=0.000687$; $\sigma^2=1.33$	−24.18
II. $E[Ln(R_e)]=\delta+\alpha X^\tau$ $\delta=2.04$; $\alpha=0.00406$; $\tau=0.803$; $\sigma^2=1.29$	−21.56
III. $E[Ln(R_e)]=\delta+\alpha (X-X^o)$ $\delta=2.14$; $\alpha=0.000687$; $X_0=0$, $\sigma^2=1.33$	−24.18
IV. $E[Ln(R_e)]=\delta+\alpha [(X-X_0)]^\tau$ $\delta=2.10$; $\alpha=0.0149$; $\tau=0.663$; $X_0=449$; $\sigma^2=1.24$	−18.58
Analyses Based on Matched Data	
I. $E[Ln(R_e/R_r)]=\alpha X$ $\alpha=0.000690$; $\sigma^2=3.22$	−42.10
II. $E[Ln(R_e/R_r)]=\alpha X^\tau$ $\alpha=0.00515$; $\tau=0.774$; $\sigma^2=3.05$	−40.22
III. $E[Ln(R_e/R_r)]=\alpha (X-X_0)$ $\alpha=0.000690$; $X_0=0.0$; $\sigma^2=3.22$	−42.10
IV. $E[Ln(R_e/R_r)]=\alpha [(X-X_0)]^\tau$ $\alpha=0.147$; $\tau=0.408$; $X_0=1040$; $\sigma^2=2.75$	−36.37

R_e—Urinary RBP in subject exposed to X μg-year/m^3 cadmium.

R_r—Urinary RBP in matched.

Note: In these expression, $X-X_0$ is taken to be zero if $X<X_0$.

[6] The 95% upper and lower confidence bounds presented in Table 19, when considered in combination, define 90% confidence intervals.

With no threshold in the model (Cases I and II), a non-linear model (Case II) provides a significantly better fit than a linear model (Case I) [based upon a likelihood ratio test (Cox and Hinkley, 1974)]. The better-fitting non-linear model is supralinear ($\tau=0.803<1$ for the unmatched analysis, and $\tau=0.774<1$ for the matched analysis). Based on linear models only (Cases I and III), the data do not provide any evidence of a threshold, because even if a threshold is permitted in the model (Case III), it is estimated as zero (i.e., no threshold). However, a non-linear model with a threshold (Case IV) provides a significantly better fit than either a non-linear model with no threshold (Case II) or a linear model with a threshold (Case III). Again, the better-fitting model is supralinear for doses above the threshold ($\tau=0.663<1$ for the unmatched analysis and $\tau=0.408<1$ for the matched analysis). These conclusions hold both for analyses based on matched data and those based on unmatched data.

The extra risk of proteinuria in a person exposed to X μg-yr/m^3 is defined as [P(X)–P(0)]/[1–P(0)], where P(X) is the probability of proteinuria in a person with a cumulative cadmium exposure of X μg-years/m^3. Based on the model assumptions given above, it can be shown that for the unmatched analyses, P(X) is given by

$$P(X)=1-N\{[Ln(338)-\delta-\alpha*(X-X_0)^\tau]/\sigma\}$$

where N is the standard normal distribution function, and 338 μg/g creatinine is the cutoff value for RBP in urine used to define proteinuria in the Mason et al. study.

The model used for the matched analysis data provides an estimate of the ratio of the RBP level in an exposed individual relative to what his baseline RBP level would be if he had not been exposed to cadmium. (This baseline value was estimated by the RBP level in a matched control in the matched analysis.) In the calculations presented, OSHA used 111 μg/g creatinine for this baseline, which was the average value from the 96 referents in the Mason et al. study. Consequently, for the matched analyses,

$$P(X)=1-N\{[Ln(3.045)-\alpha*(X-X_0)^\tau]/\sigma\},$$

where 3.045=338/111. Thus, the matched analysis is estimating the probability that the RBP level is about tripled ($3.045\simeq3$).

TABLE VI–21.—ESTIMATE OF KIDNEY PROTEINUREA PER 1000 WORKERS WITH 45 YEARS OF OCCUPATIONAL EXPOSURE TO CADMIUM DERIVED FROM CONTINUOUS MASON DATA

8-hour TWA exposure (μg/m^3)	Models I, III	Model II	Model IV
Based on Unmatched Analyses			
1	5.2	13	0
5	28	54	0
10	60	107	2.3
20	139	224	204
50	465	606	681
100	908	947	970
200	1000	1000	1000
Based on Matched Analyses			
1	7.8	25	0
5	40	91	0
10	82	161	0
20	170	287	0
50	450	593	469
100	818	879	889
200	997	996	992

See Table 20 for definition of models.

Table VI–21 provides estimates of the numbers of cases of proteinuria per 1000 workers exposed for a 45-year working lifetime at various 8-hour TWA exposures derived from analyses of continuous data from the Mason et al. study. Models I, II, and III predict between 28 and 91 cases of proteinuria per 1000 workers exposed to a TWA of 5 μg/m^3. These estimates are considerably higher than those in Table VI–19 derived from the Mason data, and are also generally higher than those in Table VI–19 derived from other data sets. Turning to the estimates in Table VI–21 derived from Model IV (non-linear model incorporating a threshold), based on matched analyses the model predicts no risk for TWA exposures of 20 μg/m^3 or below. (This model predicted a threshold of 1040 μg-years/m^3 [Table VI–20], which is equivalent to a TWA exposure for 45 years of 1040/45=23 μg/m^3.) However, the model predicts a very high risk of proteinuria for exposures slightly higher than the predicted threshold (e.g., it predicts that 469 out of 1000 workers exposed for 45 years to a TWA cadmium exposure of 50 μg/m^3 will develop proteinuria.)

Based on unmatched analyses, Model IV predicts no risk for TWA exposures of 5 μg/m^3 or below. (This model predicted a threshold of 449 μg-years/m^3 [Table VI–20], which is equivalent to a TWA exposure for 45 years of 449/45=9.98 μg/m^3.) However, this model likewise predicts a sharply-increasing risk of proteinuria for exposures higher than the predicted threshold (e.g., it predicts that 204 out of 1000 workers exposed for 45 years to a TWA cadmium exposure of 20 μg/m^3 will develop proteinuria.)

To further explore the relationship between cadmium exposure and urinary RBP in Mason et al. study, OSHA developed three plots showing the Mason et al. data and the fit of the various models to these data. Figure VI–1 is a log-log plot of the ratios of RBP level in cadmium-exposed subjects to the RBP level in matched referents versus cumulative exposure to cadmium. (For Figures VI–1–VI–4, see the end of this section VI—Quantitative Risk Assessment.) This figure shows there is a considerable amount of variability in the data points about the mean curve, no matter which model is used to describe the mean. Figure VI–2 is a similar plot for the unmatched analyses, and this plot likewise shows a considerable amount of variability in the data points about the mean curves. For visual reference, the referent RBP values are plotted along the left vertical axis in Figure VI–2 (although since a log scale is being used for dose, theoretically they should be plotted infinitely far to the left at an x-axis value of minus infinity). Visually, there appears to be little difference between the fits of the different models in Figure VI–2. Figure VI–3 is exactly the same plot as Figure VI–2, except than in Figure VI–3 a linear scale has been used for cumulative cadmium exposure (the x-axis) rather than a log scale. Use of a linear scale also allows both referents and cadmium-exposed subjects to be legitimately included in the same graph. The dose response suggested by Figure VI–3 appears less "threshold-like" than that suggested by Figure VI–2 and suggests that any indication of a threshold by Figure VI–2 may be an artifact stemming from the use of a log-scale for cadmium exposure.

The models applied to the continuous data only estimated a threshold in conjunction with a supralinear dose response ($\tau<1$). If the models were not allowed to be supralinear [i.e., constrained to be linear or sublinear, $\tau\geq1$], the model predicted no threshold. This superlinearity causes the models to predict a very rapid rise in risk at cadmium exposures slightly above the estimated threshold (Figures VI–1–VI–3). Consequently, if this supralinearity is in fact real, if the threshold is slightly overestimated, the risk at the estimated threshold could be significant. Moreover, there are questions regarding whether supralinear dose responses are biologically plausible (Crump, 1985).

In addition, there are plausible biological augments that indicate a threshold may not occur for kidney

effects of cadmium exposure. As pointed out by epidemiologist Richard Peto (1978), whenever a chemical exposure augments a health effect that occurs to some degree even among non-exposed persons by the same general mechanisms through which the background health effects occur, there is unlikely to be a threshold for that effect.[7] OSHA notes that proteinuria occurs among persons not exposed to cadmium and, further, there are sources of cadmium exposure other than the workplace. These facts, when applied to Peto's reasoning, argue that there may not be a threshold for kidney effects from cadmium exposure.

OSHA concludes that in order to insure adequate protection for exposed workers, it should give greater weight to the non-threshold models than to the models that predict a threshold. The reasons for this are threefold. First, there are plausible biological arguments that a threshold may not exist for cadmium effects upon the kidney. Second, a threshold is only estimated in conjunction with a supralinear dose response which is of questionable biological plausibility. Third, even if the estimated threshold is real, slight errors in estimation of the threshold could result in significant risk at the estimated threshold.

Thun et al. Study of Kidney Effects in Cadmium Workers

In their study of workers exposed to cadmium at the same cadmium recovery plant that was studied by Ellis et al. (Ex. 4–27), Thun et al. (Ex. 19–43B) found that increasing cadmium dose was associated with reduced absorption of β_2-microglobulin and retinol binding protein. Cadmium dose remained the most important predictor of serum creatinine levels after controlling for age, blood pressure, body size, and other factors. Although Thun et al. did not report the data in their paper in a form that could be used for quantitative dose response modelling, Thun et al. present a graph that represents the result of their own modelling (Ex. 19–43B, Figure VI–3). Based on values read from this graph, it appears that the probability of renal abnormality in unexposed subjects is about 0.12 and the corresponding probability among subjects with a cumulative cadmium exposure of 500 mg-days/m^3 (equivalent to a 45-year TWA occupational exposure to 30 μg/m^3) is about 0.2, which means that the extra risk of renal abnormality from cadmium exposure is about (0.2–0.12)/(1–0.12)=0.091, or 91 per 1000 workers. Similarly, the probability of renal abnormality among subjects with a cumulative cadmium exposure of 1000 mg-days/m^3 (equivalent to a 45-year TWA occupational exposure to 60 μg/m^3) is about 0.34, which translates to an extra risk of about 0.25, or 250 per 1000 workers. These values appear to be within the range of the quantitative estimates obtained by OSHA from other studies, and which appear in Tables VI–19 and VI–21. Thus, although OSHA was not able to conduct an independent analysis of the data from the Thun et al. study of kidney effects in cadmium-exposed smelter workers, it appears that the quantitative predictions from this study are consistent with the those developed by OSHA from other studies.

Thun et al. Review of Studies of Kidney Dysfunction in Cadmium Workers

Thun et al. (Ex. L–140–50) reviewed seven occupational studies that examined the relation of kidney dysfunction to cumulative exposure to airborne cadmium. The seven studies included the five used by OSHA for quantitative modelling [Falck et al. (Ex. 4–28), Ellis et al. (Ex. 4–27), Elinder et al. (Ex. L–140–45), Jarup et al. (Ex. 8–661), and Mason et al. (Ex. 8–669)], the study of Thun et al. (Ex. 19–43B), which was discussed above, and a study by Kjellstrom et al. (Ex. 8–233) of the same cohort of Swedish battery workers that was studied by Jarup et al. They considered both the dose-response relationship and the potential lowest cadmium exposure at which kidney effects are detectable. Figure VI–4 reproduces Figure 1 of Thun et al. (Ex. L–140–50), which presents the dose-response data for kidney dysfunction from these studies along with a risk assessment model developed by OSHA in the proposed rule and the prevalence estimated from a metabolic model by Kjellstrom (1986d, ref. in Ex. L–140–50). Thun et al. noted that, "the OSHA model generally follows the upper range of the empirical data and agrees well with the Kjellstrom and Nordberg metabolic model."

For comparison purposes, OSHA has superimposed on Thun et al.'s figure, a representation of a dose-response model estimated by fitting the modified logistic model to the data of Mason et al. (the Mason II analysis reported in Tables VI–16, VI–17, and VI–19). This particular dose-response model appeared to give results that were within the range of the results obtained by OSHA from the remaining models (see Table VI–19 and Figure VI–4). Table VI–19 indicates that this model appears to give results that are generally intermediate between those obtained using the OSHA model from the proposed rule and the metabolic model, and that, overall, the three models are in good agreement.

After reviewing the available data on the dose response of renal dysfunction, Thun et al. (Ex. L–140–50) concluded that it was impossible to identify a no-effect level for the renal effects of cadmium with certainty. Reasons for this included limited sample sizes of the studies, methodological differences between the studies, and imprecision of the exposure data. Thun et al. concluded that "The overall data suggest that the PEL for cadmium should not exceed 5 μg/m^3 to protect workers from kidney dysfunction and lung cancer over a working lifetime." This conclusion supports the independent analyses conducted by OSHA. Indeed, OSHA's analyses indicate that the risk of kidney dysfunction from 45 years of occupational exposure to a PEL of 5 μg/m^3 may be well in excess of one case per 1000 workers.

Discussion of Issues Related to Risk Assessment for Kidney Dysfunction

Two-phase Model Used by Mason et al.

Mason et al. (Ex. 8–669A) used a two-phase linear regression to model the relationship between the logarithm of the ratio of RBP levels in exposed subjects and unexposed matched referents [Ln(R_e/R_r), where R_e is the RBP level in an exposed subject, R_r is the RBP level in the matched unexposed referent] and the logarithm, Ln(X), of the cumulative cadmium exposure of the exposed subject. This model indicated that a change of slope in the relationship between RBP and cumulative cadmium exposure occurred at a cumulative exposure of 1108 μg-yr/m^3. A larger slope was indicated for cumulative exposures larger than 1108 μg-yr/m^3, and a smaller, but still positive, slope was indicated for cumulative exposure values smaller than 1108 μg-yr/m^3 (Table 6 and Figure 3 in Mason et al.).

In its proposed rule (Ex. 18, p.4083), OSHA interpreted the Mason et al. analysis as indicating that "the excess risk threshold for cadmium was approximately 1000 μg/m^3-years." However, upon reevaluation, OSHA notes that, since the slope was still positive even at doses below 1108 μg-yr/m^3, Mason et al.'s model predicts an increasing response at all levels of cumulative cadmium exposure. Thus, it does not predict a threshold for the effect of cadmium at 1,100 μg-yr/m^3.

[7] Although Peto's argument was made specifically for cancer, it applied more generally to any health effect that is augmented by exposure to a chemical through the same general mechanism.

OSHA also notes that, whether a two-phase model is suggested by the data may depend heavily upon whether cadmium exposures are log-transformed before plotting. Figure VI–2 is a plot of the Mason data using log-transformed exposures and Figure VI–3 is a plot of the same data using untransformed exposures. Figure VI–2 appears perhaps to be suggestive of a two-phase relationship whereas Figure VI–3 does not. OSHA notes that, more generally, a wide variety of dose responses (including linear, no-threshold dose responses) can be made to appear two-phase or threshold-like by using log-transformed exposures when plotting. (This is because the log-transform has the effect of placing the exposure origin at minus infinity on the log scale and thereby exerts a "stretching" effect upon the dose response at low doses. This stretching effect can be seen by comparing Figures VI–2 and VI–3.)

OSHA also notes that the two-phase linear model as applied by Mason et al. is not meaningful at low exposures because it predicts that the RBP levels in cadmium-exposed subjects will be smaller than the RBP levels in unexposed subjects by arbitrary large factors at small exposures (e.g., the model predicts that the ratio R_e/R_r approaches zero at low exposures, whereas in actuality this ratio must approach one.) Consequently, OSHA does not consider that this model is reasonable for predicting the kidney response from low cadmium exposures. On the other hand, the models used by OSHA in fitting Mason et al. continuous data assume correctly that the ratio R_e/R_r approaches one at low exposures.

Other Recommended Models for Kidney Data

Several commenters (Tr. 6/8/90) (Ex. 19–43G) recommended modelling the dose response for kidney dysfunction using the probit distribution. These recommendations were based generally on the evidence that urinary cadmium or protein levels appear to follow a log-normal distribution. For example, ENVIRON Corp. (19–43G) cited evidence that the distribution of kidney cadmium concentrations among exposed individuals is often log-normal and concluded that the probit is a "log-normal tolerance distribution model" and consequently should be used for low-dose extrapolation of cadmium renal effects. Dr. Starr (Ex. 38) also considered the probit model to be a better choice for low-dose extrapolation purposes than the logistic model used by OSHA. In support of this position, Dr. Starr offered several pieces of evidence including the following: (1) A finding by Elinder et al. (1976, ref. in Ex. 38), based on measurements taken at Swedish autopsies, that the frequency distribution of kidney cadmium concentrations was log-normal; (2) the fact that Kjellstrom (1986b, ref. in Ex. L–140–50) used a log-normal distribution for individual critical kidney cortex cadmium concentrations; and (3) a finding by Kjellstrom et al. (Ex. 8–233) that

> The individual variation in effect at the same exposure duration is great, but in each dose group a log-normal distribution of β_2-microglobulin excretion was found.

OSHA notes that all of the evidence presented by Dr. Starr addresses the distribution of cadmium or low molecular weight proteins (e.g., β_2-microglobulin) in urine within various populations. For example, the quote by Kjellstrom et al. (Ex. 8–233) refers to a log-normal distribution for concentrations within dose groups, and consequently among individuals having similar cadmium exposures. None of this evidence addresses the issue of what is an appropriate dose-response model for relating cumulative airborne concentrations of cadmium to the probability of kidney dysfunction. Contrary to what Dr. Starr implies, a log-normal distribution for protein or cadmium in the kidney does not imply a probit model for the dose response. The model fit by OSHA to the continuous cadmium data of Mason et al. (Tables VI–20 and VI–21) assumes a log-normal distribution for the distribution of RBP among persons with the same cadmium exposures and consequently is consistent with the evidence cited by Dr. Starr. However, the corresponding dose response function is not a probit model.[8]

OSHA concludes that, even if cadmium and protein levels in urine follow log-normal distributions, this in no way implies that a probit model is appropriate to model the dose response of kidney dysfunction from cadmium exposure. Dr. Lemen from NIOSH (Tr. 8–194) supported this conclusion, commenting that it doesn't matter whether the underlying β_2-microglobulin data are or are not normally distributed because they are treated dichotomously by the model.

The Office of Budget and Management (OMB) (Ex. 17–D) suggested that, since the logistic regression analyses of kidney dysfunction involved "thresholds for classification purposes" (meaning that a cutoff was derived based on urinary concentrations of β_2-microglobulin or other low molecular weight proteins and persons with urine concentrations above the cutoff were assumed to have kidney dysfunction), this "implies that kidney dysfunction is in fact a threshold-related health effect." OMB then raises the question, "To what extent does this argue against the use of a non-threshold probability model to estimate risk?" In this comment OMB is using two unrelated notions of a threshold. On one hand, they are identifying the cutoff for the urinary concentration of low molecular weight protein used to define kidney dysfunction as a "threshold" for urinary protein. On the other hand, they are suggesting that this implies the existence of a threshold of exposure to cadmium (i.e., a cadmium threshold) below which the risk of kidney dysfunction would not be increased. Thus, in one case, they are referring to a "protein threshold" and in the other case a "cadmium threshold." These two concepts are, in fact, essentially unrelated. Use of a cutoff for urinary protein levels to define kidney dysfunction is unrelated to the use of a threshold or non-threshold model for evaluating the relationship between cadmium exposure and proximal tubular dysfunction. Since there is β_2 microglobulin excreted in the general population and cadmium augments that mechanism, there is more support for the use of a non-threshold model as compared to a threshold model.

Summary of Quantitative Estimates of Kidney Dysfunction from Cadmium Exposure

OSHA has made nine sets of estimates of the risk of kidney dysfunction (Tables VI–19 and VI–21),

[8] The probit dose response is defined as $P[X]=c+(1-c)*N[a+b*Ln(X)]$, where X is cumulative dose, N indicates the normal distribution function, Ln indicates natural logarithm, and a, b, and c are parameters estimated from data. On the other hand, the dose response obtained by OSHA from its model applied to the unmatched Mason et al. data (and which assumed a log-normal distribution of RBP in subjects with the same cumulative cadmium exposure) was $P(X)=1-N\{[Ln(338)-\delta-\alpha*(X-X_0)^\tau]/\sigma\}$, where 338 $\mu g/g$ creatinine is the RBP level used to define kidney disfunction, and α, δ, X_0, τ, and σ are parameters.

These two dose responses, while superficially somewhat similar in appearance, are not the same mathematically and may provide substantially different numerical values.

A log-normal distribution for kidney concentration after a fixed cadmium exposure does not place any restriction upon the form of the dose response, because it can be shown that any dose response model is consistent with a log-normal distribution for kidney concentrations (i.e., given, *a priori*, any dose response model for the likelihood of kidney disfunction, an expression can be found for the distribution of the kidney concentration as a function of cadmium exposure that predicts the *a priori* dose response model as well as a log-normal distribution for kidney cadmium concentrations at fixed cadmium exposures).

based on data from five different studies. In addition, OSHA has reviewed estimates based on a sixth study, that of Thun et al. (Ex. 19–43B). As indicated by Table VI–15, these six studies differ in many ways. The cohorts studied come from Sweden, the United Kingdom, Michigan, and Colorado. They were exposed to cadmium in smelters and several different types of manufacturing facilities. Exposures were to different forms of cadmium, including fume, dust, welder fume, and CdO dust. The number of cadmium-exposed subjects in the studies ranged from 33 to 440, representing a difference of more than an order of magnitude. Three of the studies included non-exposed controls, and one of these matched controls to exposed subjects by age. The cadmium exposure data were of variable type and quality and different procedures were used to quantify individual exposures.

There were also considerable differences in the procedures used in collecting the urine samples. Some of the studies involve spot urine samples. Mason et al. collected 3-hour samples, Elinder et al. collected morning samples, and Falck et al. collected spot samples, but confirmed findings in subjects with kidney dysfunction using 24-hour samples. Some of the studies were based on historical urine samples and others were collected specifically in conjunction with the associated study. Elinder et al. insured that urine pH would be acceptably high by administering sodium bicarbonate prior to the sampling. Some of the remaining studies adjusted pH after collection of the sample, and others make no mention of any adjustment for pH.

There were also differences in the type of protein and the level of protein in urine used to define kidney dysfunction. Mason et al. defined kidney dysfunction in terms of RBP in urine. Ellis et al. defined kidney dysfunction using a combination of β_2-microglobulin and total protein. The remaining four studies defined kidney dysfunction in terms of β_2-microglobulin. However, these four studies use different amounts of β_2-microglobulin in urine to define kidney dysfunction; these cutoffs range from 300 $\mu g/g$ creatinine (Ex. L–140–45) to 629 $\mu g/g$ creatinine (Ex. 4–28).

Despite these differences, each of these studies demonstrated a relationship between exposure to cadmium and kidney dysfunction. In addition to the differences among the underlying studies, two different modelling approaches were applied. The logistic model, modified to include the possibility of background response, was applied to data from six studies. A model for continuous data was applied to the continuous data from the Mason et al. study. Versions of this latter model were applied that incorporated the possibility of a threshold.

All of these differences could contribute to disparities in quantitative results obtained from dose-response modelling. Given these many differences, one would not expect necessarily to get close agreement among the studies in quantitative estimates. For example, since different studies used different definitions of kidney dysfunction, different studies are actually estimating somewhat different endpoints.

However, despite differences in study protocols and modelling approaches, quantitative results are reasonably consistent. All of the results in Tables VI–19 and VI–21 predict a high risk of kidney dysfunction at a 45-year TWA cadmium exposure of 100 $\mu g/m^3$ (at least 242 cases per 1000 workers and, except for estimates based on the Jarup et al. study, at least 700 cases per 1000 workers). It was noted earlier that, with the exception of the Mason 1 analysis, the results in Table VI–19 provide consistent estimates of the extra risk of proteinuria at TWA cadmium exposures of 5 $\mu g/m^3$, in the sense that, with the exception of the Mason 1 analysis, all of the 90% confidence intervals in Table VI–19 for the extra risk of proteinuria at a TWA exposure of 5 $\mu g/m^3$ contain the range between 14 cases per 1000 workers and 23 cases per 1000 workers. (The upper 95% confidence limit from the Mason 1 analysis is 12 cases per 1000 workers, which is just barely below this range.) However, estimates of risk from exposure to 5 $\mu g/m^3$ range as high as 95 per 1000 workers (based on data from the Ellis et al. study).

The models applied to the continuous data of Mason et al. (Table VI–21) that do not predict a threshold predict extra risks at a 45-year TWA exposure to 5 $\mu g/m^3$ of between 28 and 91 cases per 1000 workers. These values are within the range of the point estimates in Table VI–19. The models that predicted a threshold only did so in conjunction with a supralinear dose response, which is of questionable biological plausibility. These threshold models predicted a no-effect threshold at a cumulative exposure equivalent to a 45-year exposure to a TWA of between 20 and 50 $\mu g/m^3$ (matched analysis), or between 5 and 10 $\mu g/m^3$ (unmatched analysis). However, both of these threshold models predict that the risk of kidney dysfunction rises rapidly for exposures slightly above the threshold. For example, the matched model predicts that the extra risk of kidney dysfunction rises from 0 per 1000 workers to 469 per 1000 workers as 45-year TWA exposures increase from 20 to 50 $\mu g/m^3$, and the unmatched model predicts that the risk rises from 2.3 per 1000 workers to 204 per 1000 workers as 45-year TWA exposures increase from 10 to 20 $\mu g/m^3$.

OSHA concludes that it should give greater weight to the non-threshold models than to the models that predict a threshold, because (1) there are plausible biological arguments that a threshold may not exist for cadmium effects upon the kidney; (2) a threshold is only estimated in conjunction with a supralinear dose response which is of questionable biological plausibility; and (3) even if the estimated threshold is genuine, slight errors in estimation of the threshold could result in significant risk at the estimated threshold. OSHA further notes that, even if the threshold estimates are taken at face value, the PEL would need to be below 10 $\mu g/m^3$ in order to prevent kidney dysfunction from a 45 year occupation exposure at the PEL.

OSHA's preferred estimates of the extra risk of kidney dysfunction is in the range of between 14 to 23 cases per 1000 workers exposed to a TWA of 5 $\mu g/m^3$ for a 45 year working lifetime. This range is consistent with the majority of the analyses conducted by OSHA, although there are individual estimates both above and below this range. OSHA notes that this risk range is considerably in excess of one per thousand.

Overall Summary of Risk Assessment for Lung Cancer and Kidney Dysfunction

OSHA has developed estimates of the risk of lung cancer from occupational exposure to cadmium using several different types of analyses based on data from animal studies of Takenaka et al. (Ex. 4–67), Oldiges et al. (Ex. 8–694D) and Glaser et al. (Ex. 8–694B) and using human data from the cohort of workers exposed to cadmium at a cadmium smelter (Thun et al., Ex. 4–68; Stayner et al., Ex. L–140–20). These animal and human data indicate an increased risk of lung cancer from occupational exposure to cadmium.

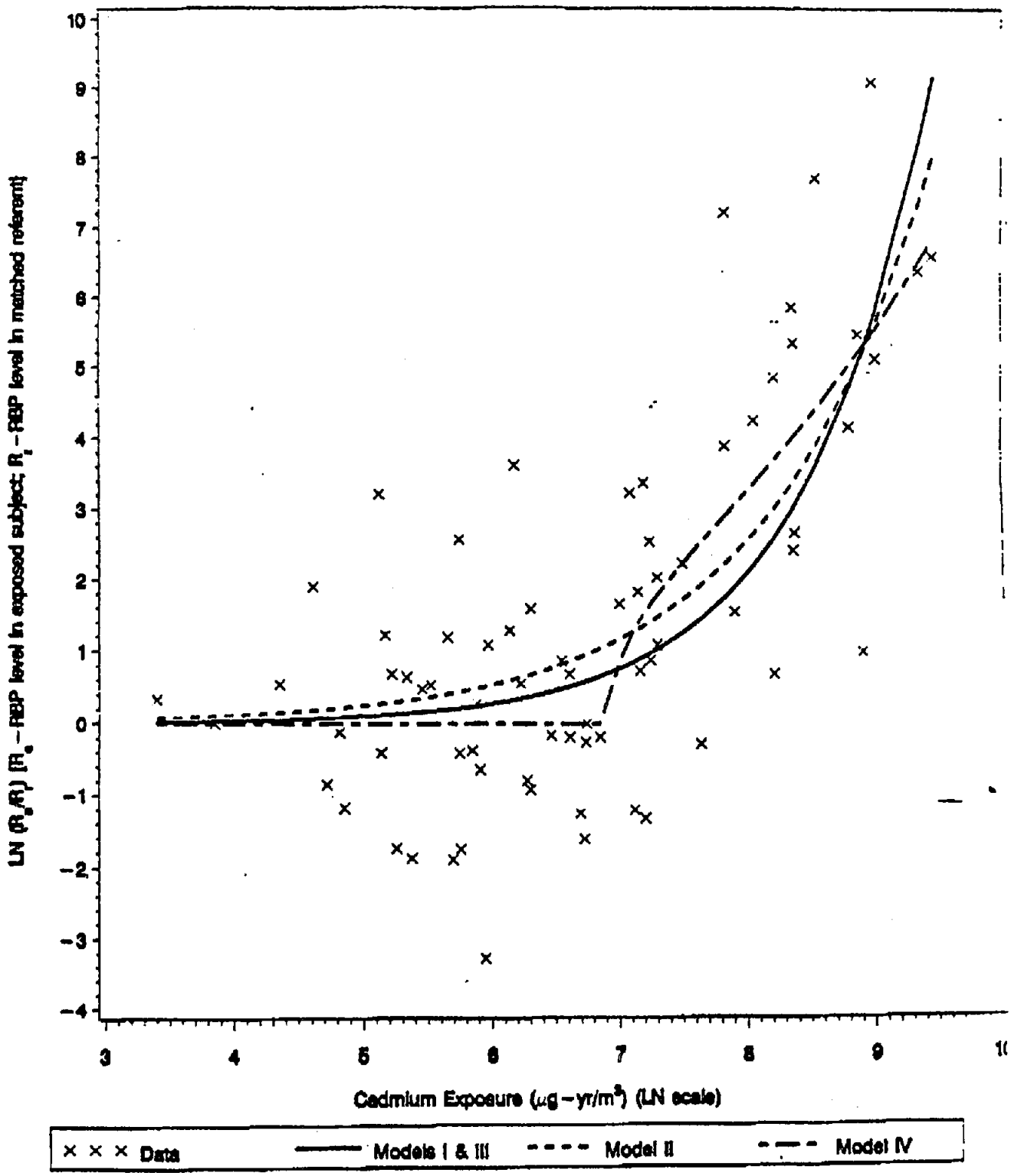
OSHA has also developed estimates of the risk of kidney dysfunction from occupational exposure to cadmium using data from five different epidemiological studies of the effect of occupational exposure to cadmium upon kidney dysfunction (Falck et al., Ex. 4–28; Ellis et al., Ex. 4–27; Elinder et al., Ex. L–140(45); Mason et al., Ex. 8–669A; Jarup et al., Ex. 8–661). All of these studies, as

well as the study of Thun et al. (Ex. 19–43B), indicate an increase in proteinuria among workers exposed to cadmium.

OSHA's preferred estimate of the excess lung cancer risk from 45 years of occupational exposure to cadmium ranges from 58 to 157 excess deaths per 1000 workers from exposure to a TWA of 100 $\mu g/m^3$, and estimates of the risk of kidney dysfunction from this exposure range above 900 cases per 1000 workers. OSHA's preferred estimates of risk from exposure to a TWA of 5 $\mu g/m^3$ range between three and nine excess lung cancer deaths based on the epidemiologic data and 15 excess cancer deaths based on the animal data and between 14 and 23 excess cases of kidney dysfunction per 1000 workers. Thus, risks of both lung cancer and kidney dysfunction are predicted to be in excess of one case per 1000 workers from 45 years of exposure to a TWA of 5 $\mu g/m^3$.

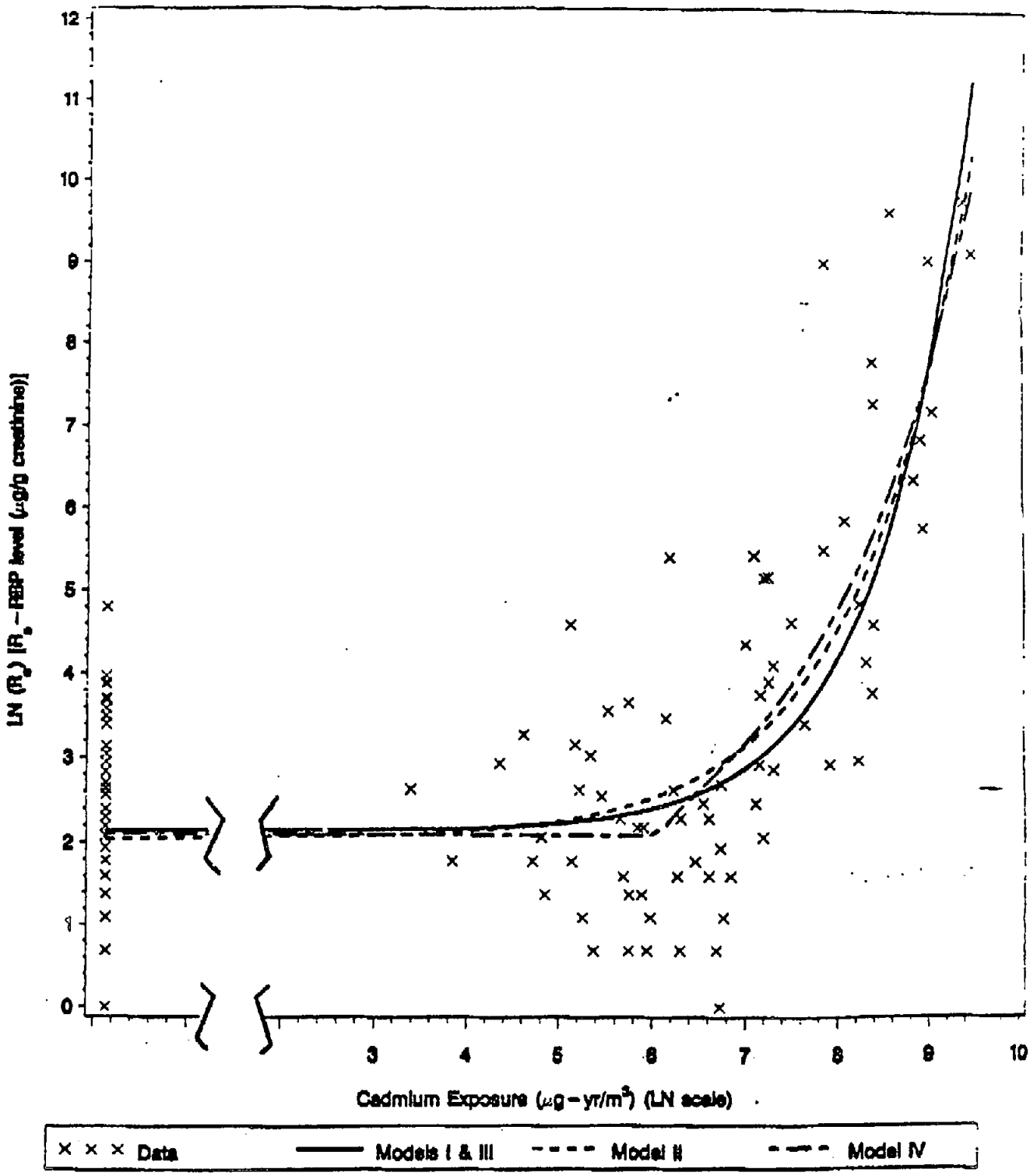
BILLING CODE 4510–26–M

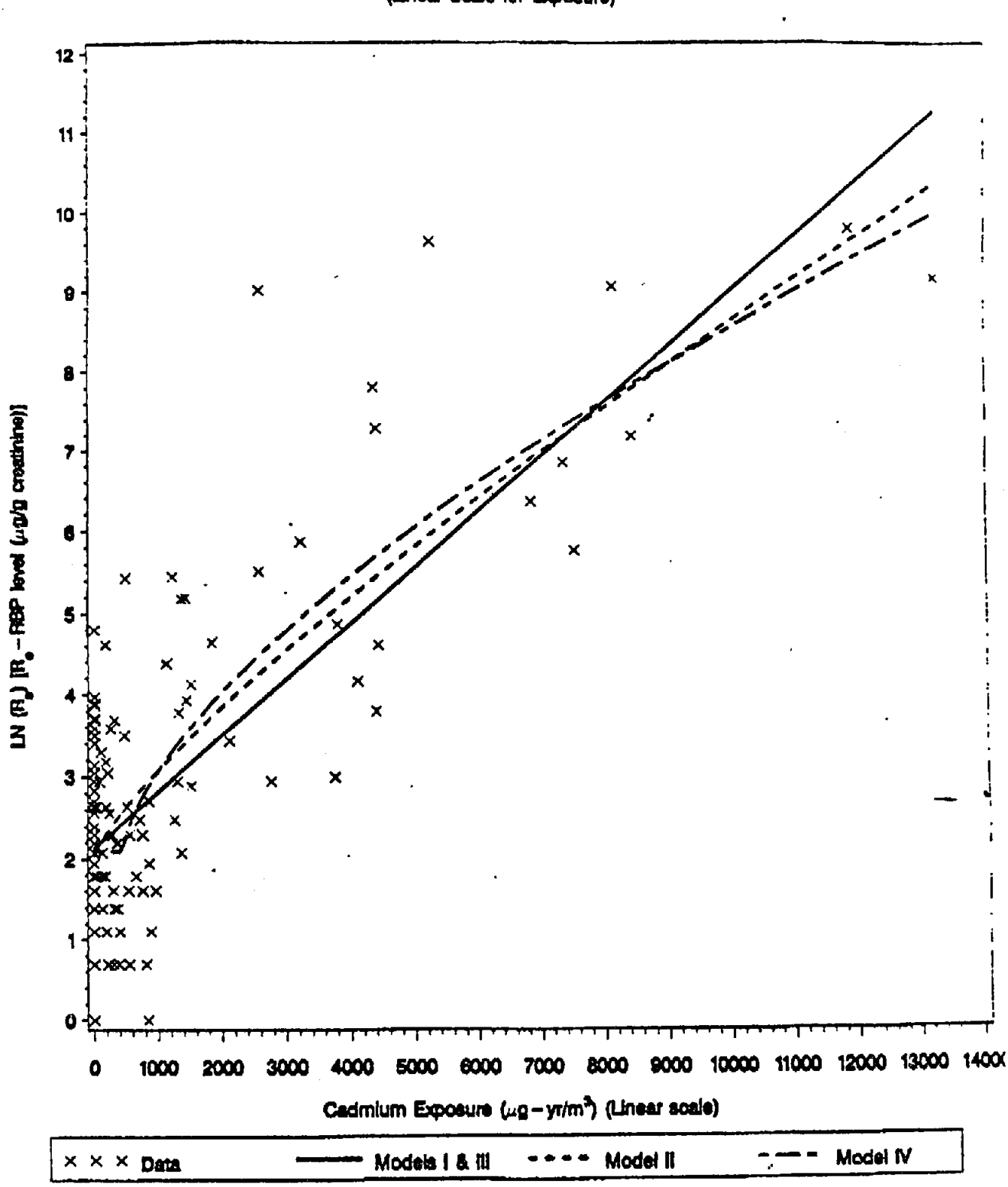
Fit of Three Models to Mason Matched Data



Fit of Three Models to Mason Unmatched Data

(Log Scale for Exposure)




Fit of Three Models to Mason Unmatched Data
(Linear Scale for Exposure)
LN (R_e) [R_e = RBP level (μg/g creatinine)]
0
1
2
3
4
5
6
7
8
9
10
11
12
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
10000
11000
12000
13000
1400
Cadmium Exposure (μg-yr/m³) (Linear scale)
Data
Models I & III
Model II
Model IV

BILLING CODE 4510-26-C

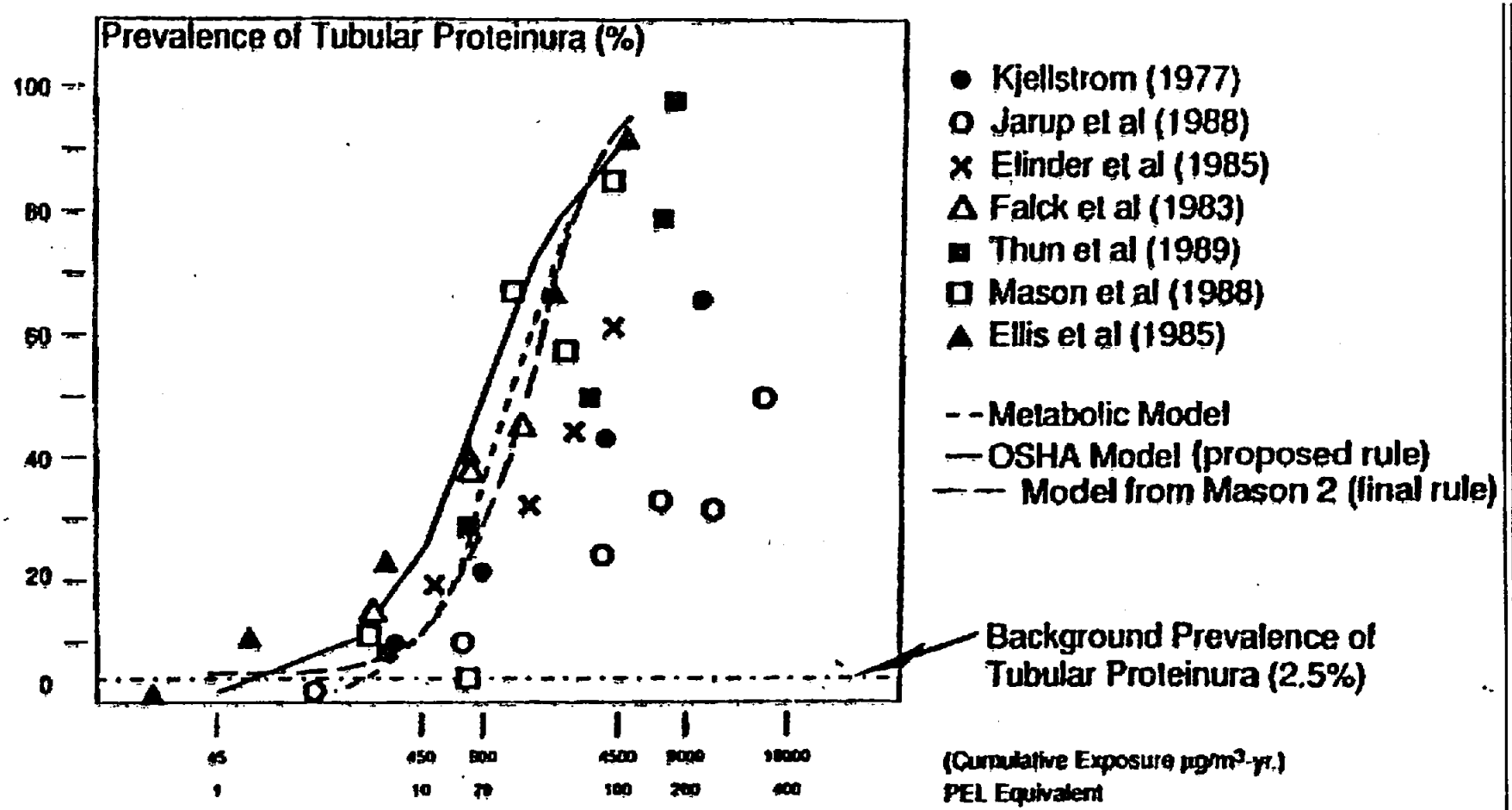


FIGURE VI-4:

~~Figure 4.~~ Prevalence of tubular proteinura by cumulative exposure to cadmium in seven cross-sectional studies compared to prediction by the OSHA risk assessment from the proposed rule, by the Kjellstrom metabolic model and by the modified logistic model applied to the Mason et al. data.

References

BEIR IV. 1988. *Health Risks of Radon and Other Internally Deposited Alpha-Emitters.* Committee on the Biological Effects of Ionizing Radiations. National Academy Press, Washington, DC.

BEIR V. 1990. *Health Effects of Exposure to Low Levels of Ionizing Radiation.* Committee on the Biological Effects of Ionizing Radiations. National Academy Press, Washington, DC.

Cox, D.R., Hinkley, D.V. 1974. *Theoretical Statistics.* Chapman and Hall, London.

Crump, K. 1984. An improved procedure for low-dose carcinogenic risk assessment from animal data. *J Environ Pathol Toxicol* 5:339–348.

Crump, K. 1985. Mechanisms leading to dose-response models. In: *Principles of Health Risk Assessment.* Ricci P., ed. Prentice Hall, Englewood Cliffs, NJ. pp. 321–372.

Crump, K., Howe, R. 1984. The multistage model with a time-dependent dose pattern: applications to carcinogenic risk assessment. Risk Anal 4:163–176.

Crump, K., Guess, H., Deal K. 1977. Confidence intervals and tests of hypotheses inferred from animal carcinogenicity data. *Biomet* 33:437–451.

Krewski, D., Crump, K., Farmer, J., Gaylor, D., Howe, R., Portier, C., Salsburg, D., Sielken, R., Van Ryzin, J. 1983. A comparison of statistical methods for low-dose extrapolation utilizing time-to-tumor data. *Fund Appl Toxicol* 3:140–160.

National Academy of Sciences (NAS). 1983. *Risk Assessment in the Federal Government: Managing the Process.* National Academy Press, Washington, DC.

National Toxicology Program (NTP). 1984. Report of the NTP Ad Hoc Panel on Chemical Carcinogenesis Testing and Evaluation. U.S. Department of Health and Human Services.

Peto, R. 1978. Carcinogenic Effects of Chronic Exposures to very low levels of toxic substances. *Environmental Health Perspectives* 22:155–159.

U.S. Department of Commerce (USDOC). 1980. Census of Population. Detailed Population Characteristics. Colorado. PC80–1–D7.

U.S. Environmental Protection Agency (USEPA). 1989. Risk Assessment Guidance for Superfund. Volume I. Human Health Evaluation Manual. OSWER Directive 9285.7–01a. Office of Emergency and Remedial Response, Washington, DC. September 29, 1989.

U.S. Environmental Protection Agency (USEPA). 1991. Health Effects and Dose-Response Assessment for Hydrogen Chloride Following Short-Term Exposure. Final Report. Prepared for Office of Air Quality Planning and Standards, Research Triangle Park, NC. Prepared by Clement International Corporation.

VII. Significance of Risk

Introduction

In the 1980 benzene decision, the Supreme Court, in its discussion of the level of risk that Congress authorized OSHA to regulate, indicated when a reasonable person might consider a risk significant and take steps to decrease it. The court stated:

> It is the Agency's responsibility to determine in the first instance what it considers to be a "significant" risk. Some risks are plainly acceptable and others are plainly unacceptable. If, for example, the odds are one in a billion that a person will die from cancer by taking a drink of chlorinated water, the risk clearly could not be considered significant. On the other hand, if the odds are one in a thousand that regular inhalation of gasoline vapors that are 2% benzene will be fatal a reasonable person might well consider the risk significant and take the appropriate steps to decrease or eliminate it. (*I.U.D.* v. *A.P.I.*, 448 U.S. at 655).

The Court further stated that "while the Agency must support its findings that a certain level of risk exists with substantial evidence, we recognize that its determination that a particular level of risk is significant will be based largely on policy considerations." The Court added that the significant risk determination required by the OSH Act is "not a mathematical straitjacket," and that "OSHA is not required to support its findings with anything approaching scientific certainty." The Court ruled that "a reviewing court [is] to give OSHA some leeway where its findings must be made on the frontiers of scientific knowledge [and that] * * * the Agency is free to use conservative assumptions in interpreting the data with respect to carcinogens, risking error on the side of overprotection rather than underprotection" (448 U.S. at 655, 656).

As part of its overall significant risk determination, OSHA considers a number of factors. These include the type of risk presented, the quality of the underlying data, the reasonableness of the risk assessments, the statistical significance of the findings and the significance of risk (48 FR 1864; January 14, 1983).

Cadmium exposure causes a number of extremely serious adverse health effects. In 1971 OSHA adopted the ANSI standard with a TWA PEL of 100 $\mu g/m^3$ for cadmium fumes and a TWA PEL of 200 $\mu g/m^3$ for cadmium dust to prevent the acute effects caused by exposure to cadmium at levels higher than the PELs. Since 1971, however, a body of evidence has developed which shows that exposure to cadmium, dust or fumes, at levels well below these PELs can also lead to very serious health effects such as kidney dysfunction and cancer. Because current occupational cadmium exposure levels generally are below 100 $\mu g/m^3$, the discussion of the significance of risk not does emphasize acute health effects, but rather focuses exclusively on two of the most common chronic adverse health effects related to cadmium exposure.

As indicated in the health effects section of this preamble, exposure to cadmium causes cancer, kidney dysfunction, reduced pulmonary function, and chronic lung disease indicative of emphysema. Other health effects, such as improper bone mineralization also have been reported. In addition to these major effects in humans, studies of experimental animals suggest that exposure to cadmium may also cause anemia, change in liver morphology, decrease in immunosuppression, and hypertension.

As discussed in the health effects section, there are numerous epidemiologic studies that show an elevated risk of lung cancer among cadmium exposed workers. Because lung cancer is almost certainly fatal, OSHA considers this disease to represent the greatest material impairment to health. A number of studies of workers also suggest an association between occupational cadmium exposures and increased deaths from other types of cancer, most notably prostate cancer. However, the relationship between cadmium exposure and prostate cancer is difficult to establish on the basis of more recent mortality studies. Most epidemiological cohort studies of workers use mortality rates to estimate risk of disease, but prostate cancer does not always lead to death. Consequently, the mortality studies probably underestimate the true incidence of the disease. In any event, although prostate cancer is not always fatal, OSHA nonetheless considers it to be a very serious material impairment to health.

Chronic exposure to cadmium is also known to cause renal dysfunction. This impairment of kidney function typically is manifested as proteinuria, a condition characterized by an excess of proteins in the urine. Early stage, cadmium induced proteinuria typically is tubular proteinuria, which is characterized by an excess of low molecular weight proteins in the urine. Chronic exposure to cadmium may also cause glomular proteinuria, a still more serious dysfunction, characterized by an excess of total proteins in the urine. The damage to the proximal tubules or glomerulus in the kidney indicated by proteinuria is likely to be irreversible in a substantial proportion of workers, except in its very earliest stages.

Because of the body's ability to accumulate and store cadmium over long periods of time, the loss of kidney function may develop even after a reduction or cessation of external

cadmium exposure. Upon prolonged exposure, tubular proteinuria may progress to more severe forms of renal dysfunction such as glycosuria, aminoaciduria, phosphaturia and glomular proteinuria. Therefore, OSHA also considers tubular proteinuria to be a material impairment of health. As discussed in the health effects section of this preamble, this conclusion is consistent with OSHA's analyses and court decisions regarding the lead and air contaminants standards [FR 52952; 11/14/78, p. 52983; *USWA* v. *Marshal* 647 F. 2d 1189 (1980), p. 1251; 54 FR 2332–2983, 01/19/89; *AFL–CIO* v. *OSHA*, Nos. 89–7185 et al., 911th Cir. 7/7/92)].

Long term exposure to cadmium appears to cause other adverse effects on the respiratory system in addition to lung cancer. Workers with prolonged exposure to cadmium dust or fumes have exhibited shortness of breath, impaired pulmonary function, and chronic lung disease indicative of emphysema. These diseases also constitute material impairment of health or functional capacity, but it has not been possible to determine a dose response relationship between them and occupational exposure to cadmium. Therefore, these diseases were not quantified in the quantitative risk assessment section of the standard.

Workers with progressive forms of proteinuria also have exhibited adverse bone effects associated with improper bone mineralization, such as osteoporosis and osteomalacia. These latter diseases are also serious, though not usually fatal. These diseases also are not quantifiable with the data available, but they are likely to occur as a result of exposure levels above the old permissible limits. The discussion of significant risk concentrates on the quantifiable diseases, cancer and kidney dysfunction. OSHA concludes that the risk of contracting each of these diseases from occupational exposure to cadmium above the new PEL is significant. The other disease risks mentioned above, though not as readily quantifiable, add to the significance of the risk presented.

In the health effects section above, OSHA discusses at length its assessments of the various relevant animal and human studies, and in the quantitative risk assessment section above, OSHA discusses in great detail its own and other's risk assessments for cadmium, including the bases and criticisms of those assessments.

The underlying epidemiologic and experimental animal studies that provide the basis for this quantification of risk are of reasonable quality and demonstrate a relationship between cadmium exposure, on the one hand, and cancer and kidney dysfunction, on the other. There is a reasonable basis for determining the exposed population, estimating dose, and excluding other potentially causal agents of the observed diseases. The Environmental Protection Agency (EPA) has concluded that the available data are adequate to quantify the risk of cancer due to cadmium exposure. This is OSHA's conclusion as well.

Cancer

OSHA used two types of data for its quantitative assessment of the risk of death from cancer. One is animal data, the rat bioassay by Takenaka and others (Ex. 4–67) and the long term bioassay by Oldiges and others (Exs. 12–10–i; 12–10–h; 12–35; 8–694). The other is human data, the human mortality study by Thun and others (Ex. 4–68). In its proposal for its preliminary quantitative risk assessment, the Agency relied on the rat data for its best estimate of total risk of cancer death, because OSHA believed that the measures of exposure were more accurate in the rat study and because the rat study can be used to predict all cancer deaths attributable to occupational exposure to cadmium. By contrast, the Thun data can be used to predict only lung cancer deaths attributable to occupational exposure to cadmium. This use of animal data to predict total cancer deaths is consistent with risk assessments conducted for other standards and upheld in the Courts (e.g. ethylene oxide).

Nevertheless, in this final standard OSHA relies on both the animal data, especially the Takenaka study, and the Thun human mortality study for its estimate of excess cancer risk. Each of these studies could, in the Agency's expert opinion, be used independently to establish the significant cancer risk associated with excess exposure to cadmium. However, OSHA recognizes that at the current state of the art reliance on either animal or epidemiolgical studies to determine human risk entails its own set of associated problems/limitations, and it is therefore prudent, where possible, to evaluate risk using both animal and human data.

For example, to determine human risk from animal studies it is necessary to extrapolate across species, and humans may be more or less susceptible than the animals studied. Moreover, animal experiments are typically carried out using relatively few animals (typically about 50 for each dose and sex group), which are often exposed for short periods of time and sacrificed often before cancer may manifest itself. With only 50 animals, it may be difficult to identify a carcinogen so potent as one that would double the background mortality rate in humans for lung cancer (overall age adjusted rate of 64 per 100,000 in white males in the USA). With a doubling of this rate, the testing of 50 animals would result in less than one additional animal per dose group developing lung cancer. So, even in this extreme situation, it is unlikely that an increased risk would be observed. To be assured of observing such an increase in cancer risk, the number of test animals would need to be tremendously increased. However, managing large numbers of animals is impractical. The more managable alternative is to increase the dose of the material being tested, often to the maximum dose that can be tolerated without causing early mortality in the animals from diseases other than cancer. However, in order to use these data to estimate human risk requires another extrapolation, from high dose in animals to low dose in humans, which in turn creates additional uncertainty.

On the other hand, epidemiological studies cannot be controlled nearly as carefully as animal studies, and information about factors potentially relevant to these studies is typically less than complete. Thus, in epidemiological studies there are inevitably confounding factors, like cigarette smoking or exposures to toxic substances other than the test substance, that may raise some doubt about findings of association between the substance under study and disease. Furthermore, detailed, complete, and accurate exposure data needed to precisely determine dose often are unavailable in such studies and must be reconstructed by applying reasonable assumptions to imperfect available data.

Notwithstanding the respective sets of problems/limitations that seem to be endemic to animal bioassays and epidemiological studies, in particular cases animal and/or human studies will provide the best available evidence of the toxicity of a substance and either or both may prove to be quite reliable. In relying in this final cadmium standard on both animal and human studies to determine risk, OSHA seeks to answer the criticism that stereotypically arises from reliance on either one alone. Thus, when one relies on the Takenaka animal study, the need to extrapolate across species may be a problem, but there is no such need and therefore no such problem when one relies upon the Thun study of cadmium exposed workers. On the other hand, when one relies upon the

Thun study, co-exposure to arsenic or cigarette smoking may be potentially confounding factors, but there are no such co-exposures and therefore no such confounding when one relies on the Takenaka study.

As a result, to the extent that the two studies are in basic agreement about the nature and extent of the risk, the concerns generated by exclusive reliance upon one type of study should be substantially alleviated by reliance upon the other as well. Such agreement, OSHA believes, would also strongly suggest that the Agency's risk determinations for cancer are realistic. It is highly unlikely that such agreement could have been produced by mere coincidence.

With regard to its quantitative risk assessment for cancer based upon the animal data, OSHA has relied upon the Takenaka (Ex. 4–67) and the Glaser/Oldiges studies (Exs. 8–694–B; 8–694–D). The Takenaka study involved exposure of male rats to cadmium chloride, while the Oldiges study involved exposure of male and female rats to cadmium chloride, cadmium oxide, cadmium sulfate, and cadmium sulfide. OSHA applied the multistage model and two variants of it to the ten data sets from these two studies to estimate excess lung cancer risk from an occupational lifetime (45 years) exposure to each of the various exposure levels for each of the cadmium compounds.

OSHA has relied upon the Takenaka rat study to derive its best estimate of risk based upon data from experimental animals. This study is particularly suitable for quantitative risk assessment, because exposure levels were well documented, the study was run with concurrent controls, there was no opportunity for confounding exposures, and the route of exposure, inhalation, is the same as the primary route of exposure in occupational settings. Two possible drawbacks to this study raised in the proposal are that the animals were exposed continuously and to cadmium chloride. By contrast, workers are exposed mostly to cadmium compounds other than cadmium chloride and generally for eight hours a day.

With regard to the carcinogenicity of particular cadmium compounds, analyses of dose response data for several cadmium compounds show a similar carcinogenic potency. With regard to length of exposure, although rats in the Takenaka study were dosed continuously, and workers are not, cancer risk assessments show a similar dose response in relation to total cadmium dose, whether the animals were exposed continuously or in an exposure pattern simulating the workplace mode of exposure (Ex. 31; See also Table VI–6 of the Quantitative Risk Assessment section). Thus, there appears to be no dose rate effect.

To quantify risk from cadmium exposure using the Takenaka rat data, OSHA in its proposal examined five low-dose extrapolation models. The choice of model involves scientific judgment. There is no certain way to determine which model is correct. The statistics that allow us to measure goodness of fit cannot provide help in judging "best" fit among the models. Consequently, the best (correct) model must be chosen on the basis of some other criterion.

OSHA prefers the multistage model as its best model because the Agency believes the multistage model has the best empirical and theoretical justification of all the models for estimating carcinogenic dose-response. The multistage model is a nonthreshold model that is linear at low doses. The Agency believes that this model conforms most closely to what we know of the etiology of cancer. OSHA's preference is consistent with the position of the Office of Science and Technology Policy, which recommends that "when data and information are limited, and when much uncertainty exists regarding the mechanisms of carcinogenic action, models or procedures which incorporate low-dose linearity are preferred when compatible with limited information. In addition, there was good general support during the rulemaking for using the multistage model to estimate cancer risk with animal data.

OSHA applied three multistage models to the data. The results are shown in Table 6 of OSHA's risk assessment. With the exception of cadmium oxide (CdO) fume (the results which might be explained on the basis of lower lung deposition) at an occupational lifetime (45 years) exposure to cadmium of 100 $\mu g/m^3$, the current PEL for cadmium fume, most of the 28 maximum likelihood estimates (MLEs) for all of the cadmium compounds and for both male and female rats project excess cancer deaths well above 100 per 1000. Even for CdO fume, the excess risk of death from cancer associated with 100 $\mu g/m^3$ ranges from 6.8 to 37 per 1000.

By contrast, with an occupational lifetime exposure to the new PEL of 5 $\mu g/m^3$, the models project dramatically reduced risks in all categories. Thus, the new PEL significantly reduces the risk of cancer among cadmium exposed workers. Nevertheless, of the 28 MLEs associated with 5 $\mu g/m^3$ for the various cadmium compounds and models using data for both male and female rats, all but three project risks of greater than 5 excess cancer deaths per thousand workers, and nearly two-thirds project 15 or more excess cancer deaths per thousand.

If OSHA were to choose a best estimate of risk based upon the animal data, for the reasons presented in the preamble to its proposed cadmium standard and in the health effects section of this preamble, it would continue to choose the risks generated by applying the multistage model to the data for $CdCl_2$ from the Takenaka study. Because the strengths and weaknesses of that study have been vetted in this rulemaking, OSHA feels assured of its reliability and appropriateness. OSHA now calculates the best estimate of risk associated with a PEL of 5 $\mu g/m^3$ from this study to be 15 excess cancer deaths per thousand. (See Table 6 in the quantitative risk assessment section.) This risk is slightly higher than the 10.6 per 1,000 risk that OSHA projected as the best estimate in its preliminary risk assessment from the Takenaka data. The reason for the difference is that OSHA calculated the dose slightly differently for its final risk assessment. In any event, both the estimates of 10.6 and 15 excess deaths per thousand are an order of magnitude above risks that previously have been considered at least minimally significant by OSHA.

With regard to its quantitative risk assessment for cancer based upon the human data, OSHA continues to rely upon the Thun study presented in the proposed cadmium rule. The cohort has been updated to include six additional years of follow-up. As discussed at length in the health effects section of this preamble, OSHA believes that the Thun study with updated information is an excellent epidemiological study. While subject to the limitations inherent in such studies, it provides a reasonably reliable basis for quantitative risk analysis. Furthermore, it is the only epidemiologic study available that has reliable data on dose and it has undergone extensive peer review. In addition, as discussed in OSHA's quantitative risk assessment in this preamble, extensive additional analyses of its data have been performed and several additional models have been used to model the data. OSHA further believes that the various challenges to the Thun study (Exs. 19–43; 12–41) have forced its authors and others, like NIOSH and OSHA, who choose to rely upon it, to thoroughly consider and respond to the questions raised. These

responses, in OSHA's judgment, have been more than adequate.

OSHA requested public comment on the uncertainties involved in using the Thun et al., epidemiological data to perform its quantitative assessment of the cancer risk associated with occupational exposure to cadmium. OSHA further requested public comment on how the Agency might resolve the issue of basing its final quantitative risk assessment on either the Thun study or the Takenaka study. Based upon additional follow-up and new analyses of the Thun cohort, OSHA has concluded that confounding from cigarette smoking and arsenic exposure played little role in the excess of lung cancer observed among the cohort members. With such an extended and comprehensive assessment of the strengths and weaknesses of the Thun study as part of this rulemaking, OSHA feels comfortable with its reliance on that study.

The Thun study is an historical prospective study of 602 white men employed in production areas of a smelter for at least six months between 1940 and 1969 and followed through 1984. It provides the strongest evidence of the carcinogencity of cadmium in humans. For workers with two or more years of employment at the smelter, mortality from lung cancer was statistically significantly elevated (SMR=229). Dividing the cohort of workers into those with low, middle and high cumulative exposures to cadmium, a significant dose-response relationship between cadmium exposure and lung cancer was observed.

The methods used to quantify risk from the Thun data closely follow those used by EPA (Ex. 4-04). In its final risk assessment, OSHA applied a relative risk model, adjusted for Hispanic ethnicity, to the updated Thun data. Because the new estimates are based upon more complete data and more reliable quantitative methods, OSHA prefers them over those in the proposal.

As shown in Table 12 of OSHA's final risk assessment, with an occupational lifetime exposure to cadmium at the new PEL of 5 $\mu g/m^3$, OSHA projects from the Thun data a risk of three excess deaths from lung cancer per 1000 workers based on the MLE. This estimate of risk at the new PEL is based exclusively on the reduction in exposure to cadmium achieved by the new PEL and does not take into account the additional risk reduction arising from the ancillary provisions of this standard. Nonetheless, this estimate constitutes a 95% reduction from the comparable estimated risk of 58.3 deaths per thousand at an occupational lifetime exposure to cadmium of 100 $\mu g/m^3$. It also represents greater than an 85% reduction of risk from the risk at an occupational lifetime exposure to 40 $\mu g/m^3$ and a 75% reduction of risk from the risk at an occupational lifetime exposure to 20 $\mu g/m^3$, both of which levels are closer than 100 $\mu g/m^3$ to typical existing occupational exposure levels in many industries with current exposures above 5 $\mu g/m^3$.

Since OSHA published its proposed rule, Dr. Leslie Stayner and others of the National Institute for Occupational Safety and Health (NIOSH) have also developed an independent quantitative risk assessment based on the updated Thun cohort. That risk assessment differs in ways discussed in the risk assessment section of this preamble from OSHA's own preliminary and final risk assessments. NIOSH, in response to criticisms of OSHA's risk assessment in the cadmium proposal and to recommendations made by various scientists, made methodological adjustments and applied three separate models to the Thun data. The results of NIOSH's risk assessment are shown in Table 9 of OSHA's final risk assessment.

With an occupational lifetime exposure at the new PEL of 5 $\mu g/m^3$, NIOSH estimates an excess risk of death from cancer ranging from 3.9 to 5.5 to 9.0 per thousand workers for the Cox Regression Analysis, the multistage model, and Poisson Regression model, respectively. These estimates of risk are statistically all very close to one another and strikingly similar to OSHA's own, independently derived estimate of 3 excess lung cancer deaths per 1000 workers.

The NIOSH risk estimates for occupational lifetime exposure at the new PEL, like the OSHA risk estimates for that level, represent a very substantial reduction of risk from risks estimated for comparable exposures at the higher, currently allowable levels and at existing levels. For example, the estimated excess risk at an occupational lifetime exposure of 100 $\mu g/m^3$ ranges from 73 to 102.2 to 157 per thousand workers according to the Cox Regression, multistage, and Poisson Regression models, respectively. Thus, under all three models the risk at 5 $\mu g/m^3$ represents a nearly 95% reduction of risk from the risk at 100 $\mu g/m^3$, a nearly 87% reduction of risk from the risk at 40 $\mu g/m^3$, and a nearly 75% reduction of risk from the risk at 20 $\mu g/m^3$. Again, the NIOSH estimates of risk at the new PEL do not take into account the additional reductions in risk arising from the ancillary provisions of this standard. OSHA expects these additional reductions to eliminate significant risk of cadmium associated cancer at the PEL of 5 $\mu g/m^3$.

Summing up the results of these various risk assessments based on animal and human data, all indicate a very high excess risk of death from cancer arising from an occupational lifetime exposure to cadmium at the current PEL (for fume) of 100 $\mu g/m^3$. All also show very high excess risks at levels much lower than 100 $\mu g/m^3$. Further, the results based upon all of the models show a very high reduction of risk associated with the new PEL of 5 $\mu g/m^3$. And all show that the risk that OSHA is seeking to regulate, without regard to the ancillary provisions, remains significant at least down to the new PEL.

Indeed, at the PEL of 5 $\mu g/m^3$ the best estimate of excess risk from the animal data, 15 deaths per thousand, and all the estimates from the human data, 3 per thousand under the OSHA model, and 3.9 to 9 per thousand under the NIOSH models also all reflect continuing significant risk without regard to the ancillary provisions. If OSHA were relying exclusively upon the PEL to reduce risk and there were no ancillary requirements that effectively eliminated remaining significant risk at the new PEL, and if there were no other circumstances that further mitigated the risk, OSHA might well have to set the PEL still lower than 5 $\mu g/m^3$ if that were feasible.

These estimates of remaining risk at the new PEL are all very similar statistically. They are all within one order of magnitude. This similarity is even more striking when one realizes that estimates based on the animal data are for total cancers, whereas, the estimates derived from the human data are based on lung cancer only. (The possibility exists that lifetime studies of the occupational cohorts might identify additional cancer sites in humans related to cadmium exposure.) Thus, OSHA feels assured by these mutually confirming results that its risk estimates for cancer are realistic and reasonably accurate. As stated above, by implementing the new PEL along with the ancillary provisions of the standard, OSHA expects the significance of the risk to be eliminated.

Kidney

For its final quantitative assessment of the excess risk of kidney dysfunction associated with occupational exposure to cadmium, OSHA applied a logistic regression model to the five independent studies that have relevant quantifiable data. These studies, discussed at length

in the health effects section above and analyzed for quantitative estimates of kidney dysfunction in relation to dose in the quantitative risk assessment section, were conducted by Falck and others, Ellis and others, Elinder and others, Jarup and others, and Mason and others. In these studies, the authors investigated the association between levels of low molecular weight proteins in the urine of workers and cumulative occupational exposure to cadmium. The low moleculator weight proteins being measured are Beta 2 microglobulin (β_2-M) or retinol binding protein (RPB), excessive levels of either of which are taken as indicative of kidney dysfunction.

The logistic model that OSHA applied to the data from each study was modified from the model presented in the proposal to take account of background levels of kidney dysfunction unassociated with occupational cadmium exposure. This explains why the results projected from the model in the final risk assessment for the Falck and Ellis data sets are somewhat lower than those projected in the preliminary risk assessment, which relied exclusively upon those two data sets.

In its final risk assessment OSHA performed analyses on seven data sets from five studies using a modified logistic model. The five studies themselves were quite different from each other in many material ways. For example, authors chose different levels of β_2-M or RPB as indicative of kidney dysfunction; some used spot urine samples, others used 24-hour samples; and the number of subjects in each ranged from 33 to 440. In part because of the small size of some of the studies and in part because of the uncertainty in extrapolating results to low TWA exposures, some of the confidence intervals in Table 19 of the risk assessment section are fairly wide. Considering this and the differences among the underlying studies, which doubtless affect the results, the analyses produced reasonably consistent results. Thus, for example, as shown in Table 19, all of the seven analyses project high rates of proteinuria at an occupational lifetime exposure of 100 $\mu g/m^3$ (24–99.8%); all continue to project relatively high rates of proteinuria down to exposures as low as 20 $\mu g/m^3$ (2.1–47.2%); and all project a risk greater than one per thousand at an exposure of 10 $\mu g/m^3$ (2.7–234 per thousand). Moreover, at the new PEL of 5 $\mu g/m^3$, all but two of the analyses show an excess risk of proteinuria greater than 1 per thousand (1.9–95). With regard to those two, both show a risk greater than two per thousand (2.7–2.8) at an exposure of 10 $\mu g/m^3$. Thus, even with regard to the two lowest results, the analyses indicate a risk greater than one per thousand at exposure levels somewhere between 5–10 $\mu g/m^3$. Furthermore, for reasons described in OSHA's risk assessment, the Agency no longer considers one of the two studies that provide the source for these low estimates, the Falck study, as reliable a basis for OSHA's quantitative risk assessment as the other studies.

In the other six risk estimates, the results range at the extremes from .37 to 95 estimated excess cases of proteinuria per 1000 workers exposed to cadmium at 5 $\mu g/m^3$ for an occupational lifetime. The four results between the extremes range between 1.9–27 cases per thousand, a range only slightly greater than one order of magnitude.

From all the analysis reflected in Table 19, OSHA's best estimate of risk at 5 $\mu g/m^3$ is 14–23 excess cases of proteinuria per thousand. OSHA arrived at this best estimate by determining the upper and lower 95% confidence intervals for each of the risk estimates at 5 $\mu g/m^3$ reflected in Table 19. With the exception of the Mason 1 analysis, the estimate of 14–23 excess cases falls within the 90% confidence intervals (95% upper bound and 95% lower bound) of the six data sets analyzed. To put this in other words, 14 represents the highest of the 95% lower bounds and 23 represents the lowest of the 95% upper bounds. So 14–23 is within the 90% confidence intervals for each of the six analyses. For example, the 90% confidence interval for Jarup 1 is 8.3–23; 14–23 falls within that interval. Similarly, the range for Elinder is 0–99; 14–23 falls within that interval. This is true for Ellis, as well: The 14–23 range falls within the 90% confidence intervals of 14–288. OSHA therefore believes that its best estimate of 14–23 excess cases reflects the central tendency of the relevant data. This risk estimate, like comparable estimates for cancer, does not take into account the additional reduction in risk arising from the ancillary provisions of the standard. OSHA expects these additional reductions to eliminate significant risk of cadmium associated kidney dysfunction at the PEL of 5 $\mu g/m^3$.

In response to a comment in the rulemaking (Ex. 17–D), OSHA also applied several types of models to the continuous data from the Mason study. The results of that analysis are shown in Table 21. At an exposure of 5 $\mu g/m^3$, with the exception of the results for the threshold model (Model IV), the results are all greater than OSHA's best estimates of 14–23 cases per thousand workers. By contrast, the threshold model predicts 0 risk at 5 $\mu g/m^3$, and, using the matched analysis, 0 risk at 10 $\mu g/m^3$ and even at 20 $\mu g/m^3$. These analyses provide estimates that are both higher and lower than the results produced by the other models and from OSHA's best estimates. For reasons discussed in OSHA's risk assessment, OSHA gives greater weight to results shown in Table 19 of the quantitative risk assessment section that were derived from the logistic models modified to incorporate background response.

With regard to reduction in risk of kidney dysfunction, the best estimate of risk, 14–23 per 1000, for occupational lifetime exposure to cadmium at 5 $\mu g/m^3$ represents a 90–94% reduction in risk from the lowest estimated risk (242 per thousand) associated with 100 $\mu g/m^3$ based on the modified logistic model. For five of the seven data analyses for exposure at 100 $\mu g/m^3$, 14–23 represents greater than a 96–98% reduction in risk. For occupational lifetime exposures to 20 $\mu g/m^3$, with the exception of the estimates derived from the Elinder data, the 14–23 best estimate of occupational lifetime risk at the new PEL represents a 62–76% reduction from the lowest estimate of risk (60 per thousand). For the next lowest estimate of risk (60 per thousand) at 20 $\mu g/m^3$, 14–23 represents greater than a 70–82% reduction in risk, and for the other four risk estimates (91, 166, 236, and 472 per thousand) at 20 $\mu g/m^3$, the reduction in risk is still greater. Even at an exposure of 10 $\mu g/m^3$, with the exception of the analyses based upon the Elinder and Falck data sets, the best estimate of 14–23 represents a 4–40% reduction in risk from the lowest estimate (24 per thousand), a 22–55% reduction in risk from the next lowest estimate (31 per thousand), and greater than a 40–60% reduction from the other risk estimates.

The conclusions of OSHA's quantitative analysis of risk for lung cancer and kidney dysfunction are further supported by a very recent review of the scientific basis for regulating cadmium in the workplace. The article (ex. L–140–50), which was written by three of OSHA's expert witnesses in the cadmium rulemaking, applies a very different approach to the analysis. The article's analysis compares OSHA's preliminary quantitative risk estimates derived from mathematical modelling of data from several studies with the results derived from other models and with published, empirical data on kidney dysfunction and lung cancer. Although the authors

find that "modelling generally implies greater certainty than exists at low doses * * *" they also find that OSHA's risk estimates generally are in line with the empirical data and the results of other modelling.

With regard to kidney dysfunction, for example, the authors find that "the empirical data and models * * * all show a similar pattern. The prevalence of kidney dysfunction increases sharply at cumulative exposures above 500 μg/m³-year * * *.[However, they point out,] the studies are too small to estimate prevalence at low[er cumulative] exposures * * *." It is therefore "impossible," the authors conclude, "to identify a no-effect level with certainty."

For cancer, the authors find that the epidemiological data provide more plausible estimates of risk than the animal data. The rat data, they find, overpredict risk.

Rather than relying upon mathematical modelling, the authors suggest using a safety margin. Based upon the analysis of both kidney dysfunction and lung cancer, the authors conclude that "occupational exposure to cadmium should be controlled as stringently as is technically feasible, with the PEL not to exceed 5 μg/m³." OSHA finds these conclusions broadly confirmatory of the results of its own analysis.

Consequently, based upon the best estimates of excess risk associated with each of various occupational lifetime exposures to cadmium, whether OSHA relies upon the cancer or the kidney data, and in connection with cancer whether OSHA relies upon the animal data or the human data, it consistently appears necessary for OSHA to set the PEL at least as low as 5 μg/m³.

Even at the new PEL of 5 μg/m³, most of the analyses and all of the best estimates of risk indicate a continuing risk of death from cancer and cases of kidney dysfunction somewhat greater than one per 1000 workers. Thus, the real problem for OSHA when it sets the PEL at 5 μg/m³ lies not in establishing that the Agency is regulating a significant risk. Rather, the problem lies in establishing that, to the extent feasible, the PEL should not be set still lower in order to eliminate what appears, without regard to the reductions in risk arising from the ancillary provisions of this standard and other factors, to be a continuing significant risk.

OSHA thinks the decision to set the PEL no lower than 5 μg/m³ involves complex policy determinations that draw upon OSHA's experience and expertise and also reflect a delicate balancing of countervailing factors. The reasons for the decision are wide ranging.

First, OSHA fully expects the medical surveillance and other requirements in the standard ancillary to the PEL (e.g., MRP, action level, regulated areas, training, etc.) to substantially lower the risk of kidney dysfunction and the risk of cancer from the estimates in the risk assessment. Although OSHA cannot quantify the reductions in risk that may be expected from these and other similar provisions of the standard, OSHA believes that the effect of including the ancillary provisions in the final standard will eliminate the remaining significant risk estimated at the new PEL.

Second, industry has stated that the best way to assure that the new PEL will be met consistently is for industry to implement work practice and engineering controls to achieve a mean exposure considerably below 5 μg/m³ (Ex. 144–6). Some industries maintain that it would be best to establish a mean 40% below the PEL. When these levels are achieved, much, if not most of the time exposure levels will be controlled to below 5 μg/μ³. As a consequence, the risk estimated at an occupational lifetime exposure level of 5 μg/m³ will overstate the actual risk, which would decline linearly.

Third, well over half the exposed workforce already is exposed below the new PEL, so that the actual risk to these employees already is below the risk estimated for an occupational lifetime exposure at that PEL.

Fourth, the vast majority of exposed employees work in industries/occupations where cadmium and its compounds are not the primary product produced or processed. Of these employees, most are not exposed above 5 μg/m³. Of the remainder who are currently exposed above 5 μg/m³, most are exposed only intermittently and will continue to be exposed only intermittently. Their cumulative exposure will be lower than the cumulative exposure used to derive the estimated risks, which are based upon an assumption that the employee is exposed to a TWA exposure at 5 μg/m³ for eight hours every day. With a lower cumulative exposure, the actual risk for employees intermittently exposed at 5 μg/m³ will be lower than the estimated risk.

Fifth, OSHA has already made an important policy decision to sever the PEL from, and set it lower than the separate engineering control air limit(s) (SECAL(s)) for six of the cadmium producing/processing industries, which is set at 15 μg/m³ and/or 50 μg/m³ because of feasibility constraints. In setting the PEL that low, OSHA has inevitably required a substantial number of employees to wear respirators full time. OSHA did this with serious reservations about the advisability of requiring full time respirator use and in the face of a NIOSH recommendation against requiring such use (Ex. 57). OSHA understands that full time respirator usage poses certain safety and health risks but, on balance, has decided that the risks of not requiring some protection for employees from airborne cadmium levels above 5 μg/m³ are more serious than those attaching to full time respirator use.

However, the vast majority of employees exposed to cadmium do not work in industries to which a SECAL applies. For them, the PEL is set at or very close to the limits of feasibility. If OSHA were to set the PEL still lower than 5 μg/m³, large numbers of additional employees would have to wear respirators full time. OSHA is loathe to go further in this direction, especially since the actual risk to employees under the new PEL in practice is likely to be considerably less than the estimated risk. For all these reasons, OSHA has exercised its professional judgment and discretion in determining that the PEL for cadmium shall be established at 5 μg/m³. As a result, OSHA concludes that its cadmium standard will protect employees and that employers who comply with the provisions of the standard will be taking reasonable steps to protect their employees from the hazards of cadmium.

OSHA's conclusion that the risk of death from cancer and the risk of kidney dysfunction resulting from exposure to cadmium at 100 μg/m³ over a working lifetime are both significant is consistent with OSHA's determination of significance of risk at the previously existing TWA PELs for two carcinogens. The two carcinogens are inorganic arsenic (Jan 14, 1983; 48 FR 1864, 1988) and ethylene oxide (Apr. 21, 1983; 48 FR 17284). The risk estimates per 1000 employees for a working lifetime exposure at the prior PEL to these carcinogens ranged from 148 to 425 lung cancer deaths from inorganic arsenic and from 63 to 109 cancer deaths from ethlyene oxide.

In addition, for both carcinogens, OSHA concluded that, if it were feasible, OSHA would seek to further reduce the predicted remaining risk at the new PELs. That remaining excess risk of death for a working lifetime exposure per 1,000 workers was 8 for

inorganic arsenic and 1 to 2 for ethylene oxide.

Further guidance for the Agency in evaluating significant risk is provided by an examination of occupational risk rates, legislative intent, and language of the Supreme Court of the United States. For example, in the high risk occupations of mining and quarrying (Division B), the average risk of death from an occupational injury or an acute occupationally-related illness from a lifetime of employment (45 years) is 15.1 per 1,000 workers. Typical occuptional risks of deaths for all manufacturing (Division D) are 1.98 per 1,000. Typical lifetime occupational risk of death in an occupation of relatively low risk, like retail trade, is 0.82 per 1,000 (Division G). (These rates are averages derived from 1989–1990 Bureau of Labor Statistics data for employers with 11 or more employees, adjusted to 45 years of employment, for 50 weeks per year.)

There are relatively few data on risk rates for occupational cancer, as distinguished from occupational injury and acute illness. The estimated cancer fatality rate from the maximum permissible occupational exposure to ionizing radiation is 17 to 29 per 1,000 (47 years at 5 rems; Committee on Biological Effects of Ionizing Radiation (BEIR) III predictions). However, most radiation standards require that exposure limits be reduced to the lowest level reasonably achievable below the exposure limit (the ALARA principle). Consequently, approximately 95% of radiation workers have exposures less than one-tenth the maximum permitted level. The risk at one-tenth the permitted level is 1.7 to 2.9 per 1,000 exposed employees.

Congress passed the Occupational Safety and Health Act of 1970 because of a determination that occupational safety and health risks were too high. Congress therefore gave OSHA authority to reduce above-average or average risks when feasible. In discussing the level of risk that Congress authorized OSHA to reduce, the Supreme Court stated that "if the odds are one in a thousand that regular inhalation of gasoline vapors that are 2% benzene will be fatal a reasonable person might well consider the risk significant and take the appropriate steps to decrease or eliminate it." (*I.U.D.* v. *A.P.I.*, 448 U.S. et 655).

Within this context, OSHA's best estimates of risk from occupational exposure to cadmium at the current TWA PELs are substantially higher than other risks that OSHA has concluded are significant, are substantially higher than the risk of fatality in high-risk occupations, and are substantially higher than the example presented by the Supreme Court. Consequently, OSHA concludes that its best estimates of risk associated with the current TWA PEL of 100 $\mu g/m^3$ are significant. Based on this reasoning, OSHA's best estimates of risk remain significant down to levels as low as the new PEL of 5 $\mu g/m^3$. As previously stated, these estimates do not take into account the additional reductions in risk that are attributable to the ancillary provisions of the cadmium standard, which OSHA fully expects will eliminate any remaining significant risk at the new PEL.

VIII. Regulatory Impact Analysis

Contents

A. Executive Summary VIII–A2
B. Discussion of Technological and Economic Feasibility Determinations. VIII–B1
C. Exposures, Costs, and Feasibility Analyses by Industry. VIII–C1
Nickel-Cadmium Battery Production. VIII–C1
Zinc Refining/Cadmium Production. VIII–C51
Pigment Production VIII–C92
Stabilizer Production VIII–C123
Lead Smelting and Refining VIII–C156
Plating VIII–C186
Dry Color Formulators VIII–C209
Electric Utilities VIII–C230
Iron and Steel VIII–C239
General Industry, Except Establishments Included Above. VIII–C257
Construction VIII–C306
D. Economic Feasibility and Regulatory Flexibility Analysis. VIII–D1
E. Environmental Impact Assessment. VIII–E1
F. Benefits VIII–F1

A. Executive Summary

Introduction

Consistent with the requirements of Executive Order 12291, OSHA has conducted a regulatory impact analysis (RIA) for the final cadmium rule. The analysis is based on the evidence in the record compiled through the rulemaking process. A preliminary analysis accompanied the proposed cadmium rule [55 FR 4052], and OSHA solicited responses from the public regarding the proposed rulemaking, its estimated potential impacts, and other relevant information.

Many interested parties contributed comments and data to the record which provided substantial evidence for the development and analysis of the final rule. Public participation in the rulemaking process enabled possible effects to be identified and appropriate consideration to be given to the concerns and views of those potentially affected.

The RIA covers several issues involved in the promulgation of the final standard. The industries potentially affected are identified, and the nature of the affected firms, the market structure, the characteristics of supply and demand, and the financial aspects are evaluated. The numbers of employees potentially exposed, the level and duration of exposures, the nature of existing controls and work practices, and the extent of current compliance with the requirements of the standard are ascertained.

The analysis then establishes the changes that would be necessary to comply with the requirements of the standard, and the corresponding costs and benefits are presented. In addition, determinations of the technological and economic feasibility of the standard are made. Finally, the potential total costs and benefits of the rule are estimated by provision and by industry.

The following pages summarize the conclusions of the RIA. This summary includes sections on the industry profile, employee exposures and benefits, technological feasibility and costs of compliance, and economic impacts.

Industry Profile

Due to the ubiquitous nature of cadmium and its usefulness in a wide variety of applications, the revised cadmium standard potentially affects establishments in many different industries. In some industries cadmium is an integral part of the manufacturing process; in other industries cadmium-containing products may be used in the production of various goods; and additional industries may be potentially affected if trace amounts of cadmium naturally present in some materials become airborne.

Table VIII–A1 lists the industries potentially affected by this rulemaking and the estimated number of employees potentially exposed in each industry. In most industries the number of potentially exposed employees represents a small part of the total work force. For example, exposures may occur during chemical mixing or during welding, but these activities may comprise only one step in a complex manufacturing process.

TABLE VIII-A1.—INDUSTRIES AND NUMBERS OF EMPLOYEES POTENTIALLY AFFECTED BY THE REVISED CADMIUM STANDARD

Industry		Potentially exposed employees
Specific sectors:		
Nickel-cadmium batteries		1,500
Zinc/cadmium refining		1,350
Cadmium pigments		100
Dry color formulators		7,000
Cadmium stabilizers		200
Lead smelting/refining		400
Cadmium plating		1,200
Electric utilities		37,500
Iron and steel		40,000
General industry, except sectors above:		
2200	Textile mill products	411
2300	Apparel	201
2500	Furniture	1,232
2600	Paper products	195
2700	Printing and publishing	1,600
2810	Inorganic chemicals	195
2820	Plastics and synthetics	870
2830	Drugs	50
2851	Paints & allied products	4,724
2860	Organic chemicals	2,533
2870	Agricultural chemicals	2,507
2890	Miscellaneous chemicals	1,024
2900	Petroleum refining	807
3000	Rubber & plastic prod.	11,133
3100	Leather products	902
3211	Flat glass	666
3220	Glassware	2,929
3250	Structural clay products	2,423
3260	Pottery products	174
3270	Concrete products	624
3280	Stone products	200
3290	Mineral products	899
3313	Alloy products	488
3315	Steel wiredrawing	500
3316	Cold-rolled steel	37
3317	Steel pipe and tubes	400
3320	Iron and steel foundries	10,808
3330	Primary nonferrous metals	1,800
3340	Secondary nonferrous mtls.	750
3350	Nonferrous rolling, etc.	3,135
3360	Nonferrous foundries	10,022
3390	Misc. primary metal	285
3410	Metal shipping containers	140
3420	Hand tools & hardware	2,761
3430	Heating & plumbing equip.	1,186
3440	Fabricated struct. metal	17,065
3450	Screws, etc.	868
3460	Forgings & stampings	612
3470	Coating and engraving	200
3480	Ordnance	265
3490	Misc. fabr. metal prod.	9,071
3510	Engines and turbines	3,036
3520	Farm and garden machinery	199
3530	Construction machinery	10,453
3540	Metalworking machinery	16,127
3550	Special machinery	6,533
3560	General machinery	11,633
3570	Computer & office equip.	1,600
3580	Refrig. & service mach.	14,180
3590	Miscellaneous machinery	19,615
3610	Elec. transmission equip.	6,386
3620	Electrical apparatus	12,460
3630	Household appliances	7,586
3640	Lighting and wiring	13,266
3650	Audio & video equip.	3,021
3660	Communications equip.	17,886
3670	Electronic components	15,412
3690	Misc. elect. equip.	350
3710	Motor vehicles	18,032
3720	Aircraft	2,776
3730	Ship building	7,907
3743	Railroad equipment	1,458
3760	Missiles & space vehicles	359
3790	Misc. trans. equip.	119
3812	Detection equipment, etc.	87
3820	Meas. & contr. instr.	216
3840	Medical instruments	337
3860	Photographic equipment	669
3870	Watches & clockwork	173
3910	Jewelry & plated ware	79
3930	Musical instruments	16
3940	Toys and sporting goods	1,004
3950	Artists' materials	50
3960	Costume jewelry & notions	29
3990	Misc. manufacturing	2,749
4011	Railroads	23
4200	Motor freight & warehsing	586
4500	Air transportation	52,147
4810	Telephone communications	2,474
4830	Radio & TV broadcasting	149
4920	Gas prod. & dist.	1,213
4950	Sanitary services	5,204
5000	Wholesale trade, durables	690
5100	Wholesale nondurables	3,080
5500	Service stations	538
7530	Automotive repair shops	3,194
7600	Misc. repair services	3,494
8060	Hospitals	277
Construction		70,000
Total		524,816

Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

Potentially affected industries include the production of various kinds of chemicals; paints and coatings; rubber and plastic products; iron and steel; nonferrous metals; machinery and other metal products; electrical equipment; and miscellaneous manufacturing, repair, and service operations.

Reflecting the emphasis of the public comments submitted to the record and other considerations, particular attention was given to several specific industry sectors. These include nickel-cadmium batteries, zinc and cadmium refining, cadmium pigments, cadmium stabilizers, lead smelting and refining, mechanical and electroplating, color compounders and formulators, electric utilities, and iron and steel production. In addition, approximately 70,000 employees in the construction industry may be exposed to cadmium primarily during welding operations.

Employee Exposures and Benefits

Mean exposures among most employees potentially exposed are generally less than 5 $\mu g/m^3$. Over half of the potentially exposed employees are engaged in welding, metal machining, or repair and utility work. In these operations cadmium is usually only present in trace quantities and the work may be intermittent. As a result, exposures are typically less than 2.5 $\mu g/m^3$.

However, exposures for some employees may be significantly higher, depending on the nature and duration of the activity and the type of material involved. Elevated exposures can be expected when dusts or fumes are generated from alloys and other products containing significant concentrations of cadmium, from metals coated with cadmium, or from cadmium-bearing dusts on work surfaces. Such situations may occur when mixing or using cadmium-containing chemicals; operating furnaces or kilns with cadmium-containing materials; machining, welding, brazing, or soldering metals containing cadmium; using paints containing cadmium pigments; and maintaining or repairing equipment involving cadmium-bearing dusts, such as pollution control devices or boilers with fly ash.

In industry sectors where cadmium is a primary component of the production process, exposures may be consistently above 5 $\mu g/m^3$ for much of the work force. Job categories with mean exposures above 20 $\mu g/m^3$ can be found in the production of nickel-cadmium batteries, in zinc and cadmium refining, and in the production of cadmium pigments and stabilizers.

The number of cases of lung cancer and kidney dysfunction attributable to cadmium exposure among the exposed employees was calculated based on the quantitative risk assessments (QRAs) discussed in a separate section of the preamble. The QRAs produce dose-response relationships which provide estimates of the excess risk of each type of health effect corresponding to different levels of exposure.

The QRAs for lung cancer and kidney dysfunction were applied to the number of employees and the exposure level in each job category to determine the number of excess cases attributable to current exposures. The calculation was repeated using the projected exposure levels estimated to be achieved under compliance with the final cadmium standard; the difference determined the number of cases potentially preventable by the standard.

Based on four risk models developed by OSHA Health Standards, compliance with the reduced exposure limit is expected to prevent from 9 to 27 cancer fatalities each year out of 13 to 40 excess cancer fatalities currently taking place. Within this range, OSHA's Multistage Model predicts 17 to 18 cancers avoided annually out of 25 excess cancer fatalities. Based upon the risk models for kidney dysfunction, the

rule should prevent from 68 to 112 kidney dysfunction cases out of 97 to 160 excess kidney dysfuntion cases, annually. For a single estimate within this range, the Jarup 1 model estimates 78 kidney dysfunction cases avoided each year out of a total 111 excess cases. The reductions would apply to risks associated with cumulative exposures over a working lifetime, and thus the annual benefits would be phased in over 45 years.

Technological Feasibility and Costs of Compliance

Compliance with the revised cadmium standard is considered technologically feasible for each of the affected industries. The standard requires engineering controls to be implemented to the extent feasible and allows the supplemental use of respirators for achieving the PEL. Respirators are capable of providing the protection required by the revised standard for the exposures encountered in each of the affected industries.

In almost all industries the application of appropriate engineering controls and work practices can keep cadmium exposures below the PEL for most employees most of the time. In some industries respirators may be necessary in some operations, but the number of employees affected would typically represent a small part of the total work force. Overall, an estimated 40,000 of the 524,000 employees exposed may require respiratory protection after the implementation of feasible engineering controls.

In a few specific industry sectors a majority of the employees may be required to wear respirators to comply with the cadmium standard. About 25 establishments in the U.S. are involved in nickel-cadmium battery production, zinc, cadmium, or lead refining, or the production of cadmium pigments and stabilizers. About 4,000 employees are exposed to cadmium in these establishments, and many are currently provided with respiratory protection. Compliance with the cadmium standard may require up to 80 percent of the workers in these plants to wear respirators full time.

For six industry sectors (nickel-cadmium batteries, zinc/cadmium refining, pigments, stabilizers, lead smelting/refining, and cadmium plating) in which the evidence on current exposures and the effectiveness of additional controls indicated that the PEL of 5 $\mu g/m^3$ is not feasible with engineering controls, separate engineering control air limits (SECALs) were specified. In order to identify the appropriate SECAL levels for employees in these industries, a process by industry methodology was adopted. High and low exposure processes were analyzed separately to avoid producing an overall SECAL which may not be relevant to either group. Table VIII–A2 shows the SECAL levels identified for these industries, and Table VIII–A3 provides a distribution of employees by SECAL or PEL level in each sector.

Compliance costs for each of the provisions of the standard were estimated for each industry. These costs are summarized in Table VIII–A4. The cost of engineering controls was determined by evaluating the additional engineering controls which establishments would introduce in each affected industry. The unit costs of feasible controls, the number of additional controls necessary, and the expected effectiveness of the controls were estimated based on the evidence in the record. Costs for engineering controls comprise the largest part of the total compliance costs and represent an estimated $82.5 million on an annualized basis.

In addition, the estimated annual costs of compliance include costs for respiratory protection ($13.5 million), exposure monitoring ($8.0 million), medical surveillance ($19.8 million), hygiene facilities and practices ($56.5 million), and information, training, and record keeping ($6.8 million). The total estimated annualized cost of the standard is approximately $187.7 million.

Economic Impacts

Based on the evidence in the record, OSHA has determined that compliance with the final cadmium standard is economically feasible in each of the affected industries.

Table VIII–A5 summarizes the economic impacts for the industries affected by this rulemaking. For most industries, the standard affects a limited number of activities and the costs of compliance represent less than 0.1 percent of revenues.

TABLE VIII–A2.—SECALS FOR PROCESSES IN SELECTED INDUSTRIES

Industry sector	Plants	Number of workers	Processes	SECAL or PEL (ug/m³)
Nickel cadmium battery	6	375	Plate making, plate preparation	50
		1,125	All other processes	15
Zinc/cadmium refining	5	202	Cadmium refining, casting, melting, oxide production, sinter plant.	50
		1,148	All other processes	5
Pigment manufacture	4	60	Calcining, crushing, milling, blending operations	50
		40	All other processes	15
Stabilizers	5	50	Cadmium oxide charging, crushing, drying, blending operations.	50
		150	All other processes	5
Lead smelting	4	60	Sinter plant, blast furnace, baghouse, yard area	50
		340	All other processes	5
Plating	400	120	Mechanical plating	15
		1,080	All other processes	5

TABLE VIII–A3.—DISTRIBUTION OF EXPOSED EMPLOYEES IN HIGH EXPOSURE INDUSTRIES

PEL/SECAL ($\mu g/m^3$)	Batteries		Zinc/Cadmium		Pigments		Stabilizers		Lead		Plating		Totals
	High	Low	High	Low	High	Low	High	Low	High	Low	High	Low	
PEL:													
5 $\mu g/m^3$				1,148				150		340		1,080	2,718

TABLE VIII-A3.—DISTRIBUTION OF EXPOSED EMPLOYEES IN HIGH EXPOSURE INDUSTRIES—Continued

PEL/SECAL (μg/m³)	Batteries		Zinc/Cadmium		Pigments		Stabilizers		Lead		Plating		Totals
	High	Low	High	Low	High	Low	High	Low	High	Low	High	Low	
SECAL:													
50 μg/m³	375		202		60		50		60				747
15 μg/m³		1,125				40					120		1,285
													2,032
Total													4,750

TABLE VIII-A4.—SUMMARY OF COMPLIANCE COSTS BY PROVISION AND BY INDUSTRY

[Thousands of Dollars]

Industry	Number of affected establishments	Engineering controls	Respirators	Exposure monitoring	Medical surveillance	Hygiene/clothing	Information, training, recdkpg.	Total
Batteries	6	881	180	16	388	495	6	1,947
Zinc/cadmium	5	728	150	17	363	459	5	1,723
Pigments	4	312	12	10	35	104	1	473
Formulators	700	4,620	525	914	1,277	0	35	7,371
Stabilizers	5	825	12	11	36	50	1	935
Lead	4	112	60	3	106	0	2	283
Plating	400	189	6	166	102	294	30	787
Utilities	4,000	0	0	1,600	600	0	188	2,388
Iron/steel	120	0	300	288	1,000	0	50	1,638
Subtotal	5,244	7,647	1,245	3,025	3,907	1,402	319	17,545
Other general industry	50,000	74,820	11,655	2,754	13,512	50,937	5,737	159,615
Construction	10,000	0	350	2,870	2,380	4,203	700	10,503
Total	65,244	82,467	13,450	8,649	19,799	56,542	6,756	187,663

Note: Costs do not include current expenditures.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

TABLE VIII-A5.—SUMMARY OF ECONOMIC IMPACTS BY INDUSTRY

[Thousands of Dollars]

Industry	Number of affected establishments	Total annual costs of compliance	Average annual cost per affected establishment	Total annual revenues	Ratio of compliance costs to revenues	Total annual profits	Ratio of compliance costs to profits
Batteries	6	1,947	324.5	185,000	0.011	7,400	0.263
Zinc/cadmium	5	1,723	344.6	230,000	0.007	NA	NA
Pigments	4	473	118.4	30,000	0.016	1,500	0.316
Formulators	700	7,370	10.5	900,000	0.008	45,000	0.164
Stabilizers	5	935	187.1	92,000	0.010	8,300	0.113
Lead	4	283	70.7	176,000	0.002	NA	NA
Plating	400	787	2.0	200,000	0.004	8,800	0.089
Utilities	4,000	2,388	0.6	140,000,000	0.000	7,000,000	0.000
Iron/steel	120	1,638	13.7	64,000,000	0.000	NA	NA
Subtotal	5,244	17,545	3.3	205,813,000	0.000	7,071,000	0.002
Other general industry	50,000	159,615	3.2	290,820,000	0.001	14,731,000	0.011
Construction	10,000	10,503	1.1	490,000	0.021	NA	NA
Total	65,244	187,663	2.9	497,123,000	0.000	21,802,000	0.009

Note: (1) Costs do not include current expenditures.
(2) Where sales or profit data provided to the record for specific companies or industries were used, the information was verified through publicly available sources such as Dun & Bradstreet, DIALOGUE, Dow Jones News Retrieval, and Nexis.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

The compliance costs are generally expected to result in slight increases in prices for goods and services associated with occupational cadmium exposures.

In some industries price increases needed to recoup compliance costs may decrease sales volume. For these establishments the standard may result in some reduction in profits. OSHA does not expect the standard to significantly affect the viability of continuing operations in any industry or to result in any plant closures. However, to the extent that compliance costs contribute marginally to increased production costs, prospects for economic expansion and employment growth in industries with cadmium exposure may be diminished.

Basically, the regulation tends to trade some of the societal benefits of producing and using products containing cadmium for greater protection among exposed employees. Compliance with

the standard ultimately causes production resources to be shifted from the regulated industries and from other sectors of the economy to compliance-related activities. Although the overall effect on the economy will probably be undetectable, a very slight increase in prices may result from the improvement in the protection of the health of employees exposed to cadmium.

B. Discussion of Technological and Economic Feasibility Determinations

Introduction

The Occupational Safety and Health (OSH) Act of 1970 requires OSHA to promulgate standards protecting the health of employees and requires that in the development of standards, one of the "considerations shall be * * * the feasibility of the standards" [Pub. L. 91-596 sec. 6. (b) (5)]. The courts have required that OSHA must bear "the initial burden of proving the general feasibility of the standard for the industry as a whole at the rulemaking stage" [1, p. 1270].

Through the rulemaking process OSHA has compiled a comprehensive record of the feasibility of controlling employee exposures to cadmium. OSHA published a proposed rule with a preliminary analysis in February, 1990 and solicited data and comments from the public. The record remained open for over eight months, and many comments were submitted by interested parties. At the public hearings each witness was available for cross-examination. Before the record closed, participants were given the opportunity to respond to all new information submitted. The resultant record provides the best available evidence for determining the feasibility of the new cadmium standard.

Legal Consideration in Determining Technological Feasibility

OSHA is obligated by the OSH Act to promulgate standards that "to the extent feasible" best protect workers. OSHA does not believe that it can satisfy this obligation by using a lowest-common-denominator approach, i.e. by protecting all workers only to the extent that the most severe feasibility constraint on protecting any worker would allow. On the contrary, OSHA believes that if a minority of workers cannot be as effectively protected as the majority, that fact is not an adequate reason to forego protecting the majority to the extent feasible.

Court decisions have supported this understanding of technological feasibility. In a decision describing the preliminary test of general feasibility that an OSHA standard must pass in a pre-enforcement review, one court summed up OSHA's burden of proof as follows: "* * * within the limits of the best available evidence, and subject to the court's search for substantial evidence, OSHA must prove a reasonable possibility that the typical firm will be able to develop and install engineering and work practice controls that can meet the PEL in most of its operations. * * * Such a standard of review for feasibility, of course, in no way ensures that all companies at all times and in all jobs can meet OSHA's demands." [1, p. 1272].

In adopting this understanding of feasibility for purposes of analysis, a related question arises. Namely, how does random variability in exposure levels affect an assessment that a particular level is technologically feasible?

OSHA recognizes that some random fluctuation of exposure levels around the average does exist. As a result, employers will generally need to control exposure levels to an average somewhat below the limit to ensure that most of the fluctuations will not exceed the limit. Further, some of the variation may be the result of identifiable and controllable causes, such as inadequate or poorly maintained engineering controls, improper work practices, or lack of oversight by qualified personnel. Correcting deficiencies in controls should reduce existing exposure levels and substantially reduce variability.

For operations where the PEL cannot be achieved with engineering controls and work practices, the employer must nevertheless implement all feasible engineering controls to reduce exposures in addition to using respiratory protection. The requirement to implement all feasible engineering controls generally applies to the existing building, equipment, and manufacturing process (although OSHA has the authority to set standards that are "technology forcing" [1, p. 1264]). For purposes of complying with this requirement, it is usually sufficient to demonstrate that every reasonable effort has been made to reduce exposures given the limitations of the plant configuration and the nature of the process.

Public Comments Regarding Feasibility Determinations

Several comments responding to the proposed standard [55 FR 4052] criticized the methodology and conclusions of the preliminary analysis concerning technological feasibility and costs of compliance. The final analysis addresses these concerns, where appropriate, by modifying analytical approaches, revising estimates, and using additional information and data submitted to develop an accurate characterization of impacts. The conclusions in this final analysis reflect these changes and are based on the best available evidence as provided by the record.

For example, OSHA reviewed the record to ensure that the full range of job categories exposed to cadmium was identified for each industry. All potentially affected industries were studied and the number of exposed employees was determined. The full spectrum of cadmium exposure sources and the corresponding prospects for additional engineering controls were assessed for each job category. The expected effectiveness of controls and the anticipated reductions in exposures were re-examined in the light of the comments and testimony submitted. Potential biases associated with the exposure data were evaluated, concerns raised in regard to statistical applications were resolved, and additional exposure data submitted to the record were incorporated into the analysis.

Many of the apparent differences among the estimates and conclusions presented in the record can be explained by differences in the perceptions of the requirement to install controls to the extent feasible.

Some commenters assumed that a feasible PEL is one that would virtually never be exceeded even by atypical monitoring results. For these commenters, the corresponding estimates of the lowest feasible PEL were often 2.5 times mean exposures, and estimates of compliance costs reflected a reduction in mean exposures to less than 40 percent of the PEL. Comments made on the basis of these assumptions tended to highlight the feasibility problems and cost of any lower exposure limit.

Process by Industry Feasibility Determinations

In addressing the legal requirements for OSHA technological feasibility analysis and the concerns expressed by affected parties during public hearings on the proposed rule, OSHA has adopted an occupation/process by industry feasibility analysis in this RIA. The approach separately analyzes worker exposure levels by occupation/process within industry segments affected by the rule. The approach was designed to extract the maximum utility from the existing data and to minimize the influence of data source differences

and inconsistencies. The occupation/process analysis became the analytical tool for identifying appropriate SECAL levels within affected industries.

As a general rule, OSHA determines whether a permissible exposure limit is technologically and economically feasible for an industry by determining whether it can be achieved in most operations most of the time with engineering and work practice controls. This approach is sensible and useful for several reasons: it permits industrial commonalities to dominate over exceptions in a constructive way; it reflects the fact that air contaminants tend to drift throughout the plant and that workers often move from one part of the plant to another during or between work assignments; and it produces a regulatory standard that is specific and accurate on the one hand, and workable from an enforcement perspective, on the other.

Although the "most operations most of the time" test is the best general rule for determining the feasibility of an engineering and work practice control limit for an industry, an exception to that rule is appropriate for six industrial sectors engaged in cadmium production operations. In nickel-cadmium battery production, zinc/cadmium refining, pigments, stabilizers, lead smelting/refining, and cadmium plating, exposure data tended to fall into distinct high and low exposure clusters, especially from process to process within industries. A unitary "most operations most of the time test" would ignore this division and either impose on the low cluster a control limit that would be needlessly high or impose upon the high cluster a control limit that would be unrealistically low.

OSHA used statistical analysis of exposure data to distinguish high and low exposure processes and represented the high and low exposure groups as high and low exposure distributions. Then OSHA used the record evidence to estimate the amount of exposure reduction that would occur from implementing controls for each distribution. OSHA applied that reduction to its respective distribution and determined the separate engineering (and work practice) control air limit (SECAL) for the processes from these distributions. This methodology allows developing different control standards where exposures in the process are substantially different and produces the lowest feasible SECAL for distinct occupation/process clusters.

Moreover, the process approach adopted here does not preclude consideration of individual plant characteristics when such characteristics can be identified. For example, in the cadmium stabilizer subsector, one plant is known to have successfully reduced exposure levels following a technology improvement program. This empirical data reinforced confidence that engineering controls could reduce exposure levels in other plants. Conversely, in lead smelting, data submitted to the record indicated that one plant has exposure levels considerably above three other plants in this subsector. Only this plant would appear to benefit from additional engineering controls to reduce exposure levels. This consideration was explicitly factored into the engineering control reduction level projected for this industry group. Finally, when inter-plant technology controls and exposure levels can not be distinguished, a cross-plant process analysis is the most neutral approach to characterizing industry exposures and technology control problems and solutions.

In technological and economic feasibility analysis attention generally concentrates on the more problematic process exposures. From an engineering design control perspective, the presumption is that high exposure processes will be more difficult and costly to control. Most engineering control remedies for high exposure processes will simultaneously lower within plant exposures for all occupations. Attention justifiably focuses on the feasibility of existing technology to control high exposure processes. In evaluating control strategies in this approach, exposure reduction factors were applied to the high and low exposure groups based on the evidence in the record addressing the ability to control exposures in each type of plant.

In designing the occupation/process approach to SECAL selection, the effort was made to take into account the many concerns expressed by industry representatives and others, that any engineering control level selected, should be capable of being met most of the time. To achieve this, all occupation/process data from all available sources were entered into a computer for analysis. Usually these data were a mixture of exposure ranges, by occupation/process, often with a median or geometric mean identified. Based on these data, a distribution of exposures was projected through the use of statistical modelling.

Occupation/process data were then depicted using a "box and whisker" diagram. The two dimensional "box" reflects the range within which 50 percent of exposure readings are found. The vertical band within a box represents the median value for the entire distribution; the "whisker" element shows the extent of exposure above and below the 50 percent block which captures the median.

Using this presentation of exposure data facilitated the identification of high and low occupational exposure by process. The Agency segregated the occupation/process data into sets of high and low exposures for six industries for whom SECALs would be required. In the text below, the nickel-cadmium battery industry is used to illustrate the verification process used to prove that certain occupation/process groups were statistically different based on exposure data.

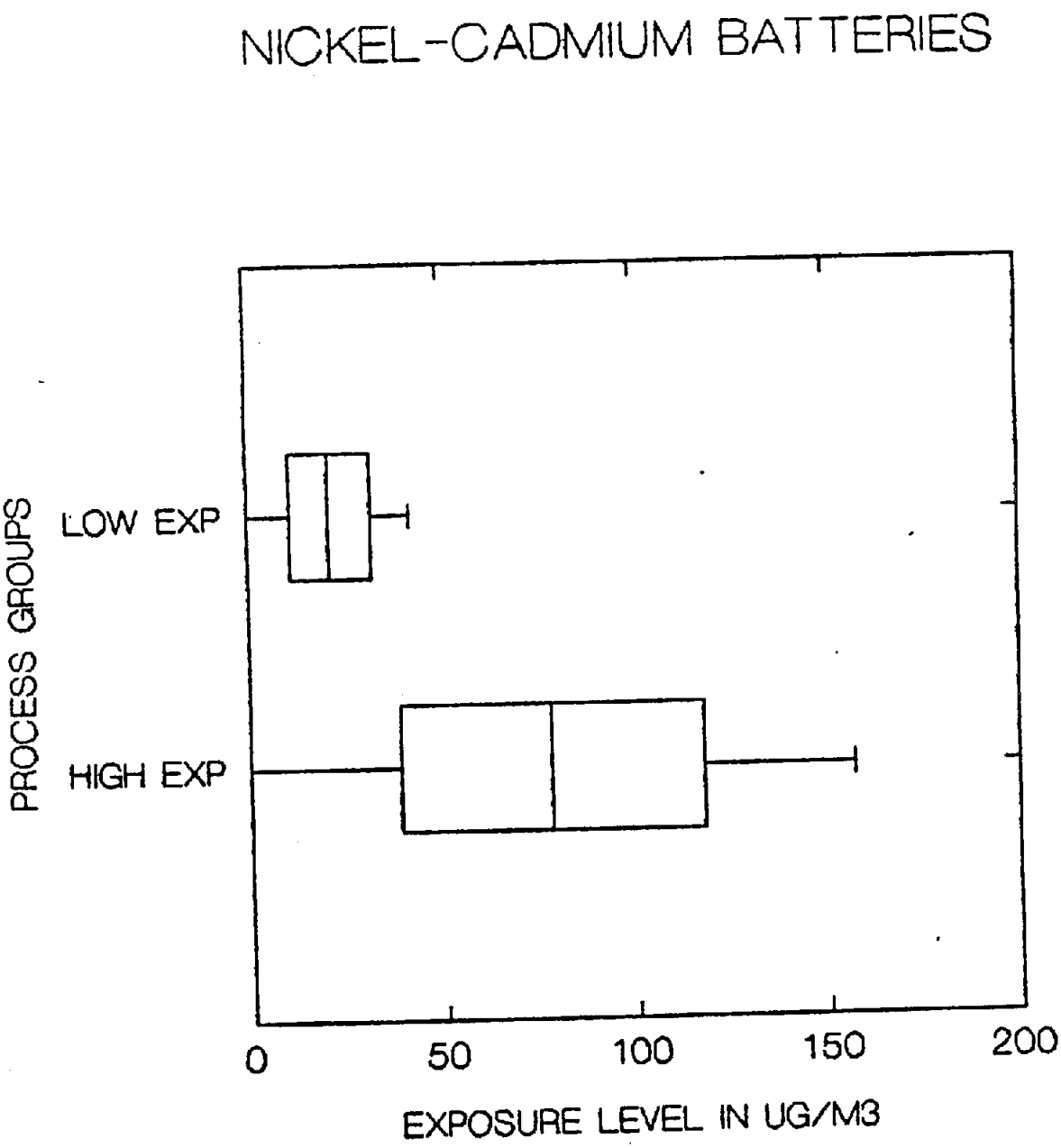
Six plants producing nickel-cadmium batteries constitute an industry. Each of the six plants produces more than one type of battery (sealed cell, vented, aerospace, commercial, etc.) involving different processes. Each plant can achieve different lowest feasible levels. To assess the lowest feasible level, high and low exposed occupation by process groups were identified and separately analyzed.

Ten sources of data on exposures in these six plants were available. All data sources are considered legitimate and no preference is expressed among them. Differences in levels may be explained by different levels of engineering controls, different points in time in the plant, different production levels, different work practices, different process modifications, or upset conditions.

In the nickel-cadmium battery industry, the following occupations/processes were identified as having high exposures: plate preparation operations and plate making operations. All other occupations and processes for which the Agency had information were identified as having low exposures. Figure VIII–B1 shows the segregated data.

BILLING CODE 4510–26–M

FIGURE VIII-B1



BILLING CODE 4510-26-C

In the nickel-cadmium battery sector the exposure data were as follows:

	High group	Low group
Number of observations.	26 (=N_H)	48 (=N_L)
Mean value	72.9 (=X_H)	14.4 (=X_L)
Standard deviation	62.7 (=S_H)	23.5 (=S_L)

To verify that the two groups within this industry were distinct, the Agency tested whether the means of the two samples were the same.

Formally, the proposed null hypothesis was that the means were equal, or equivalently, that the difference in means was zero. In general terms, if the difference in means of the two samples is large compared to its distribution, which is centered around zero, then it is unlikely that the samples are drawn from the same population. Under the assumption that the difference in means was distributed normally (central limit theorem) the appropriate test statistic is:

(mean of high exposures—mean of low exposures)—true mean÷standard error of the difference in means

The standard deviation of the difference in means is closely approximated by the square root of the sum of the squared standard errors of the means and the standard error is given by:

$$S.E._{HL} = \text{Square root}[S_H^2/N_H + S_L^2/N_L)$$

Then, the test statistic is a standard normal random variable equal to:

$$z = [(X_H - X_L) - 0]/S.E._{H\text{-}L}$$

For the standard normal distribution, there is less than a 5 percent probability that the (absolute) value of a test statistic would exceed 2.0 if its true mean was zero. The probability of the test statistic being 4.6 or larger (4.6 was the actual value for z in the formula above) under the assumption that the means are equal is less than 0.001. Therefore the null hypothesis that the means of the exposure data are equal is rejected and the conclusion that they are drawn from distinct distributions is accepted.

As the exposure samples are not large, we also tested their difference with the more conservative *t* statistic with $[N_H + N_L - 2) = 72$ degrees of freedom.

The standard error is estimated as:

$$S.E._{H\text{-}L}{}^t = \text{Square root } \{[(N_H-1)S_H{}^2 + (N_L-1)S_L{}^2] \times (1/N_L+1/N_H)/(N_H+N_L-2)\}$$

For the nickel-cadmium data the *t* statistic is 5.8. In this case, there is less than a five percent probability that the *t* statistic will be larger than 2.0 if the means are actually equal. Under the assumption that the means are equal, the probability that the *t* statistic should be as large as 5.8 is less than 0.001. We again reject the null hypothesis that the means are equal.

Once a statistical difference between high and low exposure groups was verified, the data were analyzed separately. In developing graphs of existing exposures for each occupation/process type, medians and means were used from each of the exposure sources.

The resulting distributions for nickel-cadmium battery producers are shown in Figures VIII–B2 and VIII–B3, with the high group represented by occupations directly involved in plate preparation and plate making operations and the low group by all other industry occupations, including impregnation, spiraling, cell assembly, nickel plating, sorting and stacking processes. (In these Figures and those that follow all data were "fitted" to a straight line using ordinary least squares methodology.)

The final step in identifying appropriate SECAL levels for the two groups was done through a modelling process. The current exposure pattern for each group was reduced based upon alternative engineering control efficiency levels of 80, 60, 40 and 20 percent. The higher the efficiency level, the lower the projected exposure level. Figures VIII–B4 and VIII–B5 show the reduction effect and shift in the distribution of exposures for the high and low groups in nickel-cadmium battery production.

Finally, a selection had to be made among the different efficiency reduction factors based upon evidence and testimony in the record and economic feasibility considerations. Where evidence in the record clearly indicated that an engineering control strategy would reduce exposure levels, the reduction factor range most closely approximating the new projected exposure levels was selected.

BILLING CODE 4510–26–M

FIGURE VIII-B2

BATTERIES (LOW EXP): CURRENT

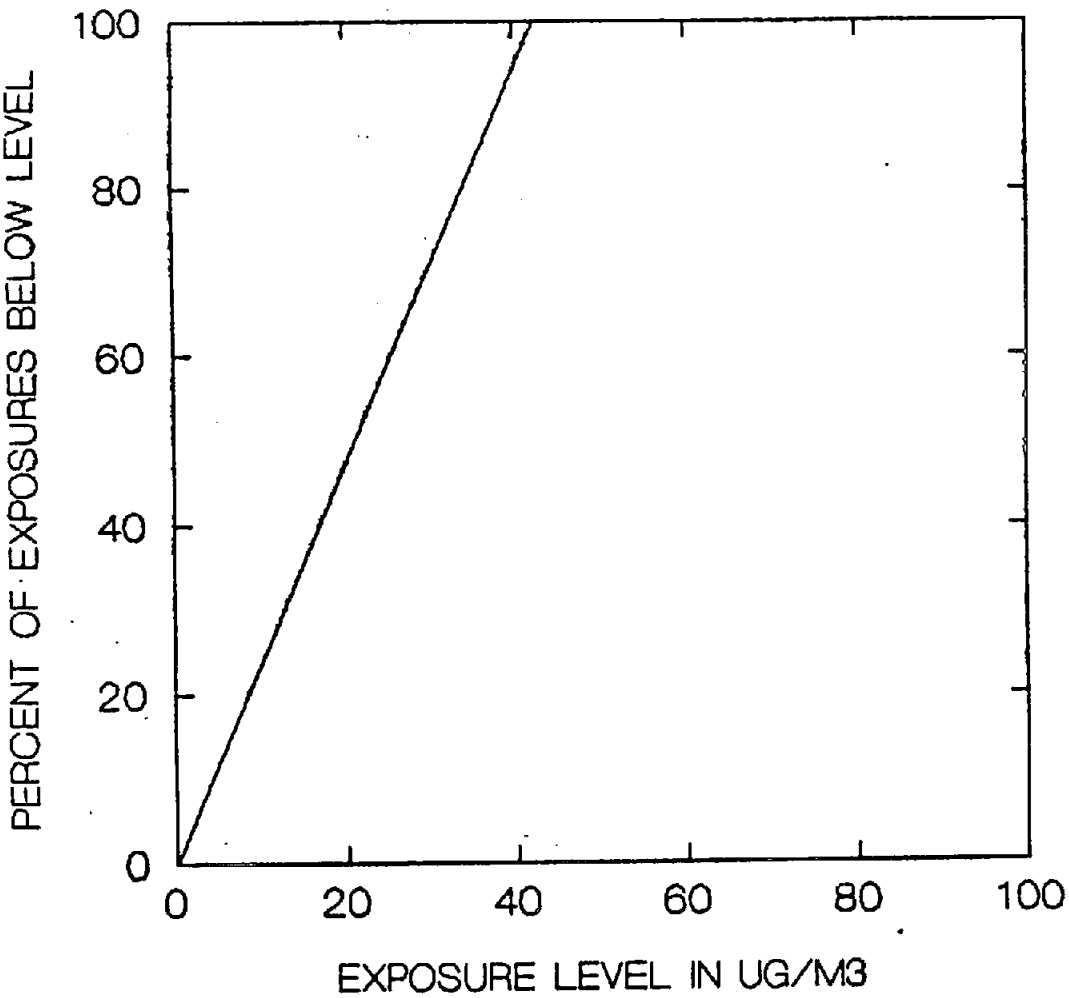


FIGURE VIII-B3

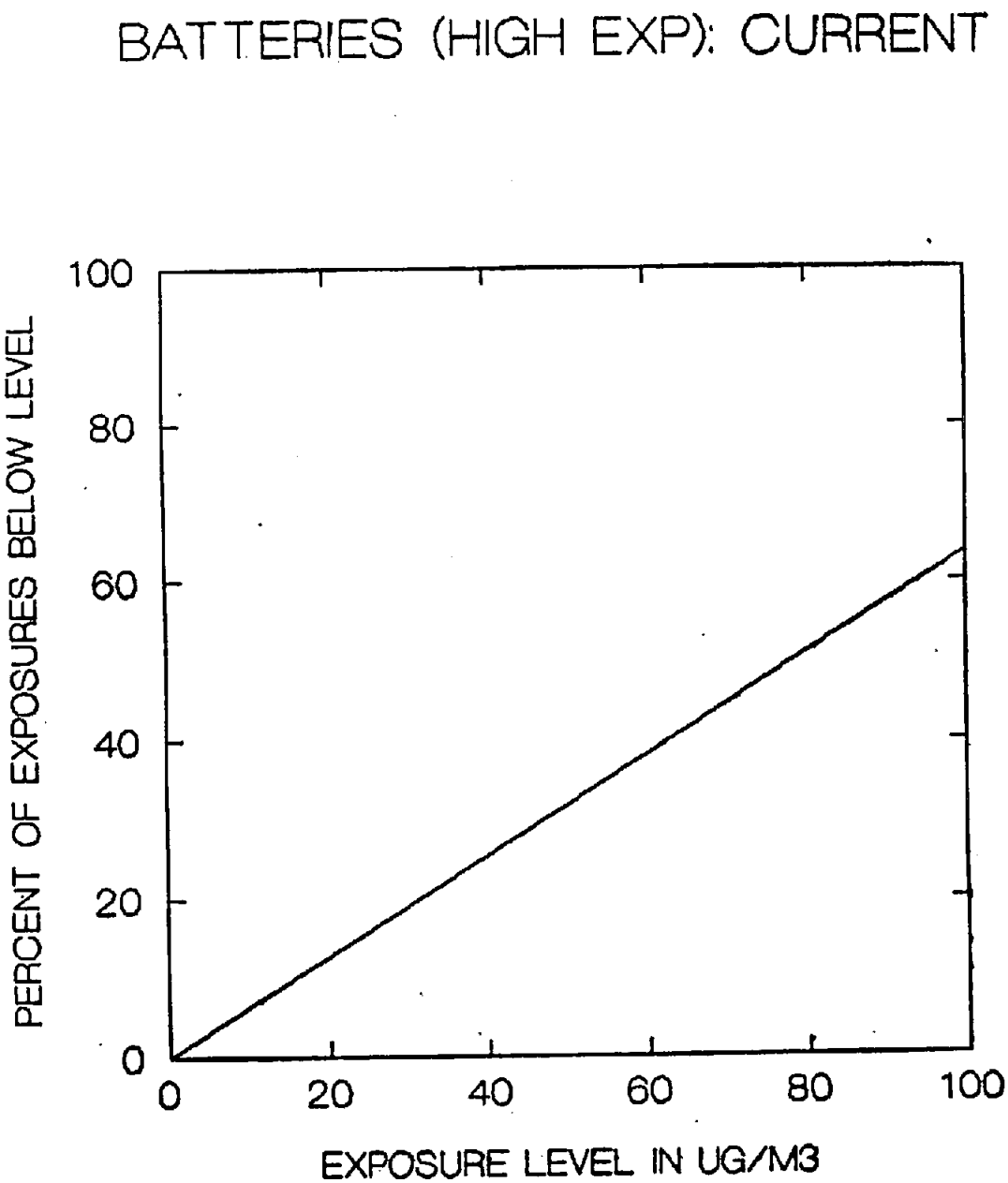


FIGURE VIII-B4

BATTERIES (HIGH EXP.): CONTROLLED 80%-20%

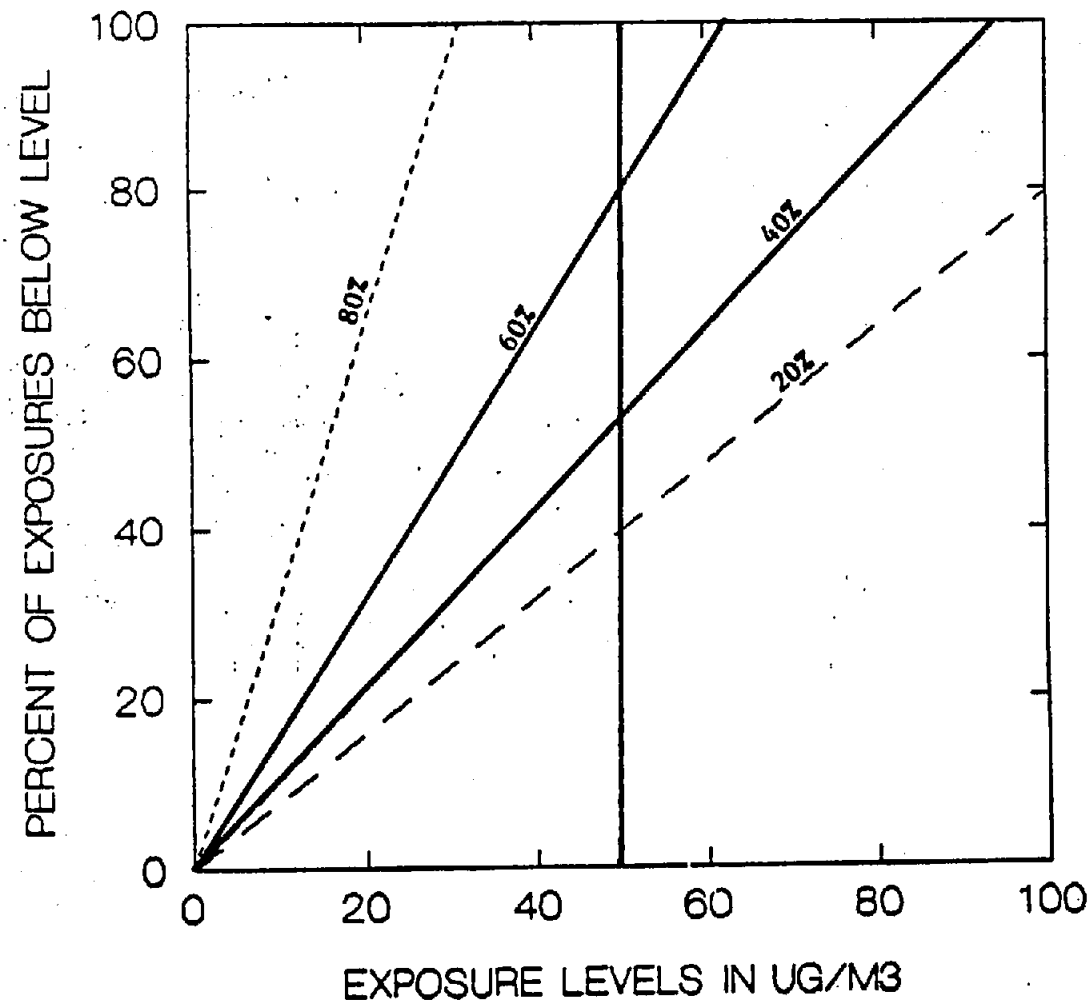
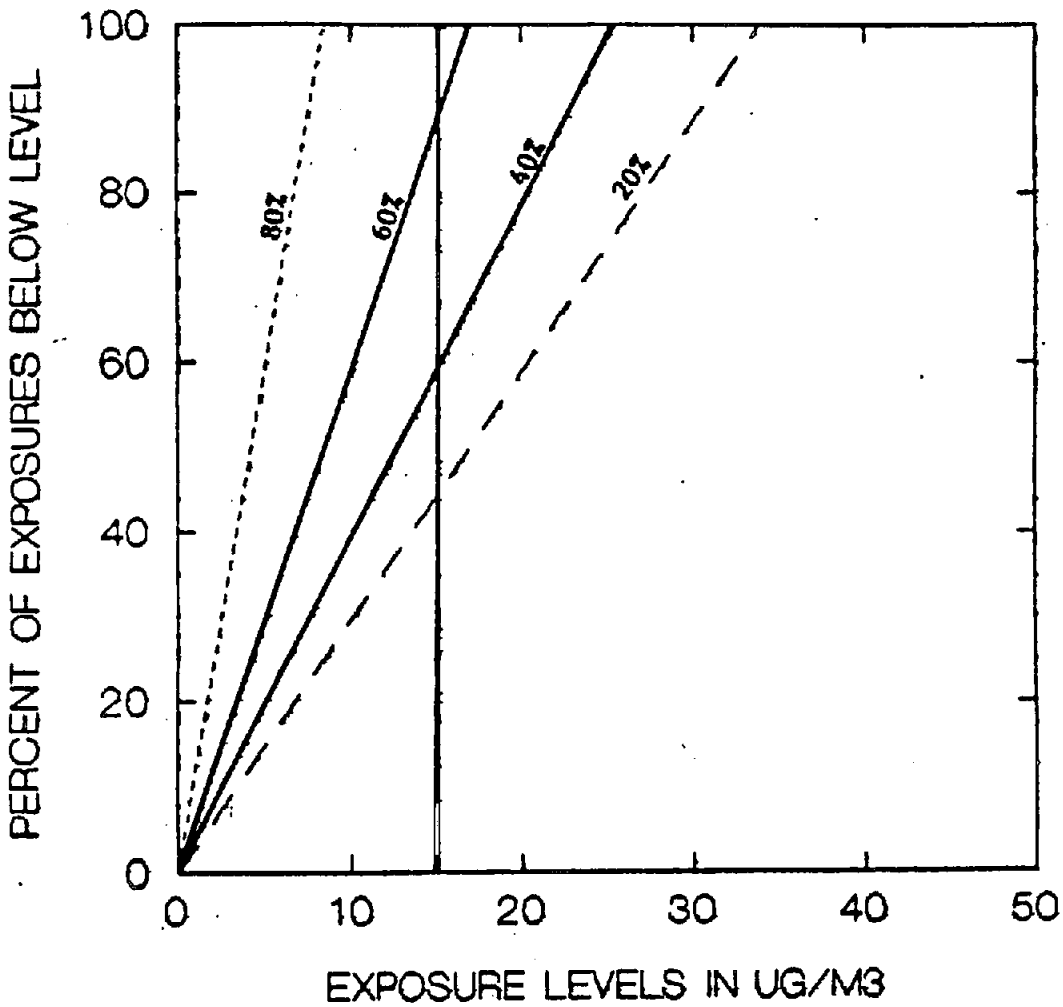


FIGURE VIII-B5

BATTERIES (LOW EXP.): CONTROLLED 80%-20%



BILLING CODE 4510-26-C

The only basis for revising this choice was if the control strategy was so costly as to make the option economically infeasible for a given industry. Industry cost and profit ratios were relied on in making a determination of economic feasibility. The higher the ratio, the more important it became. If costs represented 20 percent or more of profits, the shift to a less costly engineering control strategy and lower reduction factor (60 percent instead of 80, for example) was considered. For battery producers this reduction was made. The regulatory cost to profit ratio exceeded 20 percent and the less costly 40 - 60 percent range of reduction level was used.

Following selection of the reduction factor range, the appropriate SECAL for an exposure group was made at the level achievable for most (60 - 80 percent) of the exposure observations. For workers exposed to cadmium in battery production a SECAL of 50 $\mu g/m^3$ for plate preparation and platemaking processes was identified; for all other occupations and processes a SECAL of 15 $\mu g/m3$ was identified.

The methodology outlined above was applied to each industry in which additional analysis for determining the feasibility of achieving the PEL of 5 $\mu g/m3$ with engineering controls appeared to be useful. The sector-by-sector analysis found bifurcated exposures by process type across all industries and verified the appropriateness of different SECALs for affected industries. Table VIII-B1 shows the SECAL levels in high exposure industries and Table VIII-B2 provides a distrib'ution of employees by SECAL or PEL level in each high exposure industry sector.

Unit Cost Estimates and Economic Feasibility

*Unit costs.*OSHA developed unit cost estimates based on the engineering controls that would be required for each operation to reduce ambient exposure levels of cadmium. Some cost estimates submitted to the record included controls or measures of questionable effectiveness and very high cost. As discussed in more detail for specific industries, the data and evidence in the record provided consistent estimates of the approximate cost of additional controls once differences in underlying assumptions were taken into account.

Local exhaust ventilation systems are the predominant method of engineering control to reduce occupational exposures to cadmium, and they can be adapted to exposure sources in many different industries. JACA [3] provided estimates of the cost of local exhaust ventilation systems that ranged from $51,000 to $110,000 (in current dollars). These estimates reflect the total costs, including costs for one or more hoods, duct work, a baghouse, a stack, and installation. Annual operating and maintenance costs were estimated to be 10 percent of the capital cost. Based on these estimates, OSHA concluded that the average unit cost for a local exhaust ventilation system would be $80,000 in capital costs and $8,000 in annual costs.

Other evidence submitted to the record regarding the unit costs of local exhaust ventilation systems was generally consistent with the JACA estimates.

TABLE VIII-B1.—SECALS FOR PROCESSES IN SELECTED INDUSTRIES

Industry sector	Plants	Number of workers	Processes	SECAL or PEL ($\mu g/m^3$)
Nickel cadmium battery	6	375	Plate making, plate preparation	50
		1,125	All other processes	15
Zinc/cadmium refining	5	202	Cadmium refining, casting, melting, oxide production, sinter plant.	50
		1,148	All other processes	5
Pigment manufacture	4	60	Calcining, crushing, milling, blending operations	50
		40	All other processes	15
Stabilizers	5	50	Cadmium oxide charging, crushing, drying, blending operations.	50
		150	All other processes	5
Lead smelting	4	60	Sinter plant, blast furnace, baghouse, yard area	50
		340	All other processes	5
Plating	400	120	Mechanical plating	15
		1,080	All other processes	5

TABLE VIII-B2.—DISTRIBUTION OF EXPOSED EMPLOYEES IN HIGH EXPOSURE INDUSTRIES

PEL/SECAL ($\mu g/m^3$)	Batteries		Zinc/Cadmium		Pigments		Stabilizers		Lead		Plating		Totals
	High	Low	High	Low	High	Low	High	Low	High	Low	High	Low	
PEL:													
5 $\mu g/m^3$				1,148				150		340		1,080	2,718
SECAL:													
50 $\mu g/m^3$	375		202		60		50		60				747
15 $\mu g/m^3$		1,125				40					120		1,285
													2,032
Total													4,750

Of the additional information submitted, PACE [4] provided the most comprehensive description of controls and unit costs. For example, the installation of a local exhaust ventilation system with a hood, ducts, and a Venturi scrubber was estimated to cost $57,000 in a cadmium refining operation. In another cadmium refining operation, a collection hood and exhaust system with sloped, flushed ducts was estimated to cost $24,000. PACE also identified additions or improvements in ventilation for at least five operations in the production of cadmium stabilizers

with a total cost of less than $150,000. In conclusion, OSHA is confident that a unit of cost $80,000 provides a fair representation of the cost of implementing a substantial local exhaust ventilation system.

In addition to local exhaust ventilation systems, PACE recommended the use of other engineering controls for operations in several industries. OSHA agrees that many of these controls may provide significant reductions in exposures and included costs for these controls in the final analysis. For example, in several industries PACE recommended the use of clean air islands and estimated the cost as $3 per cfm (cubic feet per minute). The recommended systems ranged from 2,000 to 9,000 cfm and cover areas from 4 feet by 5 feet to 6 feet by 15 feet. OSHA concluded that the average unit cost for this type of control would be about $18,000.

Other types of controls referred to by PACE and other commenters involved a variety of relatively inexpensive modifications but were often applicable to specific operations or circumstances. Where the evidence suggested that such control options could be implemented effectively, costs for such controls were included in the final analysis. Since OSHA cannot realistically determine every control possibility in every operation in every plant, a unit cost of $9,000 for such controls was estimated based on the cost data submitted. Total costs per plant for such controls were approximated by estimating the appropriate number of units of these controls applicable in each type of affected establishment.

For example, estimates submitted by PACE included: partition an area from rest of building, $9,000; panel ceiling, $10,000–$15,000; complex enclosure of briquette press, $5,000; glove box hood with mechanical assist, $5,000; power conveyor for pouring, $11,000; downflow grate at front of furnace, $3,000; pass-through airlock glove box, $5,000; enclose drum fill, $1,700; enclose feed table with 10' by 3' backdraft hood, $1,600; GEMCO valve, flex boot, and flange, $2,600; modify dump enclosure for 2 tanks, $3,000; blending enclosure, $4,000; and special protection of electrical equipment, $15,000.

Unit costs for housekeeping consisted of capital costs for industrial vacuum cleaning systems and labor costs for using the system regularly. JACA assumed that a HEPA-filtered industrial vacuum cleaner could be purchased for $1,500. PACE's estimated cost for a large portable HEPA-filtered vacuum was $10,000, and the estimated cost for a central vacuum system with piping for 20,000 square feet of floor/platform area was $31,200. OSHA believes that the cost of establishing an adequate housekeeping program can be approximated by using an average unit cost of $15,000 per system; furthermore, the analysis recognizes that more than one such system may be needed in some plants. In addition to costs for power and maintenance, OSHA estimated that sufficient utilization of such a system may require annual labor costs of $7,000 (representing about 500 hours per year).

Unit costs used to estimate compliance costs for other requirements of the cadmium standard were based on information provided to the record. The annual cost of protecting an employee with a HEPA-filtered respirator, including fit testing, was about $300, according to testimony from an industry representative based on experience with respirator programs [5]. The laboratory cost of analyzing the results of exposure monitoring is an estimated $40 per sample, and the cost of collecting the samples would average about $200 per sample, according to estimates provided by an industrial hygiene firm [3]. Costs for hygiene facilities, training, and recordkeeping were evaluated for each industry based on estimates of current compliance and the extent of additional efforts needed. The unit cost for providing a daily shower during the work shift for employees exposed above the PEL was estimated at $900 annually, based on fifteen minutes per day for 240 days per year at $15 an hour.

Costs of compliance with the medical surveillance provisions were calculated based on unit cost estimates for specific elements. The analysis of samples of urine and blood for cadmium was estimated to cost $00 per sample, based on estimates from industrial medical clinics [3]. According to a public health research group, the unit cost for the analysis of a urine sample for β_2-microglobulin was $80 per sample [6]. The cost of an annual physical, including the wages paid to the employee, was estimated to be $250. This figure is based on research conducted by JACA (adjusted to current dollars), and is consistent with unit costs for comparable medical exams used in other OSHA analyses, reflecting current prices for industrial clinical services. Cost estimates provided by industry reflected unit costs for exams between $300 and $400, but these estimates may include biological monitoring costs and may not reflect the minimum cost necessary for compliance with the standard.

The unit cost associated with the medical removal of an employee was calculated by assuming that on average the employer would incur hiring and training costs of $500 per removed employee. In addition, the wage for the job the removed employee would be transferred to was assumed to average $2 an hour (generally more than 10 percent) less than the wage for the former job, and removed employees would generally have full-time (2,000 hours per year) positions. As a result, medical removal of an employee for 18 months would cost about $8,000 for the wage differential plus $500 for hiring and training costs; removal of an employee for 9 months would cost a total of about $3,500 (costs for additional medical testing are evaluated separately). OSHA concludes that the average unit cost per medical removal would be about $5,000 (on the assumption that half medically removed workers will return to work after nine months and half will receive benefits for 18 months).

Economic feasibility. Once the unit costs were assigned to engineering controls, work practice changes, new administrative requirements, and personal protective equipment, industry costs to comply with the rule provisions were calculated. The total incremental cost to comply with the rule was separately calculated for each affected industry segment. Industry differences in cost impacts reflected current baseline practices and levels of worker exposure, and the number of establishments in a particular sector using cadmium.

Industry cost estimates (the amount of capital needed to comply with the rule) were compared with revenues and profit margins for recent years in order to determine the economic impact and feasibility of the regulation. No industry sector analyzed had a cost to profit ratio in excess of 0.5. For those sectors where costs represented between 20–50 percent of profit, this fact was considered when selecting engineering control strategies to reduce existing cadmium exposure levels.

Notes

1. USWA v. Marshall, 647 F.2d.
2. OSHA Instruction CPL 2.45B CH–1, Office of General Industry Compliance Assistance, December 31, 1990.
3. Exhibit 13, "Economic Impact Analysis of the Proposed Revision to the Cadmium Standard," Final Report, JACA Corporation, March 15, 1988.
4. Exhibit 19–43, Attachment L, "Feasibility and Cost Study of Engineering Controls for Cadmium Exposure Standard," PACE Incorporated, April 30, 1990.
5. Exhibit 19–30, "Comments on OSHA Proposed Cadmium Regulation," Big River Zinc Corporation, May 10, 1990.

6. Exhibit 123, "Comments of Public Citizen Health Research Group and the International Chemical Workers Union on OSHA's Proposed Standard Governing Occupational Exposure to Cadmium," Public Citizen, October 17, 1990.

C. Exposures, Costs, and Feasibility Analyses by Industry

Nickel-Cadmium Battery Production

Industry overview. The nickel-cadmium battery industry in the United States consists of six major manufacturers operating six facilities in different states across the country. The largest establishment is located in Florida and employs over 1,700 employees. The smallest facility has 16 employees and is located in Wisconsin. The remaining facilities have between 150 and 450 employees. [1, Slide 2]. Total employment for the industry is almost 3,000, of whom about half (1,500) are involved in production and maintenance and are potentially exposed to cadmium. [1, Slide 3].

There are many different types of nickel-cadmium batteries produced and designs are often customized for specific industrial, aerospace, military, household, commercial, or specialty applications. The National Electrical Manufacturers Association (NEMA) classified battery production in the United States into two categories: industrial-military-aerospace and household-commercial-specialty. NEMA estimated that approximately two thirds of the employees exposed to cadmium in the battery industry were involved in the production of household, commercial, and specialty batteries. [1, Slide 3].

Production processes. The production of nickel-cadmium batteries can be broken down into four basic steps. Each step may involve several operations that can vary depending on the type of battery and scale of production, but these steps encompass the manufacturing process utilized for battery production regardless of the type of battery or the particular facility. NEMA preferred to characterize the manufacturing process with a generic description of these four steps; detailed descriptions were withheld "because of their highly confidential and proprietary nature." [2, p. 3].

Step 1 is called plate making in the production of large industrial, aerospace, and military nickel-cadmium batteries; this step is also referred to as sintered plate manufacture in the production of small household and commercial nickel-cadmium batteries. In both cases the process begins with the same material, nickel-plated perforated steel, and produces a porous nickel plate. [2, p. 3].

A paste of finely divided nickel metal is pressed into the open grid of perforated and nickel-plated sheet steel. This is followed by sintering or drying in an oven. The dried plate can then be rolled up into a spiral or be cut, weighed, and coined for particular specifications prior to impregnation.

Step 2 involves impregnation. The porous nickel plates are immersed in a cadmium nitrate solution, rinsed, dried, and then immersed in sodium hydroxide. After rerinsing, the plates are dried and inspected. Continuous spiral wound plates are dipped as spools on large circular holding racks and then despiraled.

Sometimes an alternate process is used for this step. A paste of cadmium oxide with fillers and binders is prepared and then continuously pressed into a moving perforated sheet which is subsequently dried.

Step 3 is plate preparation and involves cutting, inspecting, and sorting the plates. This step ensures that the plates are of proper size and quality. In addition, the plates are stacked and readied for assembly.

Step 4 is the assembly of the battery or cell. For large industrial batteries, alternate plates containing cadmium hydroxide and nickel hydroxide are welded to terminals and placed in the battery casing. The casing is filled with an electrolyte solution and sealed.

The assembly of small household cells involves winding the electrodes into a tight cylinder together with an inert separation material. The roll is fitted into a nickel-plated metal can which is sealed after the electrolyte is added. Most of these steps are performed by automatic machines. [2, p. 4].

Employee exposures. The preliminary analysis produced by OSHA for the proposed rule relied on an exposure profile developed by JACA Corporation. [3, Table 3–8]. JACA relied on two primary sources for exposure monitoring data from nickel-cadmium battery producers. The first source was seven years of sampling results from OSHA's Integrated Management Information System (IMIS) database through August 1986. The second source was a Health Hazard Evaluation (HHE) performed by NIOSH at a battery plant in 1983. JACA also visited a nickel-cadmium battery manufacturing plant to assist in the interpretation and categorization of the data. JACA's exposure profile is presented in Table VIII–C1. Geometric mean exposures in six of the seven job categories, representing over 75 percent of the exposed employees, are estimated to be less than 17 $\mu g/m^3$.

PACE Incorporated developed an exposure profile for nickel-cadmium battery production at the request of the Cadmium Council. [4, Table A4–1]. This information is summarized in Table VIII–C2. The PACE estimates were calculated from data supplied from one plant. In nine of the eighteen job categories listed, the mean exposures are less than 22 $\mu g/m^3$; in four of the seven process areas listed, the mean exposures are generally less than 25 $\mu g/m^3$. PACE did not indicate what proportion of the workforce was represented by the job categories or process areas.

Another exposure profile was developed by Multinational Business Services, Inc. (MBS) as part of their report for NEMA. [5, Exhibit 1]. Their exposure profile, presented as a frequency distribution, was based on "representative industry data correlated by MBS" and is shown in Table VIII–C3. MBS concluded that 48 percent of all worker exposures were at or below 20 $\mu g/m^3$. Based on additional information provided by NEMA [2, Table II], for three process areas representing 80 percent of the exposed workforce exposures were at or below 20 $\mu g/m^3$ for 60 percent of employee exposures.

NEMA supplied occupational exposure data in its original submission by process step for different types of batteries. The results were compiled by NEMA from data supplied by six battery manufacturers [2, Table III] and are reprinted in Table VIII–C4.

TABLE VIII–C1.—PROFILE OF OCCUPATIONAL EXPOSURES TO CADMIUM IN THE NICKEL-CADMIUM BATTERY INDUSTRY BASED ON JACA CORPORATION

Job category	Concentration in μg/m³		
	Geometric mean	Median	Range
Materials handler	0.18	0.05	0.05–14.00
Impregnation operator	16.52	20.00	10.00–22.00
Coating operator	14.19	14.00	12.00–17.00
Plate preparation operator	90.07	83.00	26.00–284.00
Assembler	7.96	9.50	3.00–12.00
Supervisor	1.11	1.05	0.05–7.00
Maintenance	3.47	3.00	0.05–1,560.0

Source: JACA Corporation, Exhibit 13, Table 3–8.

TABLE VIII–C2.—PROFILE OF OCCUPATIONAL EXPOSURES TO CADMIUM IN THE NICKEL-CADMIUM BATTERY INDUSTRY BASED ON PACE INCORPORATED

Job category	Geometric mean exposures (μg/m³)
Impregnation area operator:	
1	4.3
2	1.8
3	10.0
4	14.0
5	130.0
6	28.0
Plate preparation	15.0
Cell assembly operator:	
1	72.0
2	46.0
Cell Closing Operator:	
1	12.0
2	21.0
3	13.0
Electrical tester	3.0
Negative plate manufacturing	252.0
Negative plate preparation operator:	
1	75.0
2	78 0
3	32.9
4	83.0

Source: PACE Incorporated, Exhibit 19–43, Attachment L, Table A4–1.

TABLE VIII–C3.—PROFILE OF OCCUPATIONAL EXPOSURES TO CADMIUM IN THE NICKEL-CADMIUM BATTERY INDUSTRY BASED ON MBS INCORPORATED

[In percent]

Process	Distribution of exposures (μg/m³)					
	0–5	6–20	21–50	51–100	101–150	Over 150
Platemaking	0.9	0.9	9.8	26.8	25.0	36.6
Impregnation	37.3	40.7	16.6	2.6	0.8	0.0
Plate preparation	2.9	60.9	30.4	5.8	0.0	0.0
Cell assembly	16.5	30.8	24.4	20.8	4.9	0.8

Source: Multinational Business Services, Inc., Exhibit 19–37 B, Exhibit 1.

Unfortunately, NEMA did not submit the individual monitoring results, did not provide mean exposure levels, and did not give any indication of the distribution of exposures. However, the data do indicate that the type of battery produced does not significantly affect the ranges of exposures in most of the process steps.

As part of its post-hearing comments NEMA supplied more detailed exposure data from five facilities. [6, appendices 1–5 and 7, p. 2]. The facilities were identified as companies A through E and the data are summarized in Tables VIII–C5 through VIII–C9, respectively. At company A, average exposure levels for non-manufacturing areas, for the lab, for ambient air in the production buildings, and for three of four production processes were below 15 μg/m³. Company B submitted only a series of ranges of exposures. Some ranges included exposures from 1 μg/m³ to over 1,000 μg/m³; at least one exposure range for most processes was between 1 μg/m³ and 20 μg/m³. Company C submitted exposure data for non-manufacturing areas (all less than 3 μg/m³) and for the platemaking process. Three of the four operations in the platemaking process had mean exposures of less than 25 μg/m³. Data submitted by company D show that eight of ten job categories in production had exposures of 13 μg/m³ or less. Company E submitted data for six production job categories, and four of these had exposures of 13 μg/m³ or less.

TABLE VIII–C4.—PROFILE OF OCCUPATIONAL EXPOSURES TO CADMIUM IN THE NICKEL-CADMIUM BATTERY INDUSTRY BY TYPE OF BATTERY PRODUCED BASED ON NEMA

Process step	Ranges of cadmium concentrations (μg/m³)	
	Industrial-aerospace-military batteries	Household-commercial batteries
Platemaking	4–180	5–190
Impregnation	5–180	5–180
Plate preparation	2–104	12–190
Cell assembly		8–40

Source: NEMA, Exhibit 19–37, Table III.

TABLE VIII-C5.—CADMIUM EXPOSURE DATA FOR NICKEL-CADMIUM BATTERY PRODUCTION AT COMPANY A

Process	Average exposure level (μg/m³)	
	(1)	(2)
Platemaking:		
Press	9.0	
Dry	2.0	
Impregnation	5.3	5.3
Plate preparation:		
Weld	51.6	
Shear	57.0	
Wet scrub	8.1	
Dry scrub		3.5
Assembly:		
Stacking	14.4	
Testing	2.0	
General area, April 16, 1990		31.8
General area, except April 16, 1990		9.3
Non-manufacturing:		
Managers	4.3	3.7
Lab	1.0	
Ambient air:		
Building 1	2.9	
Building 3	12.9	

[1] Source: NEMA, Exhibit 96.
[2] Source: NEMA, Exhibit 124.

TABLE VIII-C6.—CADMIUM EXPOSURE DATA FOR NICKEL-CADMIUM BATTERY PRODUCTION AT COMPANY B

Process	Range of exposure levels (μg/m³)
Platemaking—	
Paste application:	
June, 1990	10–395
April, 1990	1–57
March, 1990	12–282
February, 1990	23–109
January, 1990	15–187
1987–1989	1–1144

TABLE VIII-C6.—CADMIUM EXPOSURE DATA FOR NICKEL-CADMIUM BATTERY PRODUCTION AT COMPANY B—Continued

Process	Range of exposure levels (μg/m³)
Seven selected sampling days	1–19
Paste preparation:	
1987–1990	1–1189
Impregnation, 1989–1990:	
Plating	1–5
Plate cleaning	1–20
Spiraling	1–2
Despiraling	1–74
Plate preparation, 1990:	
Tabbing	7–96
Cutting	1–17
Inspection	1–16
Cell Assembly, 1990:	
Assembly, 9 of 10 sampling days	1–27
Winding, 9 of 11 sampling days	1–36
Components, Formation & Test	6–13
Waste Management, 1989–1990	1–2
Maintenance, 1989–1990	3–35

Source: NEMA, Exhibit 96.

TABLE VIII-C7.—CADMIUM EXPOSURE DATA FOR NICKLE-CADMIUM BATTERY PRODUCTION AT COMPANY C

Process	Exposure levels (μg/m³)	
	Range	Geometric mean
Non-manufacturing:		
Canteen	0.6–2.3	1.2
QC Lab		0.6
West Bay		0.6
Platemaking:		
Pellet making	20–671	97.5
Breakdown	8–83	23.1
Cd-Ni production	20–29	24.1
Powder packaging		10.0

Source: NEMA, Exhibit 96.

TABLE VIII-C8.—CADMIUM EXPOSURE DATA FOR NICKEL-CADMIUM BATTERY PRODUCTION AT COMPANY D

Process	Sample results (T1μg/m³)	
	1988	1989
Platemaking	0.0	0.0
Impregnation:		
I & S operator	5.0	13.0
Plaque brusher		124.0
Plaque roller	30.0	11.0
Basket cleaning		31.0
Plate preparation:		
Shearing	6.0	6.0
Tab welding	4.0	13.0
Sort & repair	9.0	6.0
Cell assembly stacker	10.0	6.0
Salvage operator		2.0
Warehouse/storage		
Material handlers		0.0
Non-manufacturing		0.0

Source: NEMA, Exhibit 96.

TABLE VIII-C9.—CADMIUM EXPOSURE DATA FOR NICKEL-CADMIUM BATTERY PRODUCTION AT COMPANY E

Job title	Sample result (T1μg/m³)
Slitter operator	74
PEP operator	52
Electrode recovery operator	6
Sub C line operator	10
AA line operator	1
Packet inspector	13

Source: NEMA, Exhibit 96.

TABLE VIII-C10.—CADMIUM EXPOSURE DATA FOR NICKEL-CADMIUM BATTERY PRODUCTION FROM NIOSH INVESTIGATION 88-199

Process	Cadmium concentrations (μg/m³)		
	Mean	Median	Range
Platemaking:			
Nickel plating	6	1	1–31
Nickel slurry	3	1	1–14
Sintering	6	3	1–41
Sizing	8	6	1–19
Spiraling	5	6	3–9
Impregnation	9	7	1–42
Despiraling	68	58	10–144
Cleaning	31	15	1–130
Maintenance	15	13	1–53
Pressed plate:			
Paste preparation	367	185	18–1914
Tab welding	35	35	31–44
Paste machine	113	88	18–716
Tab staking	74	72	19–180
Slitting	31	26	13–47
Setting up	111	114	93–124
Maintenance	61	39	2–373
Materials handling	48	41	8–113
Dipping paste	195	195	
Rovers	66	56	16–123
Leaders	67	53	14–196

TABLE VIII–C10.—CADMIUM EXPOSURE DATA FOR NICKEL-CADMIUM BATTERY PRODUCTION FROM NIOSH INVESTIGATION 88–199—Continued

Process	Cadmium concentrations (μg/m³)		
	Mean	Median	Range
Rework/reclaim	95	89	33–198
Plate preparation:			
Slitting and blanking	20	13	1–129
Sorting and stacking	21	12	6–98
Materials handling	14	9	7–27
Rework/reclaim	16	8	4–43
Cell assembly:			
Winding	21	12	4–70
Closing	5	2	1–21

Source: NIOSH, Exhibit 128, Attachment 3.

Table VIII–C10 presents data submitted by NIOSH from an analysis of exposures at a nickel-cadmium battery plant evaluated in 1988. [8, Attachment 3, Tables 1–4]. These data were based on over 1,000 monitoring samples taken at the plant in that year. NIOSH expressed difficulties in compiling the company's sampling results "due to lack of consistent workstation terminology." In three of the four production processes, the mean exposures for almost all job categories were less than 25 μg/m³.

Existing and Feasible Additional Controls. Nickel-cadmium battery manufacturers have made an effort to control occupational exposure to cadmium. Local exhaust ventilation, automation, enclosure, and housekeeping practices are presently utilized to varying degrees. Respirator use for employees in high exposure areas is standard practice. Further reductions in exposure levels are possible through increased utilization of current control methods and through the implementation of additional controls.

JACA Corporation's description of baseline controls included local exhaust ventilation hoods for three of five production job categories (excluding supervisors and maintenance workers). Additional or improved ventilation systems were recommended for the materials handler, the impregnation operator, the coating operator, and the plate preparation operator. JACA estimated that the increased ventilation would reduce exposure levels by about 85 percent in each of these job categories. [3, Table 4–3].

JACA also recommended other controls to limit airborne concentrations of cadmium. These included increased housekeeping, such as vacuuming; additional hygiene practices, such as showering and using separate work clothing; and improved information and training programs to encourage work practices that minimize exposure levels.

PACE outlined recommendations for additional controls at each process step in its report. [4, section 4]. Additional controls during impregnation would include changes in material handling methods, improved and increased local exhaust ventilation, isolation of the process, and increased frequency of wash down of the equipment and the area. At plate preparation operations for sintered plates, feasible engineering controls would include "application of local exhaust ventilation at locations that are not significant sources under the current standard, improved ventilation at the currently significant sources, partial enclosure of some phases of the operation, * * * and significantly increased utilization of an expanded central vacuum cleaning system." [4, p. 4–9].

For operations involving paste mixing and plate preparation for pressed plates, PACE assumed that each would have to be relocated to a new building, specially constructed with a state-of-the-art inside-out design. Paste mixing involves large quantities of dry cadmium-bearing powder, and PACE conceded that even in the new building, "the exposures will be [close] to the current PEL." [4, p. 4–10]. PACE also listed modified material handling methods, isolation, and significantly increased frequency of clean-up procedures as additional feasible control methods for these operations.

During cell assembly, additional controls recommended by PACE included improved enclosures of process equipment, increased exhaust ventilation, local exhaust ventilation provided at material handling sites, and significantly increased general housekeeping by means of expanded central vacuum cleaning systems. During cell closing, "control measures would include local exhaust at specific generation points, isolation of the operation from the other cadmium generation operations, * * * and strict attention to general housekeeping." [4, p. 4–11]. The PACE report did not include estimates of the expected effectiveness of individual controls for this industry, but similar incremental controls recommended in other industries were estimated to achieve exposure reductions from 70 to over 90 percent [4]. PACE concluded that the implementation of all recommended controls for nickel-cadmium battery producers, including new buildings, would enable mean exposures in 14 of 18 job categories to be 5 μg/m³ or less and mean exposures in 17 of 18 job categories to be 13 μg/m³ or less [4, Table A4–1].

NEMA provided a general view of the exposure control technology in use at nickel-cadmium battery plants: "Companies have installed the best available feasible technology for controlling exposure to their employees * * * the most sophisticated manufacturing equipment * * * Ventilation has been engineered to the extent feasible * * * extensive respiratory protection programs are being used." [2, p. 5]. NEMA concluded that a major redesign of manufacturing plants would be required in an attempt to achieve compliance with a PEL of 5 μg/m³, which they considered technologically infeasible.

The MBS report presented the position that 5 μg/m³ is technologically infeasible with engineering controls and work practices. The MBS report assessed additional controls necessary for an attempt to achieve compliance with the standard, based on the assumption that new buildings would be required for electrode production and assembly. Methods of exposure reduction short of such extreme measures were not discussed.

In its post-hearing comments, NEMA listed controls that have been implemented at the Gates facility through 1990. [6, Table 1]. These included improved and additional

ventilation for over a dozen machines, process isolation, machine enclosures, automated paste handling, and improved environmental procedures for employees. Descriptions of controls at other companies indicated that ventilation, protective clothing, and respirators were generally employed in areas with significant cadmium exposure.

Company B submitted post-hearing comments describing the additional controls that they felt would be required to meet a separate engineering control air limit (SECAL) of 25 $\mu g/m^3$. [9, p. 1–8]. These would include new buildings for despiraling and negative platemaking operations, major process modifications throughout the plant, and new production equipment such as leak proof drying ovens. Many less drastic improvements were listed as well, including improved and additional local exhaust ventilation, improved enclosure, increased vacuuming, and periodic wash down.

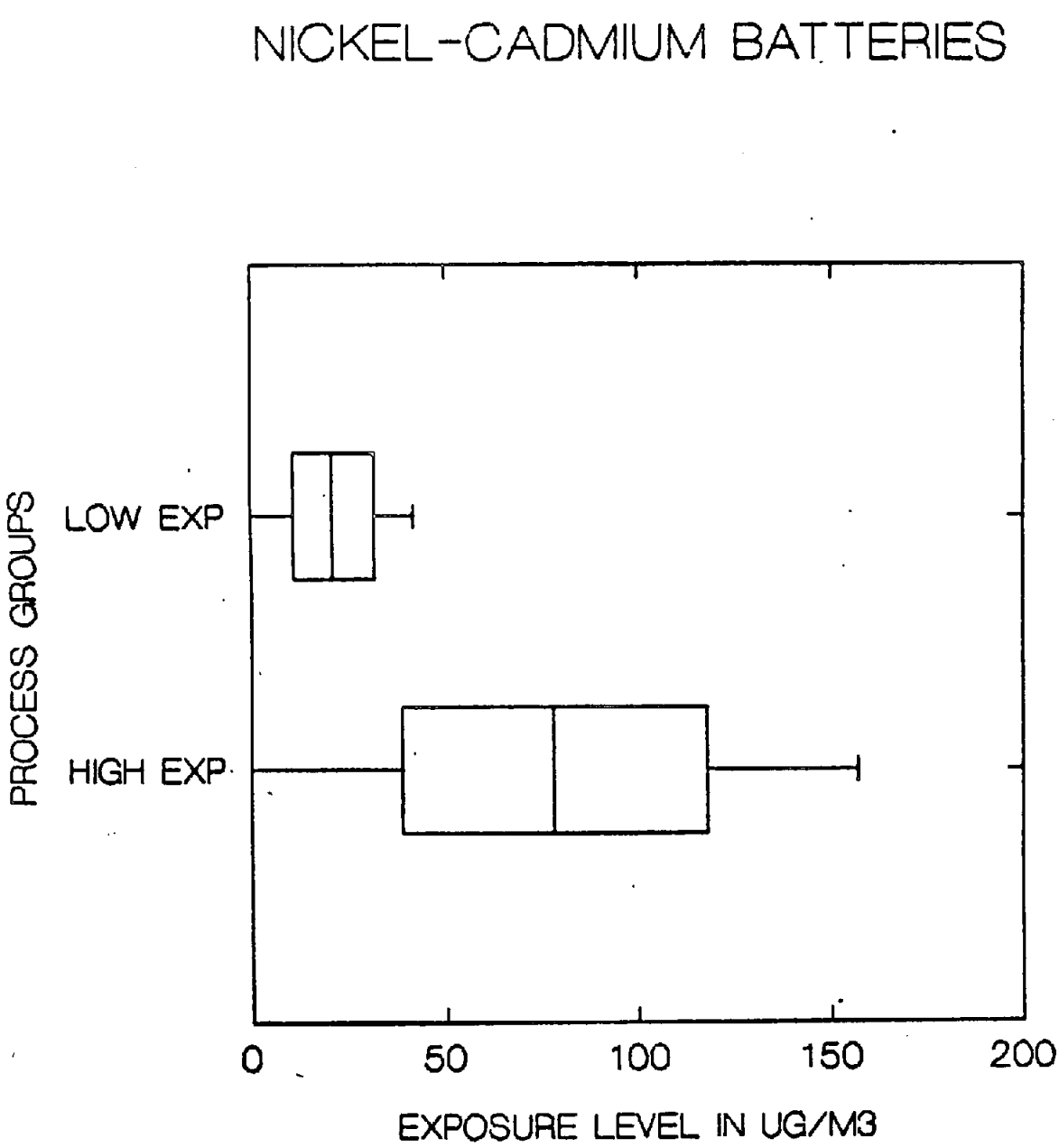
Implementing changes and exercising extra care in work practices can result in significant reductions in exposure levels. OSHA inspections und NIOSH health hazard evaluations often reveal that the total amount of a contaminant released into the air can depend heavily on how employees handle products, containers, and equipment. This factor will be of vital importance in complying with the new standard: one gram of cadmium dust is sufficient to produce an airborne concentration of 25 $\mu g/m^3$ for 40 thousand cubic meters or about 1.4 million cubic feet of air.

Technologically feasible limits for a SECAL. Given the array of existing exposure data, OSHA separated exposures into high and low occupation/process exposure groups to facilitate the feasibility analysis. (For a more detailed discussion of the approach see the preceding section B—Discussion of Technological and Economic Feasibility Determinations).

Data were divided at a breakpoint which maximized the difference between the two data sets. This exercise resulted in the identification of "high" exposure occupations/processes which included plate preparation and platemaking operations. (It is recognized that job titles differ among plants; some operators performing the same activities have different job titles in different plants.) All other occupations/processes were categorized as having "low" exposures, including impregnation and cell assembly operations and activities. Figure VIII–C1 shows the segregated data.

BILLING CODE 4510-26-M

FIGURE VIII-C1



BILLING CODE 4510-26-C

Approximately 375 workers are included in the high exposure group and 1,125 employees are in the low exposure group.

Median exposure data for the two sets were as follows:

	High group	Low group
Number of observations	26	48
Mean	72.9	14.4
Standard deviation	62.7	23.5

To verify that the two groups within this industry were distinct, a *t* test was performed on the difference in the means. The null hypothesis that the means of the exposure data were equal was rejected, and the Agency concluded that the exposure groups were drawn from separate distributions.

After the statistical difference between high and low exposure groups was verified, the data were treated separately. In developing Figures VIII–C2 and VIII–C3, individual occupation/process median or mean exposure values were drawn from each of the different data sources.

A modelling process was employed in order to correctly identify appropriate SECAL levels for the two groups. The current exposure patterns were reduced based upon alternative engineering control efficiency levels of 80, 60, 40, and 20 percent. The higher the efficiency level, the lower the projected exposure level.

Figures VIII–C4 and VIII–C5 show the reduction and shift in the distribution of exposures for the high and low groups in nickel-cadmium battery production.

BILLING CODE 4510-26-M

FIGURE VIII-C2

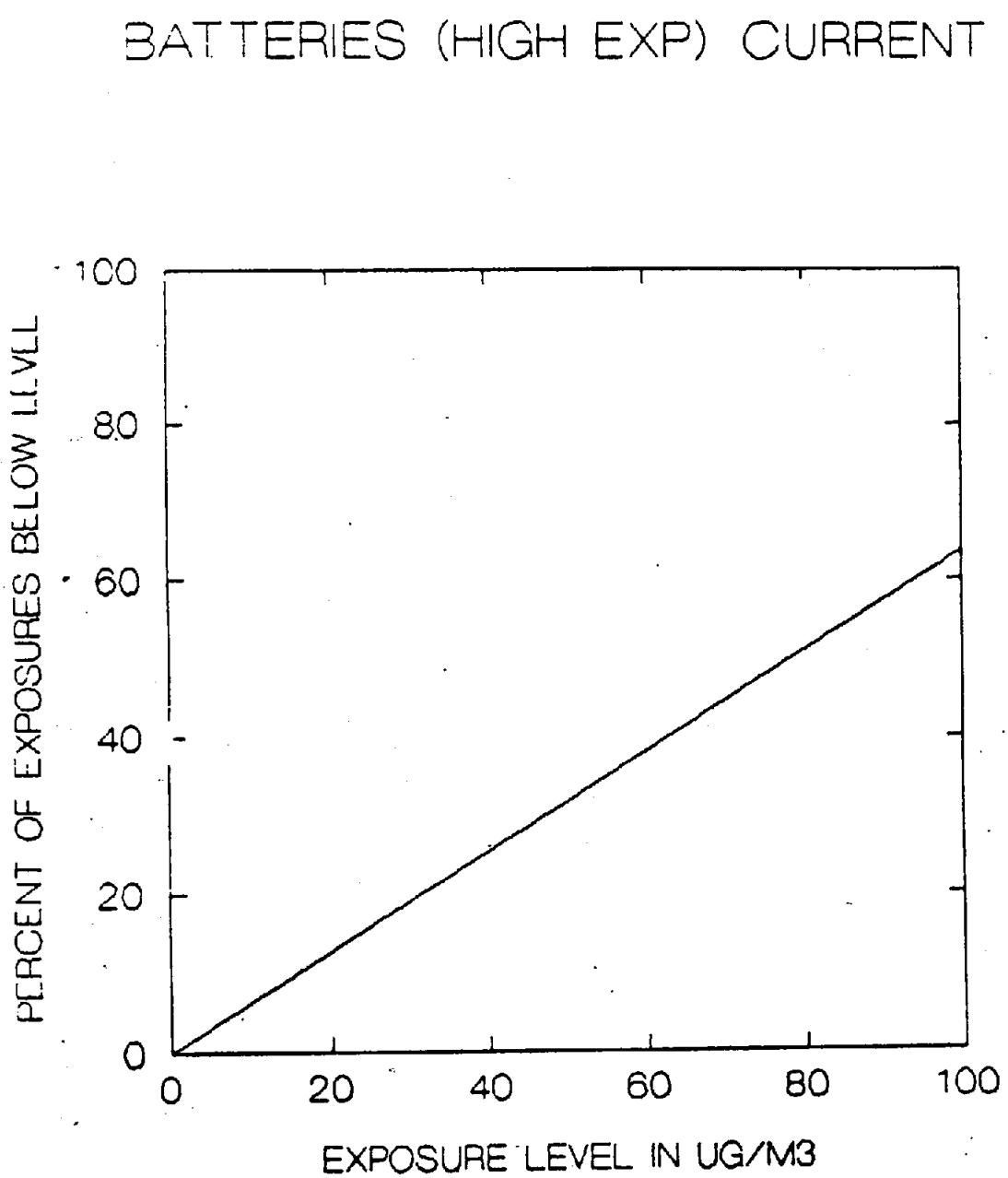


FIGURE VIII-C3

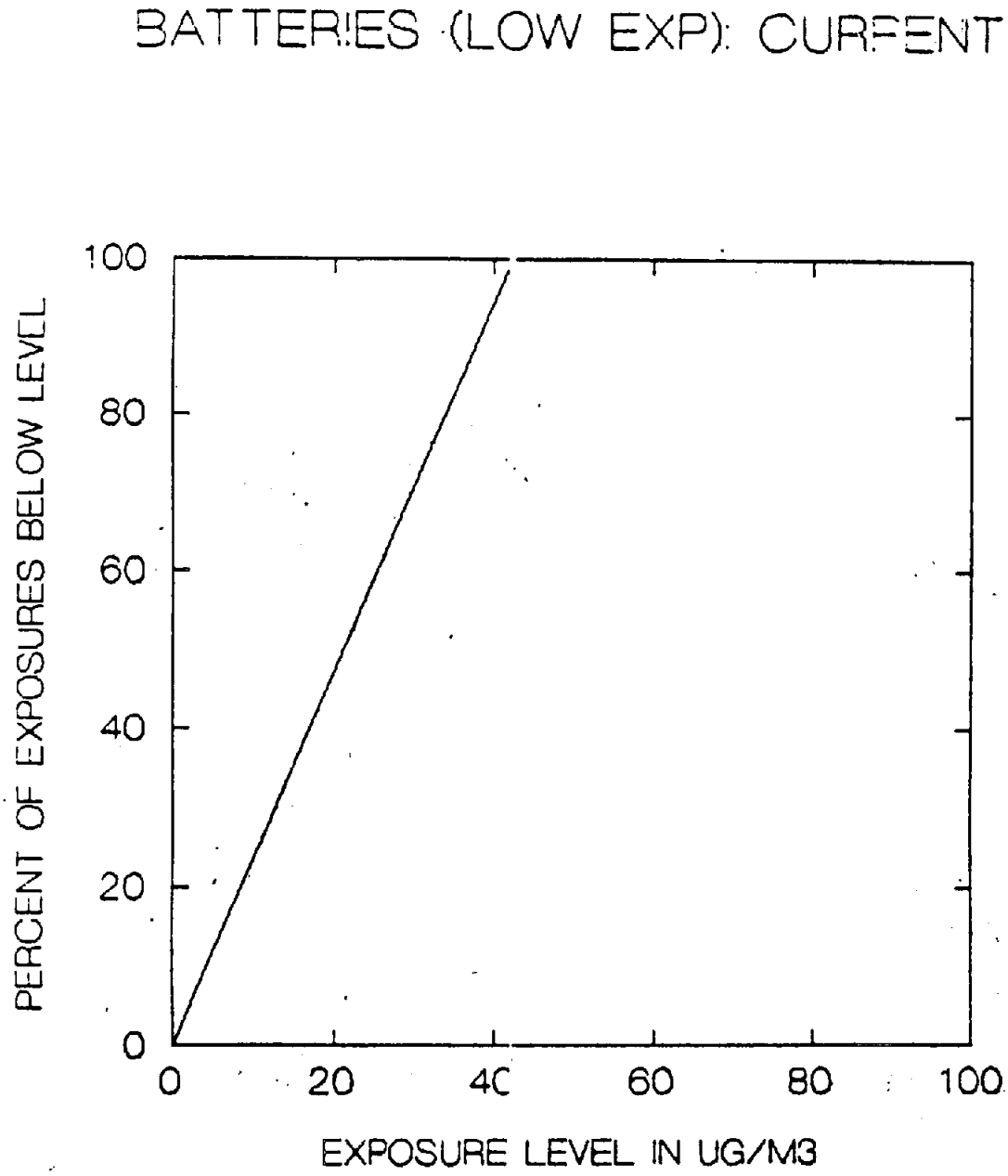


FIGURE VIII-C4

BATTERIES (HIGH EXP.): CONTROLLED 80%-2C

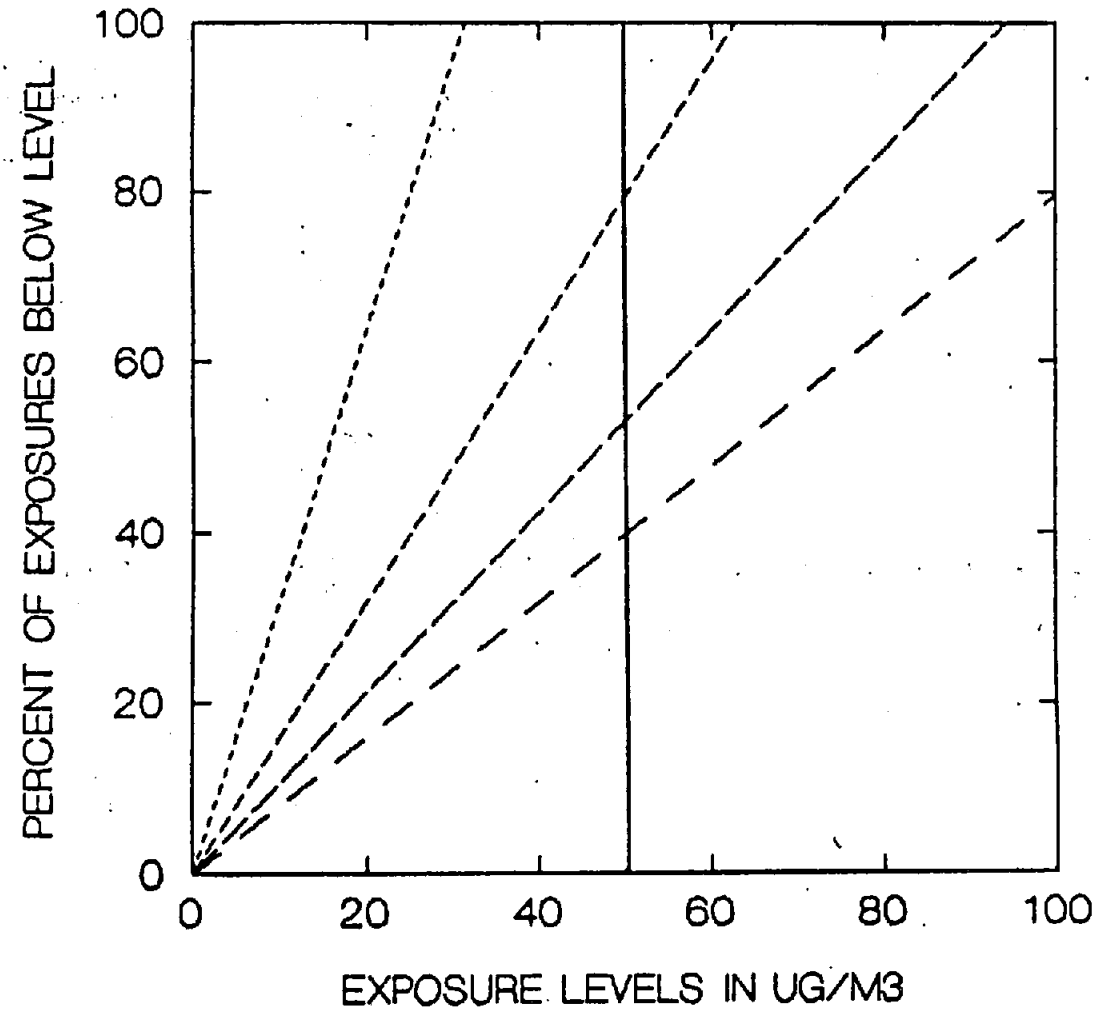
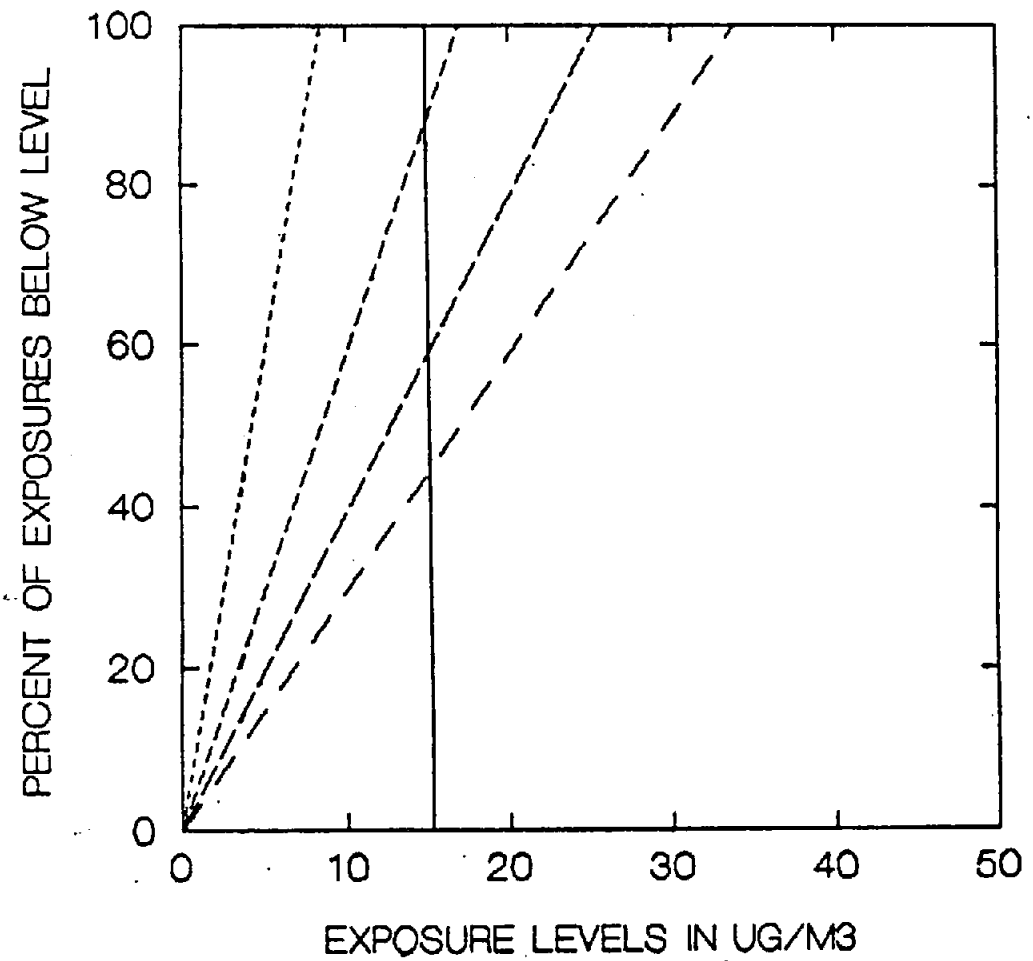


FIGURE VIII-C5

BATTERIES (LOW EXP.): CONTROLLED 80%-20%



BILLING CODE 4510-26-C

(The higher the reduction factor the closer the projected exposure line moves to the vertical axis.)

The selection of an appropriate efficiency reduction factor was based on evidence and testimony in the record and economic feasibility considerations. The only basis for revising an engineering control efficiency factor down was economic infeasibility. The industry cost to profit ratio was used as a guide in this process.

A criticism of OSHA's preliminary feasibility analysis was that the estimates of control effectiveness were overly optimistic. For example, JACA estimated that the expected efficiency of new or improved local exhaust ventilation systems for exposures in the battery industry would be 85 percent in most cases and up to 96 percent in situations where high hood efficiency was possible. [3, p. 4–9 and 13, p. 9].

The strongest criticism of the JACA estimates was presented by PACE. For the nickel-cadmium battery industry the PACE analysis concluded that a net reduction of exposure levels of approximately 75 percent could be achieved in plate preparation operations primarily through improved exhaust ventilation, improved enclosure, and improved housekeeping. [13, p. 8]. PACE also concluded that "Engineering controls can bring one of these [impregnation process] operations into compliance with a 5 μg Cd/m^3 but not a 1 μg Cd/m^3 standard. Three of these operations are amenable to separation from the cadmium source, and, therefore, can comply with the proposed 5 μg Cd/m^3 standard." [13, Appendix 5, p. 2].

PACE referred to "the installation of more extensive engineering controls" for many other operations but did not offer estimates of the effectiveness of any individual controls. PACE estimated that overall reductions of 80 to over 90 percent in mean exposures could be achieved in most job categories in the nickel-cadmium battery industry. [4, Table A4–1]. For two processes these reductions included new buildings, but for the balance the controls consisted of conventional technology, such as improved local exhaust ventilation, changes in material handling methods, partial enclosure, increased vacuuming and washdown, and partitions. [4, p. 4–8 through 4–12].

The testimony of two independent industrial hygienists [10, 11] and of the experienced experts and industrial hygienists of NIOSH [12] supported the conclusion that conventional control technology can substantially reduce cadmium exposures across all industries.

OSHA notes that controls can be used individually or in combination. If one control is not sufficient, additional ones can be used. It is the interaction of various engineering controls and work practices as part of an integrated system of controls that will produce the best overall reduction in exposure levels.

This review and analysis of the record needed to be supplemented with economic feasibility considerations before a determination could be made regarding appropriate engineering controls and their effectiveness level. For battery producers, engineering solutions to achieve an 80 percent or higher reduction in cadmium levels would have required major capital expenditures (multi-million dollars per plant) to rebuild or replace existing facilities. Yet annual profits in this sector are reported to be less than $7.5 million (see Economic Impact Section). Capital expenditures needed to achieve an 80 percent reduction in cadmium levels do not appear to be economically feasible at this time. Instead, less expensive engineering controls with a lower efficiency expectation (40–60 percent) were identified. Based on this reasoning OSHA determined that a reduction of 40–60 percent in cadmium exposures in the nickel-cadmium battery industry was both technologically and economically feasible.

Following the selection of this efficiency factor range, the appropriate SECALs for each exposure group were identified at the level achievable for 60–80 percent of the exposure observations. For the high exposure occupations/processes group, including plate preparation and plate making activities, a SECAL of 50 $\mu g/m^3$ was identified. For all other occupations/processes in this industry, a SECAL of 15 $\mu g/m^3$ was identified.

Compliance with the PEL of 5 $\mu g/m^3$ with engineering controls and work practices would be infeasible in this industry. Compliance with this standard can only be achieved through the use of respirators. Respirators are readily available with a wide range of protection factors that can adequately protect workers from the potential exposures in this industry. It is likely that respiratory protection would be required for most of the production and maintenance employees full time. This fact was recognized by OSHA in the preliminary regulatory impact analysis (PRIA); the conclusion was repeated by virtually all commenters who addressed the issue and is consistently supported by the substantial evidence in the record.

NIOSH expressed significant reservations about implementing mandatory daily respirator use for entire production shifts, even if the PEL was infeasible. "Never as a routine practice would we recommend that respirators be worn full time by employees." [14, p. 8–202]. Such respirator use has negative effects that may affect an employee's comfort, ability to communicate, and productivity. OSHA believes that the increased health risks associated with exposures to low levels of cadmium warrant the requirement for respiratory protection despite these effects.

Costs of Compliance with a 50–15 $\mu g/m^3$ SECAL and 5 $\mu g/m^3$ PEL. Estimates of total compliance costs for nickel-cadmium battery producers submitted to the record, varied greatly. The calculation of these costs can be broken down into several components, such as the types of controls that are assumed to be required, the number of controls that would be required, the unit cost of the required controls, and the costs of requirements identified in the rule. An evaluation of the evidence in the record regarding compliance costs reveals a general agreement on these cost estimates.

Disagreement on total compliance costs was invariably related to a misunderstanding of technological feasibility. One misunderstanding involved the criteria for judging technological feasibility. OSHA's approach to technological feasibility is based on concerns about employee health risks and fairness to employers. The approach incorporates a recognition that respirators may be necessary to reach a protective exposure level under certain circumstances and includes a corresponding flexibility in enforcement. A thorough discussion of this approach can be found in the lead remand analysis [54 FR 29142].

The assumption that a technologically feasible level is one which will be very rarely exceeded by any exposure sample will result in dramatically higher cost estimates for a given exposure limit. This erroneous assumption leads to the conclusion that all imaginable controls must be implemented at very high cost.

The cost estimates produced by PACE, NEMA, and MBS were based on the assumption that a level is feasible only if the probability of any sample exceeding the level is very small (less than 5 percent). PACE considered a level achievable only if the mean exposure was less than 40 percent of the level. NEMA remarked that "there are frequent excursions of 20 to 25 $\mu g/m^3$ due to process upsets so that an exposure level of 30 $\mu g/m^3$ cannot be achieved with 95% certainty even under

these rigorous controls." [6, p. 5]. OSHA's requirements for methods of compliance already take into account situations such as process upsets and maintenance by explicitly recognizing that engineering controls may not be feasible for these circumstances.

Another mistaken assumption which resulted in grossly inflated estimates of total costs involved the requirement to install engineering controls to the extent feasible. NEMA claimed that "Every U.S. manufacturer would be faced with virtual redesign of sizable segments of its production facilities in order to attempt to meet the proposed exposure standards." [2, p. 7]. PACE and MBS included the cost of new buildings in their total cost estimates; such costs comprised most of the total cost estimate. OSHA's approach to feasibility does not require employers to go to such extreme lengths.

In estimating the costs of compliance with this standard, OSHA first estimated the costs of installing feasible additional controls within existing building structures. The original estimate for this was provided by JACA in the preliminary analysis. In current dollars, the estimated cost of local exhaust ventilation systems (installed) ranged from $51,000 to $112,000. Annual operating and maintenance costs were estimated to be 10 percent of the capital cost. JACA also estimated that HEPA-filtered industrial vacuum cleaners would cost about $1,500 each and that the cost of additional vacuuming would be the current nonsupervisory wage rate. [3, p. 6–8 and 6–28].

In the PACE report, descriptions of recommended controls for the nickel-cadmium battery industry were linked to specific cost estimates. PACE identified additional controls for an operation already provided with exhaust ventilation that included "a new Venturi scrubber of 1500 cfm capacity to reduce air emissions * * * providing CAI [clean air island] air supply plenum of about 6 feet by 15 feet at the operator work station * * * The area would be steam-cleaned and painted * * * and it would then be partitioned off from the rest of the building." [4, p. 2–4]. For this operation, PACE expected mean exposure levels to be reduced from 54 $\mu g/m^3$ to 9 $\mu g/m^3$; the capital cost was estimated to be $126,000 and the estimated annual operating cost was $18,100.

For another job category, PACE expected mean exposures to be reduced from 34 $\mu g/m^3$ to 5 $\mu g/m^3$ through the installation of a new hood and exhaust system, the establishment of a clean air island over the work station, and by steam cleaning and painting the room. PACE estimated that the capital costs associated with these controls would be $43,000 and that the annual operating cost would be $16,900. [4, p. 2–5].

The PACE report included itemized costs in some tables. The cost of clean air islands was given as $3 per cfm (cubic foot per minute) with systems ranging from 2,000 cfm to 9,000 cfm that cover areas from 4 feet by 5 feet to 6 feet by 15 feet. The cost of an exhaust ventilation system with Venturi scrubbers, sloped and flushed corrosion resistant ducts, and a 4,500 cfm capacity was estimated to be $57,000. Partitioning an area from the rest of the plant with 900 square feet of material was estimated to cost $9,000. And the cost of a new vacuum cleaning system was estimated to be $15,000. [4, Table A2–4].

JACA estimated that additional engineering controls could be installed for four of five major job categories (materials handler, impregnation operator, coating operator, and plate preparation operator) identified in nickel-cadmium battery production. The battery manufacturing process description offered by PACE described additional controls that could be applied in six areas but did not give an indication of the number of such controls to be implemented. In its total cost estimate PACE included expensive modifications to the air conditioning system and the replacement of baghouses with banks of HEPA filters. While these changes may lower cadmium concentrations in air released from the building, OSHA believes that the effect on employee exposures would be negligible.

The total costs given in the PACE report also included new buildings, an expanded water treatment facility, and "a crew of janitorial personnel" that would "wet wipe any contaminated surfaces throughout the work shifts." OSHA believes that exposure levels can be sufficiently reduced without incurring such expenses. PACE also claimed that in addition to an annual expense of $1.8 million for increased maintenance, power and fuel, a single plant would incur $2.1 million annually for "increased operating labor." [4, p. 4–5 and Table A4–2].

OSHA explicitly and repeatedly asked industry sources to provide costs for individual controls recommended in each area. The costs supplied by PACE for the nickel-cadmium battery industry were aggregated and included items not needed for compliance with the standard. Similarly, the high cost estimates developed by MBS were associated with new buildings and also included over $5.9 million for "annual operating costs." MBS did not list costs for specific controls operation by operation. [5].

Company B submitted post-hearing comments describing the controls that could be implemented in nine manufacturing areas. The list of controls was based on a perceived need for "achieving 25 $\mu g/m^3$ 95% of the time" and included new buildings as well as other major rebuilding efforts. These controls go beyond what OSHA considers additional feasible controls. Costs for the engineering controls were not itemized; aggregated costs of millions of dollars were not explained, and it is unclear how over $4 million in annual expenses in addition to the capital costs were calculated. [9].

Since 72 percent of the nickel-cadmium batteries manufactured in the United States are produced by one plant [15, p. 3], it is difficult to develop a single profile of the number of controls required by a typical plant. Company A submitted exposure data for nine operations distributed among the four manufacturing process steps. Most of these currently have some degree of ventilation, and respiratory protection is used in five of the nine operations. Company B listed fourteen job titles for the four process steps in its exposure data and indicated current use of ventilation and respiratory protection to some degree. For Company C the primary location of cadmium use was in one small highly-protected room; exposure data were listed for four activities within the one process step. Potential control measures included enclosure, ventilation, and respirators. Company D listed exposures for nine production job categories. These were located in three of the four production process steps. Company E listed exposures for six job categories and indicated that ventilation controls were present at each one. [6, Appendices 1–5].

Based on a review of all comments submitted to the record, OSHA concludes that Table VIII–C11 provides a fair and accurate representation of the additional controls and costs needed to comply with the 50–15 $\mu g/m^3$ SECAL levels. Employers are able to choose among these and any other controls to reduce exposures in the most cost-effective manner for their particular circumstances. For example, an employer may already be providing ventilation in one operation and may choose to install a pneumatic conveying system, glove box technology, modifications to material handling methods, or another solution for the specific situation. The resulting costs would generally be comparable to those estimated in Table VIII–C11.

The largest plant, with approximately 50 percent of the exposed employees in the industry and "with as many as 16 to 19 discrete operations" [2, p. 5], was estimated to need new or improved local exhaust ventilation at eight locations, clean air islands at ten locations, two additional central vacuum cleaning systems, and improved enclosure or partitions for five operations. The numbers of these controls estimated to be implemented are greater than the number recommended in either the PACE or the MBS reports [4,5]. In contrast, these sources based their cost estimates on more extensive building modifications and new buildings construction.

TABLE VIII–C11.—ESTIMATED COSTS OF ENGINEERING CONTROLS FOR CADMIUM IN THE NICKEL-CADMIUM BATTERY INDUSTRY

Type of control	Controls per plant by size of plant			Total industry controls[1]	Cost per control ($thousands)			Industry costs ($thousands)				Total annualized industry cost ($thousands)
	Small	Medium	Large		Capital	Annual power and maintenance	Annual labor	Capital	Annualized capital	Annual power and maintenance	Annual labor	
Local Exhaust Ventilation	1	5	8	29	60	8	0	2,320	377	232	0	609
Clean Air Islands	1	5	10	31	18	2	0	558	91	62	0	153
Central Vacuum Systems	1	1	2	7	15	1	7	105	17	7	49	73
Enclosure	0	3	5	17	9	0	0	153	25	0	0	25
Total				84				3,136	511	301	49	861

[1]Based on one small plant, four medium plants, and one large plant.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

Additional controls at each of the four medium-sized plants were estimated to be five new or improved local exhaust ventilation systems, five clean air islands, one additional central vacuum cleaning system, and new or improved enclosures for three operations. At the smallest plant, where exposures are limited to one room and where the manufacturing exposure monitoring data were representative of two employees, feasible additional controls would include an improved local exhaust ventilation system and a clean air island.

Further reductions in exposures can be achieved at all plants through more attention to appropriate work practices and through improved housekeeping practices. Table VIII–C11 summarizes the costs associated with the additional controls. The capital costs, the annual power and maintenance costs, and the annual labor costs are presented for each control. Capital costs for the industry are estimated to be $3.1 million and annual costs are estimated to be $350,000. Total annualized costs were calculated by amortizing the capital costs over ten years with a ten percent interest rate and adding the resulting annualized cost to the other annual costs. The annualized costs of engineering controls in the nickel-cadmium battery industry are estimated to be $861,000.

Compliance with other provisions in the new cadmium standard would also require additional costs. These include costs for increased respirator use, more comprehensive exposure monitoring programs, medical surveillance requirements (including requirements for medical removal), hygiene provisions (shower and eating facilities and protective work clothing), and additional efforts associated with recordkeeping and other information-related requirements (including regulated areas, compliance programs, and training).

Nickel-cadmium battery plants generally have established respirator programs for employees in high exposure areas. In order to comply with the PEL of 5 $\mu g/m^3$ it is likely that 80 percent of the production and maintenance employees would be required to wear respirators full time after the implementation of additional feasible controls. JACA estimated that about half of the employees exposed above the new PEL already wear respirators full time, and this estimate was consistent with information supplied by industry. [3, p. 6–17]. Thus, the revised standard would require respirator costs for an additional 40 percent of the 1,500 production and maintenance employees, or about 600 workers.

Appropriate respiratory protection was estimated to cost $300 per employee per year. Most commenters did not provide estimates of the additional cost of respiratory protection except to indicate that the numbers of employees had been underestimated in the preliminary analysis. One industry commenter estimated that the annual cost of protecting an employee with a HEPA-filtered respirator, including a fit test, would be $295 [17, Attachment III]. The estimated incremental annual cost of respiratory protection for the nickel-cadmium battery industry is $180,000.

The revised standard requires semi-annual exposure monitoring of "each shift for each job classification in each work area" but also allows representative samples to be taken for workers with similar exposures. JACA's assessment that the typical battery plant already performs this sampling annually was supported by the monitoring data submitted by industry. OSHA expects that plants will need to monitor 2 to 20 job categories with an average of about 10 job categories per plant. The revised standard would require each shift to be monitored separately, and thus a total of about 180 jobs would need to be monitored (10 job categories per plant times 6 plants times 3 shifts).

The lab analysis of each exposure monitoring sample is estimated to cost $40. The services of an industrial hygienist or other qualified person necessary to perform the monitoring for the required set of samples on average would cost about $1,500 per plant. [3, p. 6–23]. Thus, the estimated annual cost to the industry attributable to increased exposure monitoring is $16,200 [6*$1,500+180*$40].

The medical surveillance requirements of the revised standard involve a complex combination of different categories of employees and a series of triggers and schedules of different types of exams. The base requirements are for annual biological monitoring, including tests for cadmium in urine, cadmium in blood, and B_2-microglobulin in urine, and for a full

medical examination every two years. More frequent biological monitoring and medical exams are required if the tests indicate elevated levels. NIOSH submitted data on the results of biological monitoring for the general population and for workers in the nickel-cadmium battery industry. [8, Attachment 3, Tables 5 and 7]. These data indicate that a number of employees would be required to receive more frequent testing and exams.

Nickel-cadmium battery producers generally indicated in the record that medical surveillance, including monitoring levels of cadmium in blood and urine, was already being provided for most employees exposed to cadmium. [18, p. 10–96]. NEMA, the trade association for the industry, stated that the "industry is currently employing medical surveillance, respirator use, protective clothing/equipment use, regulated areas designation, employee information and training, and labeling/identification." [2, Attachment 1, page 3]. This confirmed OSHA's preliminary assessment that annual medical exams were provided to employees in this industry.

The medical surveillance provisions of the final rule would require an expanded program for most establishments in the industry, resulting in both more workers covered and more extensive and more frequent medical tests. The cost of an annual physical, including the wages paid to the employee, is estimated on the basis of OSHA experience to be about $250. The cost of the lab analysis for a B_2-microglobulin sample was cited by a public health research group as $80. [18, p. 4]. Analyses of samples for cadmium in urine and cadmium in blood are estimated to be $60 each, as presented by JACA and unchallenged in the record. An additional $5 is added to the cost of each of the biological monitoring samples for costs associated with collecting the samples.

For purposes of calculating the incremental costs of compliance associated with the revised standard and consistent with the evidence submitted to the record, OSHA estimated the numbers of additional exams and tests that could be expected to be required annually. Approximately 300 additional medical exams are estimated to be needed for employees currently not covered or for whom exams would be required more frequently, including employees receiving medical removal protection. Tests for β_2-microglobulin generally are not currently provided. About 30 percent of the exposed workforce may be subject to more frequent biological monitoring, with 20 percent receiving semi-annual monitoring and 10 percent receiving quarterly monitoring. As a result, an estimated 2,000 additional tests for β_2-microglobulin, 750 additional tests for cadmium in urine and 750 tests for cadmium in blood would be necessary. The total estimated cost for additional medical exams and biological monitoring is thus estimated to be $342,500 annually.

Requirements for medical removal may involve compliance costs in addition to those for more frequent medical exams and monitoring estimated above. The criteria for mandatory removal would affect employees with high body levels of cadmium. The criteria for removal also allow for considerable physician's discretion. An estimated 3 percent of the exposed workforce may be removed initially on the basis of these criteria and the discretion of physicians.

Compliance with the new PEL for cadmium and other requirements of the final cadmium standard should prevent a continuing need to remove employees. The number of employees with relatively high past exposures who would be more likely to be removed should decline through attrition. However, as the criteria for removal become broader in future years (lower levels of cadmium in blood and urine will trigger mandatory removal), additional employees may be subject to removal. The costs associated with the medical removal provisions are approximated by assuming that on average, 3 percent of the exposed workforce may be removed every 5 years.

The number of employees removed should be small enough to enable establishments to provide removed employees with alternative positions. Costs to the employer would include paying possible wage differentials and hiring and training employees in new positions. OSHA estimates that the average cost per removed employee would be no greater than $5,000. An estimated 45 employees may be removed every five years on average, in the nickel-cadmium battery industry, and the average annual cost for the industry would be $45,000.

The total annual cost for the medical surveillance and medical removal provisions is estimated to be $387,500.

Other provisions of the revised standard that involve compliance costs include those related to hygiene facilities and to additional recordkeeping. As previously described, most plants already comply with requirements for work clothing, regulated areas, information, and training. Some of these requirements are currently covered by other standards.

Employers in the nickel-cadmium battery industry indicated that although lunch rooms and shower rooms were already provided, some costs would have to be incurred to increase their capacity and/or modify the facilities as required by the standard. Employers would also have to pay wages to the additional employees required to shower and change. Estimates of the costs of facility modifications range from zero to over $2 million. The high estimate was submitted by company B which did not itemize costs. OSHA believes that an average of $200,000 in capital costs and $5,000 in annual operating costs would be representative of most firms. These figures are supported by estimates from one firm [17, Attachment 3] and are generally consistent with other comments in the record. The estimated cost of showering on work time is $900 per employee annually (based on fifteen minutes per day for 240 days per year at $15 an hour) and would apply to an estimated 300 additional employees. This cost estimate was supported by one industry estimate [17, Attachment 3]. Thus, the costs associated with the hygiene requirements are estimated to be $1.2 million in capital costs and $300,000 in annual costs; the estimated annualized cost is $495,000.

Comments that addressed recordkeeping usually pointed out that the requirements were burdensome and unnecessary. Comments did not contradict the costs, which were estimated to be $5 per employee annually; this estimate was confirmed by one industry commenter [17, Attachment 3]. This cost estimate includes the need for additional equipment and staff time. For the nickel-cadmium battery industry, the total annual incremental cost would be $7,500.

A summary of the estimated costs of compliance for the nickel-cadmium battery industry is presented in Table VIII–C12. The total annualized cost is estimated to be $1.95 million. Over half of this cost is for exposure controls and respirators; most of the remainder is associated with medical surveillance and hygiene facilities.

Economic feasibility of 50–15μg/m³ SECALs and 5 μg/m³ PEL. The MBS study submitted by NEMA concluded that additional annual compliance costs of $2.25 million would be economically feasible for this industry. These costs were calculated for a PEL of 50 μg/m³.

NEMA subsequently urged OSHA to adopt a PEL of 40 $\mu g/m^3$, indicating that costs at this level would be economically feasible. The arguments on feasibility limitations submitted by industry generally focused on the technological infeasibility of achieving 5 $\mu g/m^3$; extremely high cost estimates were generated at this level.

OSHA has determined that the costs associated with the revised cadmium standard are economically feasible for the nickel-cadmium battery industry. Although the impact of these costs may not be negligible and can be expected to include reduced profits, the effects of the cadmium standard should not be substantial in comparison to the general market forces affecting this industry.

TABLE VIII-C12.—ESTIMATED COSTS OF COMPLIANCE WITH THE CADMIUM STANDARD FOR THE NICKEL-CADMIUM BATTERY INDUSTRY

Provision	Annualized cost ($thousands)
Exposure control	661.0
Respirator use	180.0
Exposure monitoring	16.2
Medical surveillance	387.5
Hygiene facilities/practices	495.0
Recordkeeping and information	7.5
Total	1,947.2

Note: Costs do not include current expenditures.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

The demand for nickel-cadmium batteries continues to be strong and growing in the United States and worldwide. Nickel-cadmium batteries offer the best overall performance for energy storage and retrieval; the advantages over other cells include a high ampere hour capacity, performance capability in a wide temperature range, long service life, safety, high energy density, efficient recharge capability, and low cost. Nickel-cadmium cells are used in most commercial and military aircraft, spacecraft, satellites, and ships. Rechargeable nickel-cadmium cells have a wide variety of uses. Equipment currently dependent on this technology includes phones, pagers, toys, tools, emergency naval and communication radios, police and fire transceivers, cameras, computers, heart monitors, portable surgical equipment, emergency lights, intrusion alarms, and back-up power.

Annual sales of nickel-cadmium batteries in the United States are approximately $350 million. Imports currently supply about 45 percent of domestic demand, up from about 18 percent in 1985. The domestic nickel-cadmium battery industry currently has revenues of about $185 million. Profits are estimated to be $7.4 million annually, resulting in a return on sales of 4 percent and a return on equity of 7 percent. [5, p. 3 and Exhibit 2].

The prospects for recouping compliance costs by raising prices are limited. Foreign competition is strong and there is reportedly sufficient production capacity outside the U.S. to meet the entire global demand. [16, p. 10–81]. A rise in prices is likely to be accompanied by an offsetting decline in sales. The elasticity of demand faced by individual establishments may be as high as 1, based on the experience of one domestic producer's attempt to raise prices in response to increases in the price of cadmium in 1988. This producer is currently operating at about 50 percent of capacity. [16, p. 10–167 and p. 10–171].

Assuming that all compliance costs would be absorbed from profits, the estimated costs may reduce the return on sales to about 3 percent and the return on equity to about 5 percent. The maximum reduction in profits would be approximately 26 percent. Alternatively, an increase in revenues of about 1 percent would completely offset the compliance costs without any reduction in profits. This would be possible if the level of demand increased. Although imports have increased their share in the U.S. market, the expansion in worldwide demand has enabled the U.S. domestic industry to maintain production levels.

The promulgation of this standard is not expected to result in plant closures and any effect on investment decisions or job creations, are uncertain. The incremental effects of this standard are not expected to produce any substantive overall production changes.

Sources

1. Exhibit 65, Testimony of Douglas Bannerman, on behalf of the National Electrical Manufacturers Association, July 19, 1990.
2. Exhibit 19–37, Comments of the National Electrical Manufacturers Association, May 11, 1990.
3. Exhibit 13, "Economic Impact Analysis of the Proposed Revision to the Cadmium Standard," Final Report, JACA Corporation, March 15, 1988.
4. Exhibit 19–43, Attachment L, "Feasibility and Cost Study of Engineering Controls for Cadmium Exposure Standard," PACE Incorporated, April 30, 1990.
5. Exhibit 19–37 B, "The Cadmium Rule—Destroying Workers' Jobs To Protect Them?" Multinational Business Services, Inc., September, 1989.
6. Exhibit 96, Comments of the National Electrical Manufacturers Association, September 14, 1990.
7. Exhibit 124, Comments of the National Electrical Manufacturers Association, October 9, 1990.
8. Exhibit 128, Attachment 3, "Health Hazard Evaluation 88–199," National Institute for Occupational Safety and Health, October, 1990.
9. Exhibit 121, Comments from 'Company B,' October 11, 1990.
10. Exhibit 26, Comments of Robert D. Soule, CIH, CSP, PE, May 9, 1990.
11. Exhibit 27, Testimony of Leslie Ungers, CIH, Ungers and Associates, Inc., May 18, 1990.
12. Exhibit 57, Testimony of NIOSH, July 17, 1990.
13. Exhibit 19–43, Attachment M, "Analysis of OSHA's Preliminary Conclusions Concerning the Technological Feasibility of Achieving a 5 or a 1 $\mu g/m^3$ Permissible Exposure Limit for Cadmium Fume and Dust," PACE, Inc., May 10, 1990.
14. Hearing Transcript, Tuesday, July 17, 1990.
15. Exhibit 130, Comments from NEMA, October 17, 1990.
16. Hearing Transcript, Thursday, July 19, 1990.
17. Exhibit 19–30, Comments from Big River Zinc, April 3, 1990.
18. Exhibit 123, Comments of the Public Citizen Health Research Group and the International Chemical Workers Union, October 17, 1990.
19. Exhibit 100, Comments of NIOSH, September 18, 1990.

Zinc Refining/Cadmium Production

Industry overview. Cadmium is primarily produced as a byproduct of zinc refining and is also recovered from cadmium-bearing scrap and waste products. Cadmium is not mined independently because sufficient deposits occur naturally in zinc ores. U.S. zinc concentrates have a relatively high cadmium content and may contain between 0.3 and 1.0 percent cadmium.

There are currently four primary zinc smelters in the U.S. with a combined annual capacity of 300,000 metric tons. [13, p. 2–2]. Three of these plants produce finished cadmium as well as zinc products; one zinc refiner ships out its cadmium concentrates for processing at another facility. While world output has been increasing, U.S. zinc mine and refinery production has decreased steadily in the past twenty years. The domestic production of zinc has fallen to about 30 percent of the peak level in 1969. The reduction in domestic production has resulted from excess world capacity, environmental control costs, and higher production costs.

Cadmium is currently produced at four facilities in the U.S. In addition to the three primary zinc smelters that operate cadmium refining circuits, one

plant produces cadmium from materials supplied by other refineries and secondary sources. The production of cadmium in the U.S. has declined steadily, and current levels are about 30 percent of the peak levels reached in the late 1980s. The decline in U.S. cadmium production is generally the result of the decline in domestic zinc production because of the naturally close link of these minerals. In 1979, eight facilities refined cadmium metal; half of these have shut down due to declining demand and poor market conditions. [1, pp. 2–2 through 2–5].

Total employment for the zinc refining and cadmium producing facilities is about 1,800 workers. Of these, approximately 75 percent (1,350) are production and maintenance employees. The four zinc plants have a total of 300 to 600 employees each and the cadmium plant has about 45 employees. The total number of workers directly involved in the production of cadmium at the four cadmium refining facilities is about 200. [11, p. VII–59 through VII–97, p. 10–194].

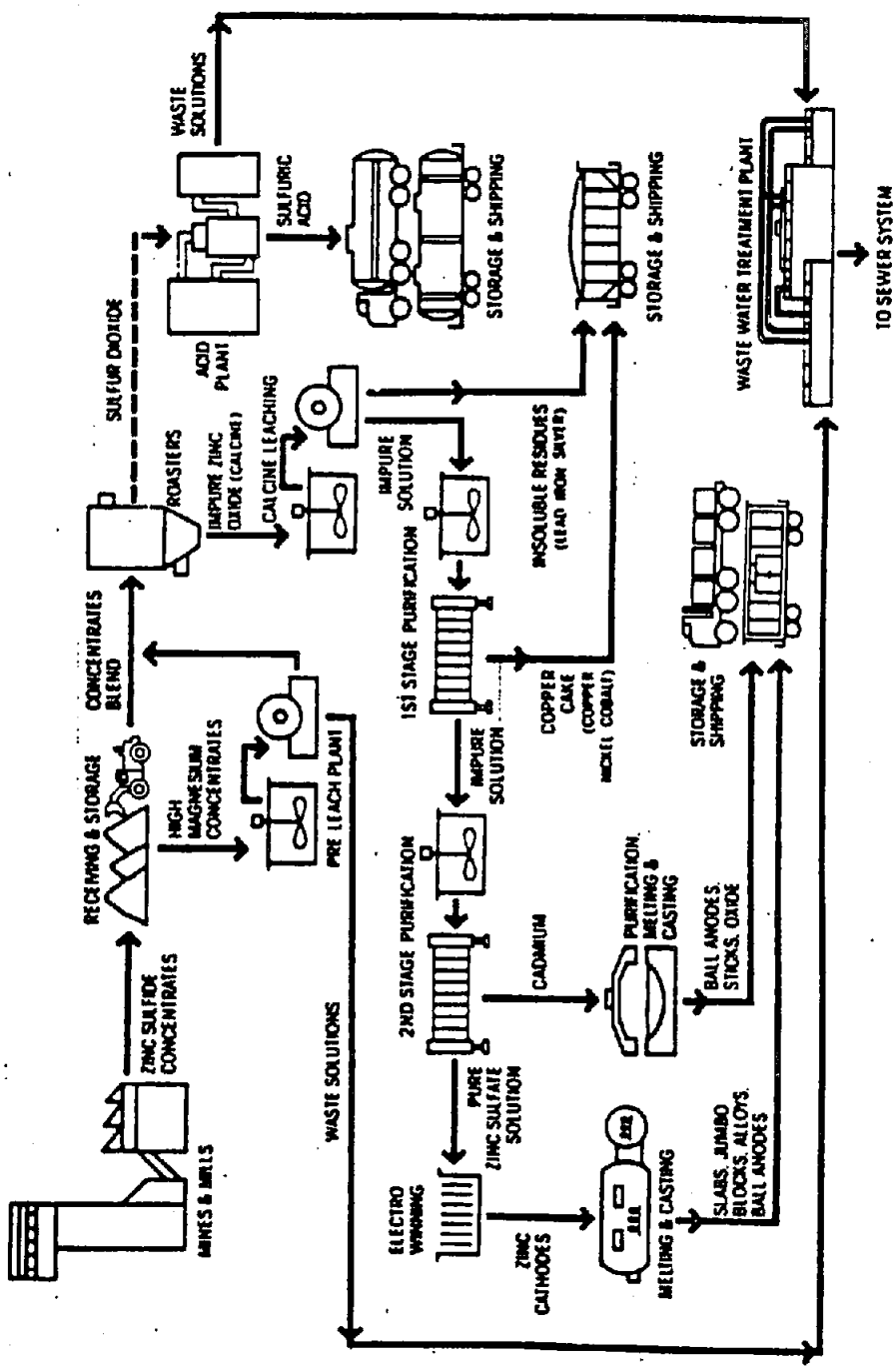
Production Processes. Zinc smelters convert zinc concentrate and zinc bearing secondary materials to metallic zinc. The two basic methods used to accomplish this are the electrolytic process and the electrothermic process. In both types of processes the feed streams contain several metals in addition to zinc. As the zinc is separated, the other metals are also separated and become raw materials for other smelters. Cadmium is one of the metals that is separated from the feed during the production of zinc. The cadmium concentrate then becomes an input for the cadmium refining process. Figure VIII–C6 presents a flow sheet for a typical zinc smelter.

In both the electrothermic and electrolytic processes, the zinc concentrate is converted from zinc sulfide to zinc oxide in fluid bed roasters. The hot oxide is separated from the roaster flue gas and is called calcine.

BILLING CODE 4510-26-M

FIGURE VIII-C6

TYPICAL FLOW CHART FOR ELECTROLYTIC ZINC SMELTERS



Source: Exhibit 19-43, Attachment K, Appendix A, Figure 1.

BILLING CODE 4510-26-C

In the electrolytic process the calcine is leached and the dissolved cadmium product is precipitated and filtered. In the electrothermic process the calcine is fed into the sinter machine with other materials, and the cadmium is concentrated in the dust contained in the sinter machine exhaust gas. The cadmium is leached from the baghouse catch, and then precipitated and filtered. The cadmium concentrate obtained in both zinc refining processes is further processed by melting and refining in an independent operation. The cadmium is recovered either as sponge by a final precipitation with zinc dust or by electrolyzing the solution and causing the cadmium to be deposited on the cathode. In either case, the cadmium is melted and cast or converted to cadmium powder or cadmium oxide.

Employee exposures. Data on employee exposures to cadmium in the zinc refining and cadmium production industries have been submitted to the record from several sources. The exposure profile used for the preliminary analysis was developed by JACA Corporation. [1, Table 3-3]. This profile was based on seven years of sampling results from OSHA's Integrated Management Information System (IMIS) database through August 1986 and on a Health Hazard Evaluation (HHE) performed by NIOSH at a refinery in 1977. JACA also visited a cadmium production plant to facilitate the interpretation and categorization of the data.

JACA's exposure profile represented employees involved in cadmium refining only; other operations in the zinc refining industry were analyzed separately as part of the generic cross-industry occupations. In response to concerns raised by several commenters, the following analysis covers the zinc refining and cadmium production industries as a whole. JACA's exposure data for cadmium production operations are presented in Table VIII-C13. Three of the six job categories have mean exposures above 100 $\mu g/m^3$.

At the request of the Cadmium Council, PACE Incorporated conducted a study on cadmium exposures in the primary zinc industry [2] and also analyzed cadmium exposures at a primary cadmium production plant as part of another report [3]. Table VIII-C14 shows the PACE exposure profile for employees involved in cadmium refining only (as in the JACA exposure profile). [3, Table A2-1]. Of the 14 job categories listed, six have mean exposures under 25 $\mu g/m^3$ and three have mean exposures above 100 $\mu g/m^3$.

The cadmium refinery plant submitted detailed exposure monitoring data to the record that are generally consistent with the JACA and PACE exposure profiles. [7, Attachment I]. A summary of these data is presented in Table VIII-C15. Approximately half of the job categories have mean exposures below 25 $\mu g/m^3$.

In its report on the zinc industry, PACE provided exposure profiles for both electrolytic and electrothermic zinc refining (including cadmium refining operations). [2, Appendix A, Table 1 and Appendix B, Table 1]. Table VIII-C16 presents the exposure data for electrolytic zinc refining, and Table VIII-C17 presents the exposure data for electrothermic zinc refining. Exposures in the two types of refining processes are generally similar.

TABLE VIII-C13.—CADMIUM EXPOSURE DATA FOR CADMIUM PRODUCTION BASED ON JACA

Job category	Concentration in $\mu g/m^3$		
	Geometric mean	Median	Range
Solution operator	123.6	155.0	10.0–580.0
Cement operator	105.7	185.0	10.0–780.0
Furnace operator	189.3	310.0	20.0–1,650.0
Materials handler	0.3	0.1	0.1–49.0
Process supervisor	1.4	1.1	0.7–7.0
Maintenance technician	146.8	110.0	30.0–1,560.0

Source: Exhibit 13, JACA, Table 3-3.

TABLE VIII-C14.—CADMIUM EXPOSURE DATA FOR CADMIUM PRODUCTION BASED ON PACE

Job category	Geometric mean exposures ($\mu g/m^3$)
Solution charger	226
Solution operator	54
Sponge operator	34
Sponge presser	65
Neutralization operator	17
Weigh and pack	41
Premelt operator	302
Retort operator	1,396
Maintenance	55
Laboratory	7
Mechanical equipment	23
Thalium operator	17
Litharge operator	13
Utility and extra	19

Source: Exhibit 19-43, Attachment L, Table A2-1.

TABLE VIII-C15.—CADMIUM EXPOSURE DATA FOR CADMIUM REFINING BASED ON COMPANY DATA

Process	Exposure levels ($\mu g/m^3$)	
	Range	Geometric mean
General (Lab, Utility, Laundry)	1–125	12
Transport/unloading	6–2,957	32
Mechanical/ maintenance	1–379	16
Cadmium refining	5–230	34
Cadmium casting	4–1,007	117
Retort department	80–9,425	653
Thallium operator	12–21	16
Litharge operator	4–1,373	15

Source: Exhibit 19-32, Attachment I.

TABLE VIII-C16.—CADMIUM EXPOSURE DATA FOR ELECTROLYTIC ZINC REFINING BASED ON PACE

Process	Exposure levels ($\mu g/m^3$)	
	Range	Geometric mean
Yard department:		
Equipment operator	1–9	3
Concentrate charger	1–7	3
Laborer	2–45	13
Concentrate beltman	3–51	16
Sampler	6–12	9
Janitor	4–4	4
Warehouse trucker	.....	.....
Pre-leach:		
Pre-leach operator	ND–2	2
Roaster department:		
Roaster operator	1–19	8
Roaster helper	1–18	7
Acid plant:		
Acid plant operator	2–2	2
Acid plant helper	.....	1
Acid loader	.....	1
Leach/purification plant:		
Head leacher	ND–3	2
1st stage operator	ND–2	2
2nd stage operator	2–5	3
Residue dryer	3–9	5
Laborer, 2nd stage	5–96	17
Other areas	4–14	8
Line reamer	5–6	6
Pressman (both stages)	5–19	12
ZSM/Cd operator	4–27	10
Cadmium leach helper	4–11	8
Cadmium department:		
Finish operator—Melter	17–198	56
Finish operator—Oxide	46–600	220
Lead casting	14–35	23
Lead sheering	12–12	12
Cell room department: (represents over 40% of total employees)	<1–2	1

ND: Not Detectable.
Source: Exhibit 19-43, Attachment K, Appendix A, Table I.

Table VIII-C17.—Cadmium Exposure Data for Electrothermic Zinc Refining Based on PACE

Process	Exposure levels (μg/m³)	
	Range	Geometric mean
Acid Plant:		
Acid plant operator	1-1	1
Shift utility	1-1	1
Day utility	1-1	1
Roaster Plant:		
Foreman	1-1	1
Feed utility ore	1-16	6
Roaster plant operator	ND-2	1
Shift utility	1-36	10
Mechanical repairman	1-1	1
Sinter Plant:		
Foreman	ND-111	19
Utility men	4-116	24
Sinter machine operators	7-70	24
Sinter plant weighmen	10-216	95
Material handlers	3-373	57
Laborers	ND-319	64
Mechanical repairmen	1-118	20
Slag Plant:		
Slag plant operators	ND-24	5
Coke & Residue Plant:		
Coke & residue operator	3-31	11
Furnace Plant:		
Foremen		
Furnace group leader	1-7	2
Furnace operators	1-5	1
Utility men	2-29	4
Shift utility men	1-18	5
Top operators	1-29	13
Ass't top operators	3-47	14
Slag operators	1-10	2
Casting operators		
Compressor operators		
Laborers	1-8	3
Mechanical repairmen	ND-37	6
Zinc Sulfate Plant:		
Supervisor	17-21	19
Operator	10-42	23
Secondary Materials Plant:		
Materials handler	1-32	8
Heavy equipment operators	1-14	4
Zinc Dust Plants:		
All operators	ND-5	1
Refinery:		
All operators	ND-2	1
Maintenance:		
Mechanical utility (not in production area)	2-3	2
Electrical Repairmen	1-50	7
Bricklayers	1-5	2

Notes: Utility/Maintenance data excludes work on dust collectors.
ND: Not Detectable.
Source: Exhibit 19-43, Attachment K, Appendix B, Table I.

In electrolytic refining, 25 of the 27 job categories have mean exposures below 25 μg/m³, and 18 job categories have mean exposures less than 10 μg/m³. In electrothermic refining, 32 of the 35 job categories have mean exposures below 25 μg/m³, and 23 job categories have mean exposures less than 10 μg/m³.

Data on cadmium exposures during zinc and cadmium refining were also provided for the record by a zinc refining company [5, Attachment I, p. 5] and are summarized in Table VIII-C18. The company employs 385 people of whom 162 are considered exposed. Among the exposed production workers, only four employees have average exposures above 20 μg/m³; 21 of 27 production job categories had average exposures below 10 μg/m³. For this company over 85 percent of the monitoring samples were less than 20 μg/m³ in every area except the cadmium plant. [5, Attachment I, Table I].

Existing and feasible additional controls. The JACA report described hoods ducted to baghouses as part of existing controls for the solution operator, furnace operator, and materials handler in the cadmium refining plant which they visited. JACA recommended the installation of additional and improved local exhaust ventilation for the solution operator and the furnace operator. JACA also recommended enclosed screw conveyors as an alternative to manually transferring materials between tanks. Mechanized systems would be implemented for the transfer of moist cadmium cement from the cementation tank to the oxidation bins and for the transfer of dried cement to the leach tanks.

Table VIII-C18.—Cadmium Exposure Data for Electrolytic Zinc Refining Based on Company Data

Process	Exposure Levels (μg/m³)
	Arithmetic mean [1]
Yard workers	8.37
Roaster operators	6.30
Acid plant operators	1.50
Leach/purification operators	7.06
Cellroom attendant	0.50
Cadmium finishing (4 employees)	102.35
Casting	1.55
Lab analyst (when in Cd plant)	57.00
Test plant technician (for new Cd projects)	93.50

[1] Generally higher than geometric mean.
Source: Exhibit 19-30, Attachment I, page 5.

JACA also recommended improved housekeeping measures such as vacuuming, damp mopping, and improved cleanup prior to maintenance. [1, pp. 4-4 through 4-7].

PACE provided a more detailed analysis of the cadmium refining plant. PACE identified 14 separate job categories at the plant which had a total of 45 workers exposed over two shifts. Both existing and recommended additional controls were described. Additional controls were recommended for most job categories and included local exhaust ventilation systems, enclosed material handling systems, clean air islands, and vacuum cleaning systems. [3, pp. 2-3 through 2-13].

The cadmium refining plant provided descriptions of existing controls for each of eight departments. [7, Attachment III]. The company stated that all feasible controls and housekeeping methods were utilized for control of exposure to arsenic and lead and that these same controls also reduced cadmium exposure. [7, p. 4].

PACE provided the most detailed analysis of existing and additional controls for zinc refining plants [2]. In the yard department, the roadway could be relocated and the dry sweeper could be replaced with a wet sweeper. Equipment operators could be protected by providing enclosed, ventilated cabs. An enclosed work station, a clean air island, and a side draft ventilation system could be provided for the concentrate beltman. For the roaster department PACE described several specific controls, summarized by "improved housekeeping, ventilation at specific sources and changes in work practices will reduce exposures." [2, appendix A, page 17]. For the leach/purification plant PACE recommended isolation of the calcine hoppers by means of a sheet metal wall with additional ventilation inside the enclosure, the installation of two central vacuum cleaning systems, local exhaust ventilation at the cyclone feeder, improved ventilation at the roll filters, general ventilation for negative pressure in the residue tower area, enclosure and ventilation of the briquette press, and a clean air island for the briquette press operator. To lower exposures in the cadmium plant, the PACE analysis described significantly revised exhaust ventilation systems and tighter fitting furnace enclosures.

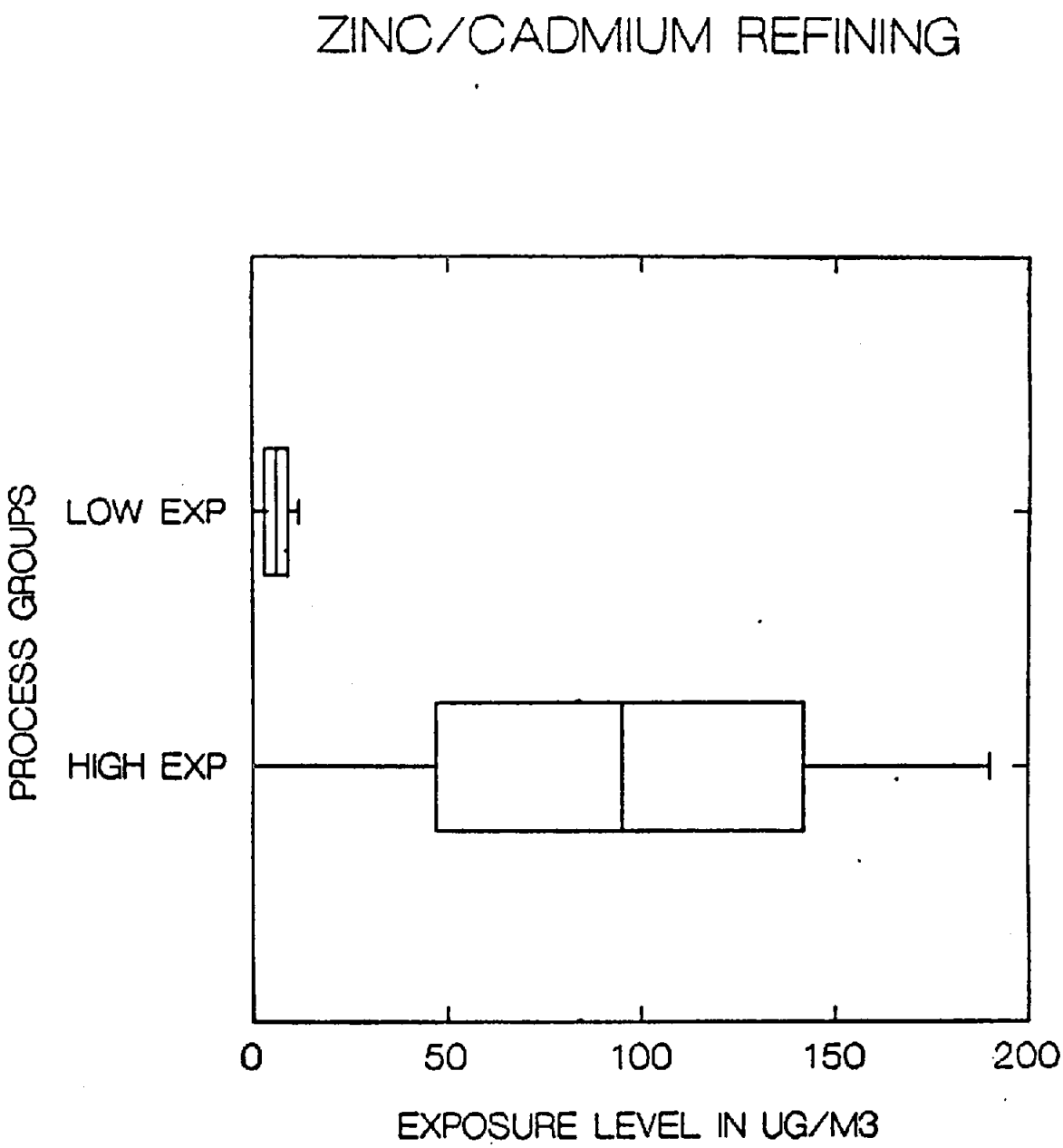
Technologically feasible limit for a SECAL. In order to determine the appropriate SECAL level for this industry sector, OSHA separated exposures into high and low occupation/process exposure groups to facilitate the analysis (see Section B for a more complete description of this approach). Data were divided at a breakpoint which maximized the difference between the mean values for the two separated data sets.

The data segregation resulted in the identification of a "high" occupation/

process exposure group which included cadmium refining, cadmium casting, cadmium oxide production, and sinter plant operations, involving about 202 workers. All other plant operations including zinc leaching operations, yard department, acid plant, cell room, etc., were included in the "low" exposure group involving about 1,148 employees. Figure VIII–C7 graphically presents the segregated data. The vertical line within each box depicts the median value for the distribution.

BILLING CODE 4510–26–M

FIGURE VIII-C7



BILLING CODE 4510-26-C

Mean exposure data for the two sets were as follows:

	High group	Low group
Number of observations	39	51
Mean	91.4	5.8
Standard deviation	141.7	5.3

To verify that the two groups within this industry were distinct, a *t* test was performed on the difference in the means. The null hypothesis that the means of the exposure data were equal, was rejected and the conclusion that they were drawn from separate statistical distributions, was accepted.

After the statistical difference between high and low exposure groups was verified, the data were analyzed separately. In Figures VIII–C8 and VIII–C9, separate process mean exposure values were drawn from each available data source. All process data in each group were "fitted" to a straight line using ordinary least squares methodology. For the high exposed cadmium group over one half of the exposures were at or below 100 $\mu g/m^3$ (figure VIII–C8).

For each group a model was developed to graphically show the effect on the exposure distribution after current exposures are reduced using alternative engineering control efficiency factors of 80 percent down to 20 percent, in 20 percent increments. The higher the efficiency level, the lower the projected exposure level and the closer the projected exposure line moves to the vertical axis. Figures VIII–C10 and VIII–C11 show the reduction and shift in the distribution of exposures for the high and low groups in zinc refining/cadmium production operations.

BILLING CODE 4510–26–M

FIGURE VIII-C8

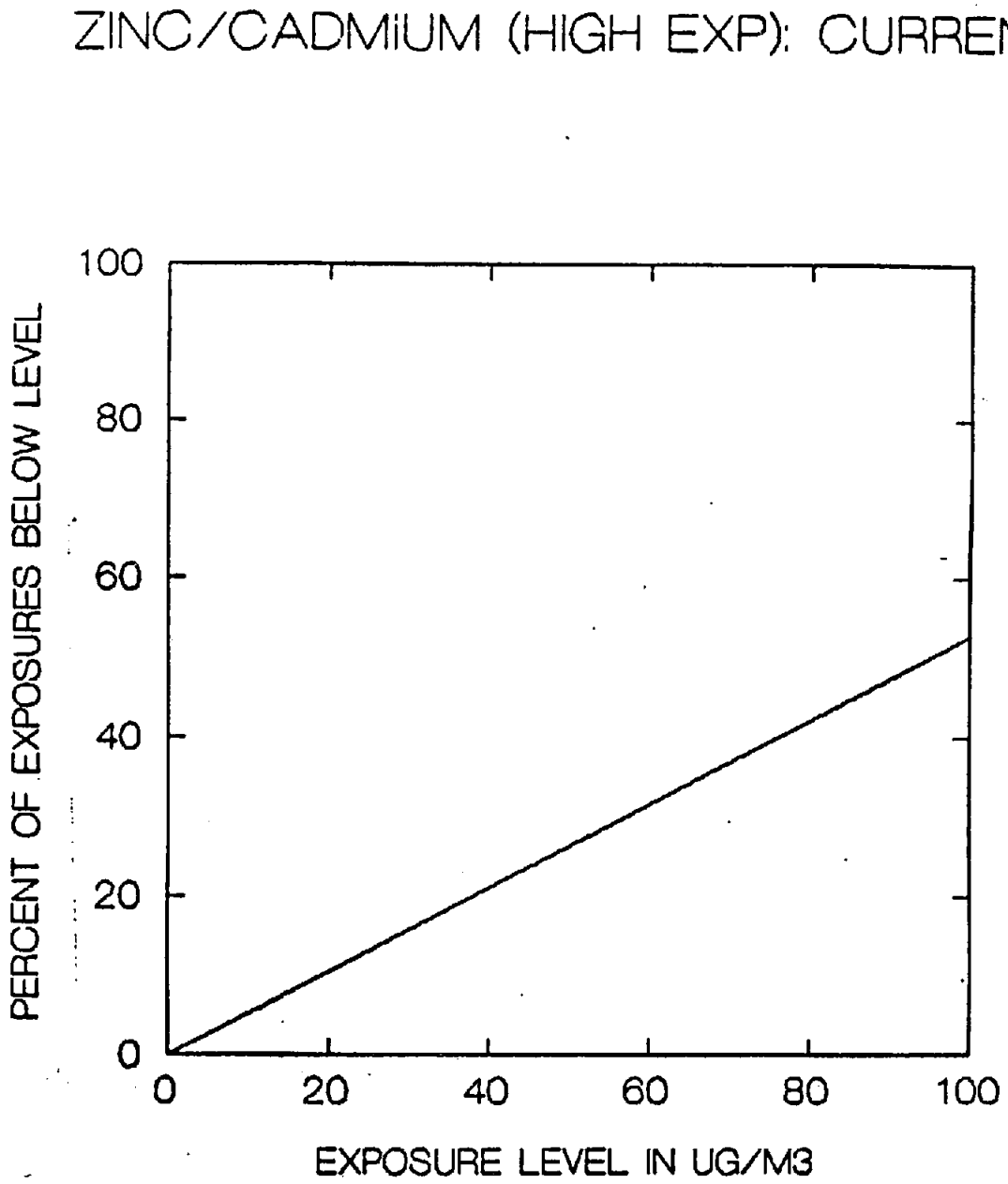


FIGURE VIII-C9

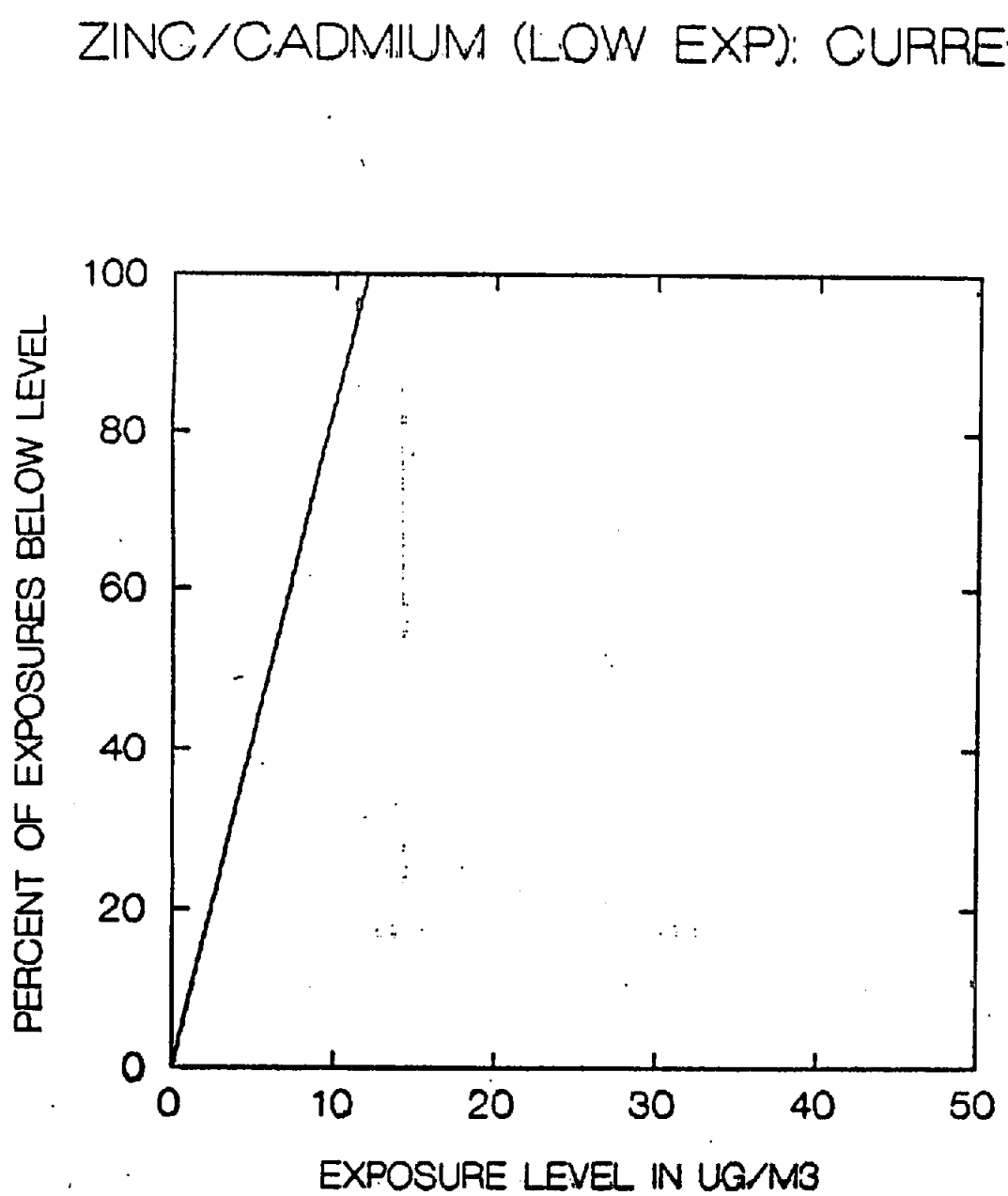


FIGURE VIII-C10

ZINC/CADMIUM (HIGH EXP.): CONTROLLED 80%-20%

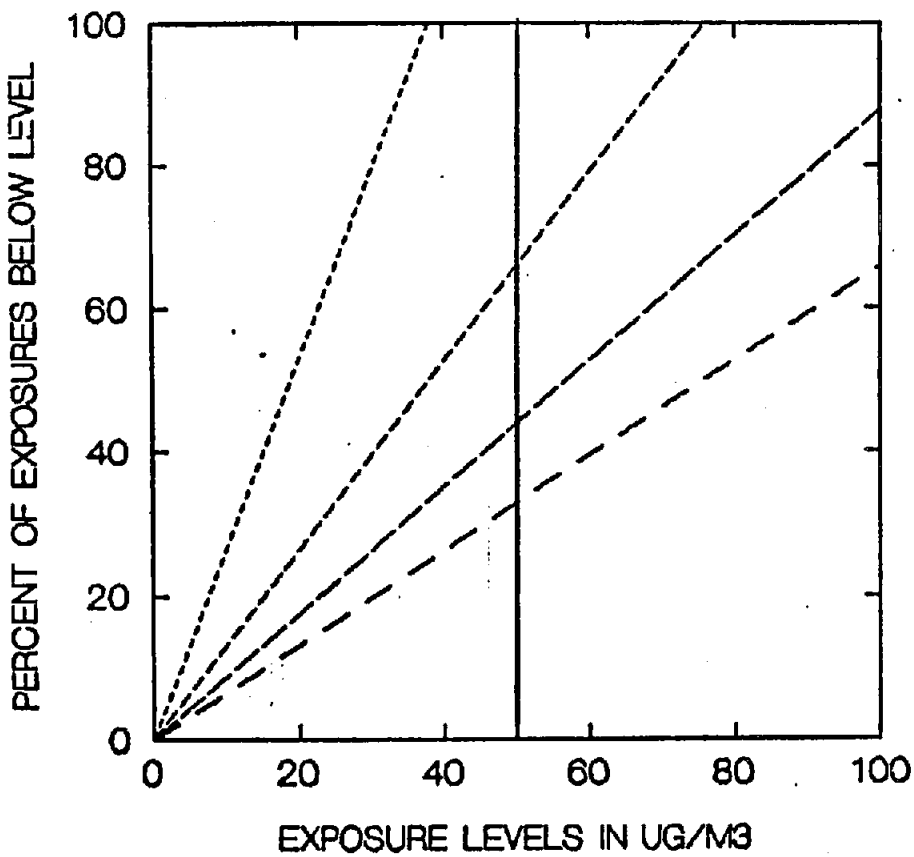
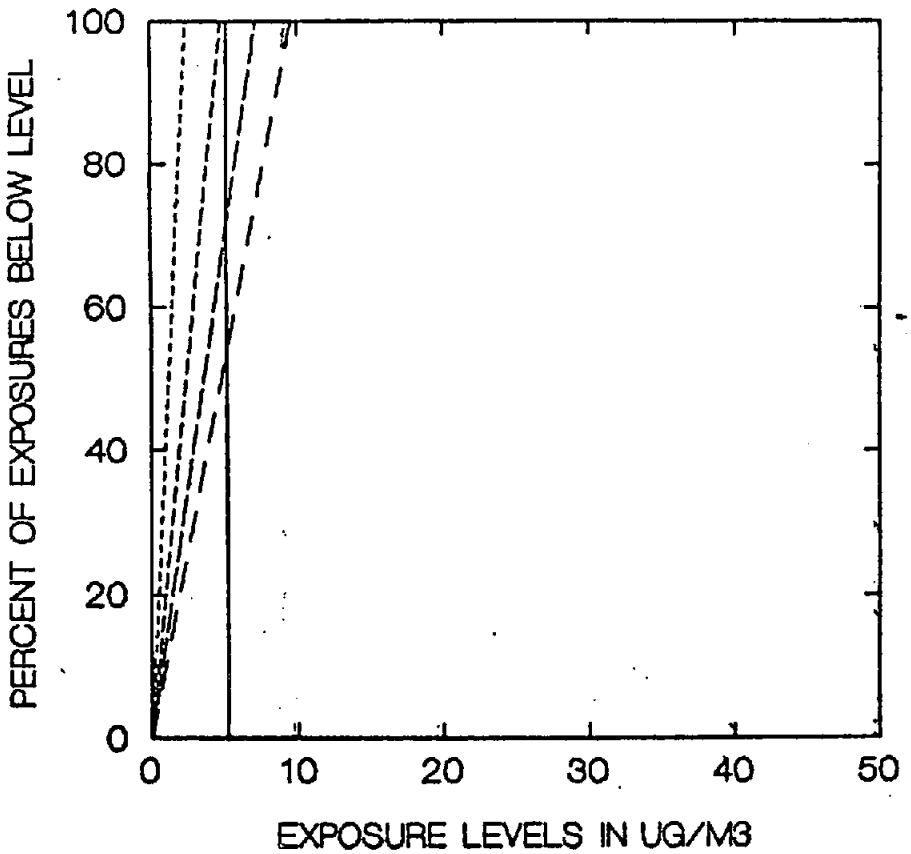


FIGURE VIII-C11

ZINC/CADMIUM (LOW EXP.): CONTROLLED 80%-20%



VIII-C72

BILLING CODE 4510-26-C

The selection of an appropriate engineering control reduction factor was based on evidence and testimony in the record and economic feasibility considerations. The only basis for selecting an engineering control solution with a lower efficiency than an alternative strategy with a higher factor, was economic infeasibility of the latter.

The evidence in the record substantiates the finding that additional feasible controls are available and can be implemented to further reduce exposure levels. The extent of current controls in place and the applicability of specific additional controls will vary depending on the individual plant, but the relevant comments in the record all basically agree that a multitude of control options exists to limit airborne cadmium concentrations. These are generally conventional technologies that are commonly known, readily available, and to some degree currently used in the industry, as described above.

The controls can be used individually or in combination. If one control is not sufficient, additional ones can be used. It is the interaction of various engineering controls and work practices as part of an integrated system of controls that can produce the needed overall reduction in exposure levels. OSHA does not specify which control must be implemented. Rather, OSHA allows the employer the choice best suited to the particular characteristics of the workplace.

JACA estimated that the expected efficiency of new or improved local exhaust ventilation systems for exposures in the cadmium refining industry would be over 90 percent in situations where high hood efficiency was possible. [1, Table 4–2]. PACE provided a detailed analysis of the expected effectiveness of engineering controls for both zinc refining and cadmium refining. [2, 3]. For each job category PACE determined the percent of the total exposure that was attributable to different exposure sources and then applied control effectiveness estimates to each source. Estimates of the effectiveness of specific controls were not given, but they can be derived by comparing descriptions of recommended controls in one section with the expected reductions in exposure levels presented in tables supplied by PACE.

In cadmium production operations, PACE's expected percent reduction due to controls at specific sources ranged from 75 to 95 percent. Overall exposure reductions for operators ranged from 75 to over 90 percent (60 percent for maintenance). In zinc refining operations, where cadmium exposures are much lower, controls at individual sources were expected to achieve reductions of up to 80 percent. Background and variability of exposure levels would be reduced significantly. Overall, mean employee exposures would consistently be less than 10 $\mu g/m^3$ except in cadmium refining areas.

This review and analysis of the record needed to be supplemented with economic feasibility considerations before a determination could be made regarding appropriate engineering controls and their effectiveness level. According to PACE, engineering solutions to achieve an 80 percent or higher reduction in cadmium production would require major capital expenditures and the rebuilding and replacement of existing facilities. Capital costs to achieve this reduction margin could reach over $3 million per affected plant according to PACE [3, p. 2–3]. Achieving an 80 percent reduction in cadmium levels does not appear to be economically feasible at this time. (Total annual revenues in this sector average less than $50 million per plant. If the profit margin on this amount was five percent, per plant profits would be $2.5 million. Since 1979, four cadmium refining facilities have closed, leaving four domestic producers nationwide.) Instead, less expensive engineering controls with a lower efficiency expectation (60 percent) were identified. Based on the evidence in the record, OSHA believes that an engineering control reduction level of 60 percent is reasonable for this industry segment and is both technologically and economically feasible.

Following the selection of this efficiency factor, the appropriate engineering control level for each exposure group was identified at the point achievable for 60–80 percent of the exposures. For the high exposure processes including cadmium refining, cadmium casting, cadmium oxide production and sinter plant operations, a SECAL of 50 $\mu g/m^3$ is identified. For all low exposed processes, OSHA believes that the PEL level of 5 $\mu g/m^3$ is achievable through engineering controls.

For the high exposure group, compliance with the PEL of 5 $\mu g/m^3$ with engineering controls and work practices is infeasible at this time and can only be achieved through the use of respirators. Respirators are readily available with a wide range of protection factors that can adequately protect workers from the potential exposures in this industry. Respiratory protection will be required for many of the production and maintenance employees full time. This result was anticipated in the preliminary analysis and was consistently supported by the substantial evidence in the record.

Costs of Compliance with the 50 $\mu g/m^3$ SECAL and 5 $\mu g/m^3$ PEL. The costs of compliance with the revised cadmium standard consist of costs for additional engineering controls, increased respirator use, more comprehensive exposure monitoring programs, medical surveillance requirements, hygiene provisions (shower rooms, work clothing, etc.), and training and recordkeeping requirements.

Estimates of the costs of installing new or improved local exhaust ventilation systems were provided by JACA. In current dollars, the costs of these systems range from $51,000 to $112,000. [1, Table 6–1]. Annual operating and maintenance costs were estimated to be 10 percent of the capital cost.

PACE provided cost estimates for several types of controls in its analysis of the cadmium production industry. [3, Table A2–4]. A pneumatic conveying system was estimated to cost $60,000 with $4,000 in annual operating and maintenance costs; exhaust ventilation systems with hoods and ducts were estimated to cost $24,000 to $254,000; costs for clean air islands ranged from $6,000 to $27,000; partitioning an area from the rest of the building was estimated to cost $9,000; a complex enclosure of a machine was estimated to cost $5,000; the cost of installing a central vacuum cleaning system was estimated to be $15,000; relocating an operation would cost about $25,000; and a decontamination booth for maintenance work, with exhaust system, monorail and hoist, and vacuum and steam cleaning facilities was estimated to cost $47,000. These estimates were consistent with the evidence in the record for costs of similar engineering controls.

JACA recommended additional engineering controls for three of the six job categories identified in cadmium production. PACE recommended significant additional control measures for ten of fifteen job categories. In its analysis of a zinc refining plant (including cadmium production operations), PACE recommended control measures in four of the seven departments, representing about twenty job categories. Both the PACE and JACA analyses were based on an attempt to achieve 5 $\mu g/m^3$.

For purposes of estimating the costs of additional engineering controls in this industry, OSHA developed estimates of the number of different types of controls that are expected to be installed. The additional feasible controls

recommended and described in the record for this industry are generally common methods of controlling airborne exposures. Each plant would choose the control methods that represent the best solution for their particular situation, depending on the configuration of the operation, the extent of current controls, and the applicability of additional controls.

For example, in some situations ventilation may already be present and exposures may be more effectively controlled by installing glove boxes or mechanized material transfer equipment, or by relocating the operation rather than improving ventilation. Costs for these alternatives would be comparable to the costs for the control methods identified. Thus, OSHA's estimates of the numbers of controls serve to identify work stations where exposures need to be reduced; additional controls provide the basis for estimating total costs. As noted, these control costs may serve as a proxy for the cost of alternative solutions at some operations, in some firms.

Based on a review of the relevant comments submitted to the record, Table VIII–C19 presents the additional controls and their potential costs, needed for compliance with the 50 $\mu g/m^3$ SECAL and the PEL. The three plants with both zinc refining and cadmium refining operations are estimated to need new or improved local exhaust ventilation at six operations, clean air islands at five locations, two additional central vacuum cleaning systems, and improved enclosure or partitions for seven operations. Additional controls for cadmium refining operations would include four local exhaust ventilation systems, three clean air islands, one central vacuum cleaning system, and enclosure of four operations. Zinc refining operations are estimated to need two local exhaust ventilation systems, two clean air islands, one central vacuum cleaning system, and enclosure of three areas.

TABLE VIII–C19.—ESTIMATED COSTS OF ENGINEERING CONTROLS FOR CADMIUM IN THE ZINC REFINING/CADMIUM PRODUCTION INDUSTRY

Type of control	Controls per plant by type of plant [1]			Total industry controls [2]	Cost per control ($thousands)			Industry costs ($thousands)				Total annualized industry cost ($thousands)
	A	B	C		Capital	Annual power and maintenance	Annual labor	Capital	Annualized capital	Annual power and maintenance	Annual labor	
Local exhaust ventilation	4	6	2	24	80	8	0	1,920	312	192	0	504
Clean air islands	3	5	2	20	18	2	0	360	59	40	0	99
Central vacuum systems	1	2	1	8	15	1	7	120	20	8	56	84
Enclosure	4	7	3	28	9	0	0	252	41	0	0	41
Total				80				2,652	432	240	56	728

[1] Type A plant: cadmium refining only; Type B plant: zinc refining and cadmium refining; Type C plant: zinc refining only.
[2] Based on one type A plant, three type B plants, and one type C plant.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

Table VIII–C19 shows the capital costs of additional controls, $2.65 million, and the annual costs, $296,000. Total annualized costs are calculated by amortizing the capital costs over ten years with a ten percent interest rate and adding the resulting annualized cost to the other annual costs. The total annualized costs of engineering controls in the zinc refining/cadmium production industry are estimated to be $728,000.

Three companies submitted lengthy comments and testimony about the extent of current programs for respirator use, exposure monitoring, medical surveillance, hygiene facilities, information and training, and recordkeeping [5, 6, 7, 8, 9, 10, 11]. The industry generally already provides extensive programs in these areas, but the revised standard may require some of these programs to be expanded.

The plants involved in zinc and cadmium refining currently have established respirator programs for employees in high exposure areas. In order to comply with the PEL of 5 $\mu g/m^3$ it is likely that about 80 percent of the production and maintenance employees in the industry would be required to wear respirators full time even after the implementation of additional feasible controls. Employees in cadmium refining areas are already provided with respirators, but many employees with exposures below 20 $\mu g/m^3$ do not wear respirators. One zinc refiner estimated that regular respirator use would have to be expanded from 20 employees currently to 289 employees working in the plant. [11, p. VII–30]. Another comment from a zinc refiner indicated that almost all of the 120 employees exposed at or above 1 $\mu g/m^3$ currently wear respirators. [5, Attachment I, pp. 5–7].

The incremental costs associated with respirator use as a result of the revised cadmium standard are based on providing respirators for an estimated 500 additional employees in the industry. The industry currently employs about 1,800 workers, of whom about 75 percent are production or maintenance employees [11, p. VII–59]. Given that all employees in the cadmium refining operations already wear respirators, the 500 employees represent about half of the remaining workers who would be required to wear respirators under the revised standard.

The annual cost per employee of providing a respirator, HEPA filter changes, and a fit test was estimated by one zinc industry employer to be about $300. [5, Attachment III, p. 1]. Thus, the annual cost for the industry for additional respirator use is estimated to be $150,000.

As evident from employers' submissions of monitoring results to the record, zinc and cadmium refining facilities already conduct exposure monitoring regularly. The revised standard requires semi-annual exposure monitoring of "each shift for each job classification in each work area." Plants refining zinc and cadmium have an average of 20 job categories, and plants refining only zinc or cadmium have an average of about 10 job categories affected by this requirement. Counting each shift separately, a total of 240 job categories would have to be monitored

semi-annually. Since about half of this monitoring is already conducted, approximately 240 additional samples would have to be taken each year in this industry.

The lab analysis of each sample is estimated to cost $40. The services of an industrial hygienist required to perform the monitoring for each plant would cost on average about $1,500. [1, p. 6-23]. Thus, the estimated annual cost attributable to increased exposure monitoring is $17,100.

The medical surveillance requirements of the revised standard involve a complex combination of different categories of employees and a series of triggers and different schedules of various exams and tests. The standard basically requires annual biological monitoring, including tests for cadmium in urine, cadmium in blood, and β_2-microglobulin in urine, and a full medical examination every two years.

Most employees at cadmium refiners are already provided with annual medical exams and biological monitoring including blood and urine cadmium analyses and urine protein analyses. [8]. About half of the exposed employees at zinc refiners are included in biological monitoring programs, and those with high cadmium exposure (less than 10 percent of all exposed workers) are given annual physicals. [11, pp. VII-49 through VII-51]. Expanding the medical surveillance programs in this industry to meet the basic requirements of the revised cadmium standard would involve approximately 600 additional physicals (1,200 employees every two years) and an additional 600 of each of the three biological monitoring tests.

More frequent medical exams and biological monitoring may be required for some employees, including employees who may be medically removed. An estimated 50 additional medical exams and 150 additional sets of biological monitoring may be necessary annually for this purpose.

The cost of a physical, including the wages paid during the exam, was estimated to be about $250. The cost of the lab analysis for a β_2-microglobulin sample was cited by a public health research group as $80. [4, p. 4]. Analyses of samples of cadmium in urine and in blood are estimated to be $60 each. An additional $5 is added to the cost of each of the biological monitoring samples for costs associated with collecting the samples. Thus, the total incremental annual costs of compliance with the medical surveillance requirements are estimated to be $323,750 [650*$250+750*($65+$65+$65)].

Requirements for medical removal may involve compliance costs in addition to those for more frequent medical exams and monitoring (estimated above). The criteria for mandatory removal would affect employees with the most extreme biological monitoring levels. The criteria for removal also allow for considerable physician's discretion. An estimated 3 percent of the exposed workforce may be removed initially on the basis of these criteria and the discretion of physicians.

Compliance with the new PEL for cadmium and other requirements of the final cadmium standard should prevent a continuing need to remove employees. The number of employees with relatively high past exposures who would be more likely to be removed, should decline through attrition. However, as the criteria for removal become broader in future years (lower levels of cadmium in blood and urine will trigger mandatory removal), additional employees may be subject to removal. The costs associated with the medical removal provisions are approximated by assuming that on average, 3 percent of the exposed workforce may be removed every 5 years.

The number of employees removed should be small enough to enable establishments to provide removed employees with alternative positions. Costs to the employer would include paying wage subsidies to employees moved into lower wage jobs, and hiring and training new employees. The average cost per removed employee would be an estimated $5,000. An estimated 40 employees may be removed every five years, on average, in the zinc and cadmium refining industry, and the annual cost for the industry would be $40,000.

The total annual cost for the medical surveillance and medical removal provisions is estimated to be $383,750.

Cadmium refining plants generally have established hygiene programs, including clean/dirty side change rooms, work clothing, and separate lunch rooms. [11, p. 10-216]. One zinc refiner currently provides showers and change rooms but stated that the modifications necessary to meet the requirements of the cadmium standard would cost about $200,000. This commenter also stated that disposable work clothing would have to be provided for about 200 additional employees at an annual cost of $184 per employee. [5, Attachment III, p. 1].

Based on the record, OSHA has concluded that for the industry as a whole the costs of the hygiene provisions would include about $300,000 for shower room and/or lunch room modifications with $50,000 in annual expenses for work clothing and operating costs. In addition, the estimated annual cost of showering on work time is $900 per employee (based on fifteen minutes per day for 240 days per year at $15 an hour) and would apply to an estimated 400 employees. The total annualized costs of compliance with the hygiene provisions is thus estimated to be $459,000.

Incremental costs for recordkeeping and other information-related requirements are estimated to be about $5 per employee annually. Up to 1,000 additional employees may be affected by these requirements which would result in an annual compliance cost of about $5,000.

The total annualized costs of compliance with the cadmium standard for this industry are estimated to be $1.72 million. These costs are summarized by provision in Table VIII-C20.

Economic feasibility of a 50 $\mu g/m^3$ SECAL and 5 $\mu g/m^3$ PEL. Cadmium prices have generally ranged from $1 to $4 per pound over the past 25 years. [14, p. 6]. From 1983 through 1987 the average prices were below $2 per pound. In 1988, the average price per pound rose to over $7, and as of August 1989 the price had fallen back to about $4 per pound. [13, p. 8].

TABLE VIII-C20.—ESTIMATED COSTS OF COMPLIANCE WITH THE REVISED CADMIUM STANDARD FOR THE ZINC REFINING/CADMIUM PRODUCTION INDUSTRY

Provision	Annualized cost ($thousands)
Exposure Control	728.0
Respirator Use	150.0
Exposure Monitoring	17.1
Medical Surveillance	383.8
Hygiene Facilities/Practices	459.0
Recordkeeping and Information	5.0
Total	1,722.9

Note: Costs do not include current expenditures.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

From 1984 to 1987 U.S. production of cadmium remained relatively stable, ranging from 1,488 to 1,686 metric tons. Preliminary data for 1988 suggest that U.S. cadmium production increased to nearly 1,900 metric tons as a result of increased zinc production and in response to higher zinc and cadmium prices. [13, p. 2-2].

Since cadmium is a necessary by-product of zinc refining, decisions

regarding its production are not made independently of conditions in the zinc market. From 1984 to 1987 U.S. production of zinc was about 260,000 metric tons while the price of zinc was about 40 cents per pound [13, Table 2–3]. Thus, revenues from zinc production have been about $230 million.

At a price of $2 per pound, total revenues from cadmium production would amount to less than $7 million. Based on the average New York dealer price of $6.28 per pound in 1989, the value of domestic cadmium metal output in that year was $21.5 million. [14, p. 10].

Cadmium and other by-product revenues are usually considered credits (i.e., negative costs) by zinc refiners. [14, p. 9]. These revenues partially offset the production costs of the principal product (zinc). The magnitude of the credit fluctuates according to by-product prices, but tends to be a relatively small portion of total revenues.

Zinc refiners are unlikely to discontinue cadmium production unless the total costs of producing zinc and cadmium outweigh the total revenues. Zinc refiners and cadmium refiners did not discontinue operations when the price of cadmium remained below $2 per pound for several years in the 1980s. For cadmium and zinc producers, the estimated compliance costs associated with this standard would be completely offset by an increase in the price of cadmium of less than fifty cents per pound. Since the price of cadmium has recently risen by two to five dollars per pound over prices a few years ago, refiners should be earning sufficient revenues to cover compliance costs.

For zinc refiners the estimated compliance costs represent a fraction of 1 percent of revenues. Given the inherent fluctuations in the price of zinc, costs of this magnitude could not alone cause a zinc refiner to cease production. An independent study by the U.S. Department of Interior, Bureau of Mines, concluded that annualized costs for engineering controls for the industry of $983,000 represented "a reasonable cost." [14, Attachment I, p. 1]. Some commenters raised concerns that the impact of the standard could hinder the ability to recover cadmium from scrap and other forms of recycling. At current prices cadmium production is financially viable. Cadmium-containing residuals are classified as hazardous waste and their disposal is estimated to cost $0.50 per pound of cadmium. Thus, "the price of cadmium metal would have to drop about $0.50 below the operating costs before primary cadmium producers would actually shut down their cadmium circuits and dispose of residuals instead." [13, p. 4–2]. Due to the high costs associated with the disposal of cadmium-bearing waste, cadmium refiners should be able to obtain supplies at relatively low prices.

Cadmium refining operations are currently conducted with extensive use of respiratory protection and would have to continue to do so with or without the revised cadmium standard. The feasibility of cadmium recycling efforts would depend on the price of cadmium and other factors in the business environment. The incremental compliance costs associated with this standard would be a very minor factor in investment decisions on this scale.

Due to environmental regulation, labor costs, and other factors, the costs of domestic cadmium refining may be higher than in other countries. Prior to 1974, the United States was the world's leading refiner of cadmium with 11 plants producing cadmium. Cadmium production dropped 82 percent by 1982 even though demand remained strong. By 1989 the United States had gone from being nearly self-sufficient in cadmium to a net import reliance of 62 percent. [14, p. 9].

The impacts of the revised cadmium standard are completely overshadowed by more fundamental circumstances and developments in this industry. Cadmium refining operations can continue in this country under the revised cadmium standard. The survival of or investment in such plants depends on many factors. The revised standard would have a negligible influence in this area because (1) the incremental costs represent a small fraction of revenues and return on equity and (2) the basic nature of cadmium refining operations with the need for respiratory protection would not be changed.

OSHA concludes that the revised cadmium standard is economically feasible for the zinc refining/cadmium producing industry. This determination is based on the evidence submitted to the record, including the costs imposed by the standard and the industry's ability to absorb these costs.

Notes

1. Exhibit 13, "Economic Impact Analysis of the Proposed Revision to the Cadmium Standard," Final Report, JACA Corporation, March 15, 1988.

2. Exhibit 19–43, Attachment K,"Technical Feasibility of a Workplace Standard for Airborne Cadmium in the Primary Zinc Industry," PACE Incorporated, December 5, 1989.

3. Exhibit 19–43, Attachment L,"Feasibility and Cost Study of Engineering Controls for Cadmium Exposure Standard," PACE Incorporated, April 30, 1990.

4. Exhibit 123,"Comments of Public Citizen Health Research Group and the International Chemical Workers Union on OSHA's Proposed Standard Governing Occupational Exposure to Cadmium," Public Citizen, October 17, 1990.

5. Exhibit 19–30,"Comments on OSHA Proposed Cadmium Regulation," Big River Zinc Corporation, May 10, 1990.

6. Exhibit 19–31, "Statement of Zinc Corporation of America on the OSHA Proposed Rulemaking on Occupational Exposure to Cadmium," Zinc Corporation of America, Thomas E. Janeck, May 11, 1990.

7. Exhibit 19–32, Comments of ASARCO Incorporated, May 9, 1990.

8. Exhibit 107, Comments of ASARCO Incorporated, September 18, 1990.

9. Exhibit 111, Comments of ASARCO Incorporated, September 26, 1990.

10. Exhibit 125, Comments of Big River Zinc Corporation, October 16, 1990.

11. Hearing Transcript, pages VII–29 through VII–110 and pages 10–204 through 10–216.

12. Exhibit 106, Comments of NIOSH, September 18, 1990.

13. Exhibit 19–43, Attachment I, "Economic and Technological Feasibility of a 5 Microgram per Cubic Meter Workplace Standard for Airborne Cadmium," Putnam, Hayes & Bartlett, Inc., April 30, 1990.

14. Exhibit 105, Studies submitted by Bureau of Mines, U.S. Department of Interior, September 18, 1990.

Pigment Production

Industry overview. Cadmium pigments are manufactured at four plants in the United States. Approximately 600 tons of cadmium are used in the production of cadmium-based pigments annually. A total of about 100 employees are exposed to cadmium in these facilities. [1, p. 5].

Cadmium pigments are inorganic compounds that range in color from yellow to red. They are used to color plastics, paints, ceramics, and printing inks. The pigments are usually produced as powders but are also available in other forms such as pastes and liquids. For applications in the plastics industry, cadmium pigments are available in master batch pellets, which incorporate the pigment in pellets of compounded polymer resins.

Compared to other inorganic pigments, cadmium pigments are relatively expensive. Cadmium pigments are preferred and essential for many uses because other pigments lack the qualities that cadmium pigments provide. The advantages of using cadmium pigments include heat stability for manufacturing plastics at high temperatures or coating high-temperature surfaces; coloring power that is strong and bright; and resistance to fading due to aging or sunlight.

Production processes. The process for manufacturing cadmium pigments differs among companies, and

manufacturers may utilize different combinations of job classes depending on the process. In general the process entails the addition of cadmium metal to a tank which contains an acid solution. Depending on the color desired, sodium sulfide and selenium or zinc sulfide are added. The resulting precipitate is filtered, washed, and dried. The dried precipitate is then calcined, forming the desired cadmium pigment. The pigment is further milled or blended to meet customer specifications. Finally, it is packaged, usually in fiber drums.

The cadmium pigment manufacturing process generally involves the following job classes in addition to supervisors, maintenance mechanics, and laboratory technicians: Solution operators, wet solids operators, calcine operators, and dry solids operators. [1, p. 6].

The solution operator is in charge of adding cadmium metal flakes to the preparation tank and may also be involved in the striking operation which is a wet process. Depending on the manufacturer, this position may be two different jobs, an operator and a striker. The wet solids operator transfers the wet presscake either manually or automatically to the drying department. In some pigment plants the material is manually transferred from drying trays to the crushing operation where it is packed in drums and sent to the calcining department. In other facilities, the pigment is dried in a closed system using either a belt dryer or pan dryer. Depending on the facility, pigment is either added to the calcine manually by the calcine operator or it is transferred to the calcine by air from a portable container. Dry solids operators are responsible for further grinding, milling, or blending of the cadmium pigment. When product specifications are met, the pigment is packaged.

Employee exposures. The preliminary analysis accompanying the proposed rule relied on the exposure profile developed by JACA Corporation. [2, Table 3–6]. JACA's exposure profile was based on seven years of sampling results from OSHA's Integrated Management Information System (IMIS) data base through August 1986. JACA also visited a pigment manufacturing plant to better understand and interpret exposure data. Their exposure profile is presented in Table VIII–C21. Four of the six job categories identified have geometric mean exposures of less than 6 $\mu g/m^3$; the remaining two job categories have mean exposures between 40 $\mu g/m^3$ and 50 $\mu g/m^3$.

PACE Incorporated developed an exposure profile for the pigment manufacturing industry at the request of the Cadmium Council. [3, Table A10–1]. This information is summarized in Table VIII–C22. The PACE estimates were calculated from data supplied from one plant. Three of the eight job categories listed have mean exposures of less than 50 $\mu g/m^3$; four of the job categories have mean exposures of 100 $\mu g/m^3$ or more.

One pigment manufacturing plant submitted personal monitoring data to the record as part of its post-hearing comments, including samples taken during 1990. [4, Section D–1]. These data are summarized in Table VIII C–23. The average eight-hour time-weighted average exposures vary from less than 30 $\mu g/m^3$ in some job categories to over 100 $\mu g/m^3$ in others.

TABLE VIII–C21.—CADMIUM EXPOSURE DATA FOR CADMIUM PIGMENT PRODUCTION BASED ON JACA

Job category	Concentration in $\mu g/m^3$		
	Geometric mean	Median	Range
Solution operator	46.2	28.0	22.0–160.0
Wet solids operator	5.6	17.5	0.1–470.0
Calcine operator	40.3	243.0	0.1–1,020.0
Dry solids operator	3.9	2.0	0.1–1,200.0
Process supervisor	1.1	1.1	0.1–7.0
Maintenance technician	3.5	3.0	0.1–1,560.0

Source: Exhibit 13, JACA, Table 3–6.

TABLE VIII–C22.—PROFILE OF OCCUPATIONAL EXPOSURES TO CADMIUM IN THE CADMIUM PIGMENT INDUSTRY BASED ON PACE INCORPORATED

Job category	Geometric mean exposures [$\mu g/m^3$]
Attack operator	79
Strike operator	29
Pressman	43
Crusher operator	140
Calcine operator	100
Wet system operator	44
Millman	222
Blend operator	145

Source: PACE Incorporated, Exhibit 19–43, Attachment L, Table A10–1.

TABLE VIII–C23.—OCCUPATIONAL EXPOSURES TO CADMIUM DURING CADMIUM PIGMENT PRODUCTION BASED ON SCM PLANT DATA

Job category	Arithmetic mean[1] exposures [$\mu g/m^3$]
Attack operator	27
Strike operator	12
Pressman	56
Crusher operator	278
Calcine operator	50
Wet system operator	43
Millman	348
Blend operator	53
Mixer operator	163
Maintenance mechanic	24
Supervisor	9

[1] Generally higher than geometric mean.

Note: Based on 1990 eight-hour time-weighted average personal monitoring data for all job categories except attack operator and pressman, for which 1990 data were not available and 1988–1989 data were used.

Source: SCM Chemicals, Post-Hearing Documentary Evidence, Exhibit 112, Part D–1.

Existing and Feasible Additional Controls. Descriptions of existing controls and feasible additional controls were provided to the record from three primary sources.

JACA Corporation described the limited use of ventilation systems observed during a site visit to one plant; most operators were not protected by engineering controls [2, page 4–10]. JACA recommended an extensive expansion and improvement of the ventilation system, including additional high-efficiency local exhaust ventilation hoods at four work stations.

The plant visited by JACA subsequently implemented a major exposure reduction project, the details of which are described in exhibit 112. The project was completed by early 1989. The improvements and modifications listed as part of this effort

include a variety of controls and were based on a comprehensive approach to reducing exposures levels throughout the plant. According to evidence supplied by the plant,

> The design of the exposure reduction project involved a number of components, including improvement of the existing ventilation system, installation of extensive new ventilation equipment, installation of central vacuuming equipment, installation of pneumatic transfer equipment, and other improvements to the processes and work practices. [4, Section D-2, p. 3].

PACE Incorporated evaluated existing controls and prospects for additional controls in the pigment manufacturing industry [3]. The plant visited by PACE and considered representative of the industry was the same plant that was visited by JACA. By the time of the PACE site visit, the plant had completed its exposure reduction project as outlined above. Additional controls recommended by PACE included the enclosure of the box opening and dumping operation at the attack tanks and adding back-draft exhaust ventilation. Together with improved work practices and reduced background concentrations of airborne cadmium, mean worker exposures at the attack tanks would be expected to be reduced by over 80 percent to 13 $\mu g/m^3$ [3, p. 10-4].

PACE suggested that exposures at the strike tanks would be significantly reduced by providing more effective exhaust ventilation for the tanks and by establishing frequent wash down of surfaces in this area to prevent contaminant accumulation.

PACE's recommendations for pigment transfer and calcining included improved ventilation and establishing dedicated equipment and enclosed chutes for multiple production lines which would also involve building modifications.

PACE identified improved ventilation and enclosure as feasible additional controls for the milling and blending operations. The use of parallel production lines may also reduce exposures in these operations, assuming that a sufficient number of production lines could be built and that the lines would remain dedicated to a particular color without the need for clean out.

According to PACE, exposures during pressing and washing operations could be reduced by replacing recessed plate filter presses with automatic pressure filters. Manual material handling would be eliminated as the discharge from the belt filters would be maintained in enclosures. However, implementing parallel production equipment to sufficiently accommodate manufacturing needs may not be feasible and would also create additional exposures during cleaning and maintenance of the chutes and enclosures.

PACE further proposed that controls for the drying operation include an extension of the semi-automatic processing from the pressure filters, eliminating manual handling of trays, tray drying racks, and the use of static drying ovens. Drying would be accomplished with continuous screw dryers from the pressure filter discharge in a closed system. Dedicated dryers would be required for each of the dedicated pressure filter lines.

Pigment manufacturers contend that establishing dedicated production lines would not be feasible given the need to make a variety of products. In order to compete effectively, the plants offer a wide range of products and need to maintain the flexibility to change specifications frequently by producing custom blends using a batch process. The batch nature of the production process requires frequent clean out of equipment.

The capability for batch production seems necessary and likely to continue in plants which compete globally in this industry; and the total number of clean outs are not likely to be reduced. OSHA concludes that feasible controls are available to minimize exposures to cadmium during pigment manufacturing. These would include ventilation systems, enclosures, and housekeeping measures. The industry appears to have implemented some controls already, although further improvements should be possible based upon the PACE report analysis.

Technologically feasible limits for a SECAL. In order to determine appropriate limits for this industry segment, occupation/process exposures were separated into high and low categories (see section B for a more complete discussion of this approach). In general, high exposure occupations/processes had average exposure readings above 100 $\mu g/m^3$; the low exposure group had average exposures at or below 50 $\mu g/m^3$.

Separated data indicate that the high exposure processes include calcining, crushing, milling, and blending operations (with a total of 60 exposed employees) while low exposure occupations/processes include wet system, attack, and strike activities, maintenance and supervision (about 40 employees exposed). Figure VIII-C12 graphically shows the separated data.

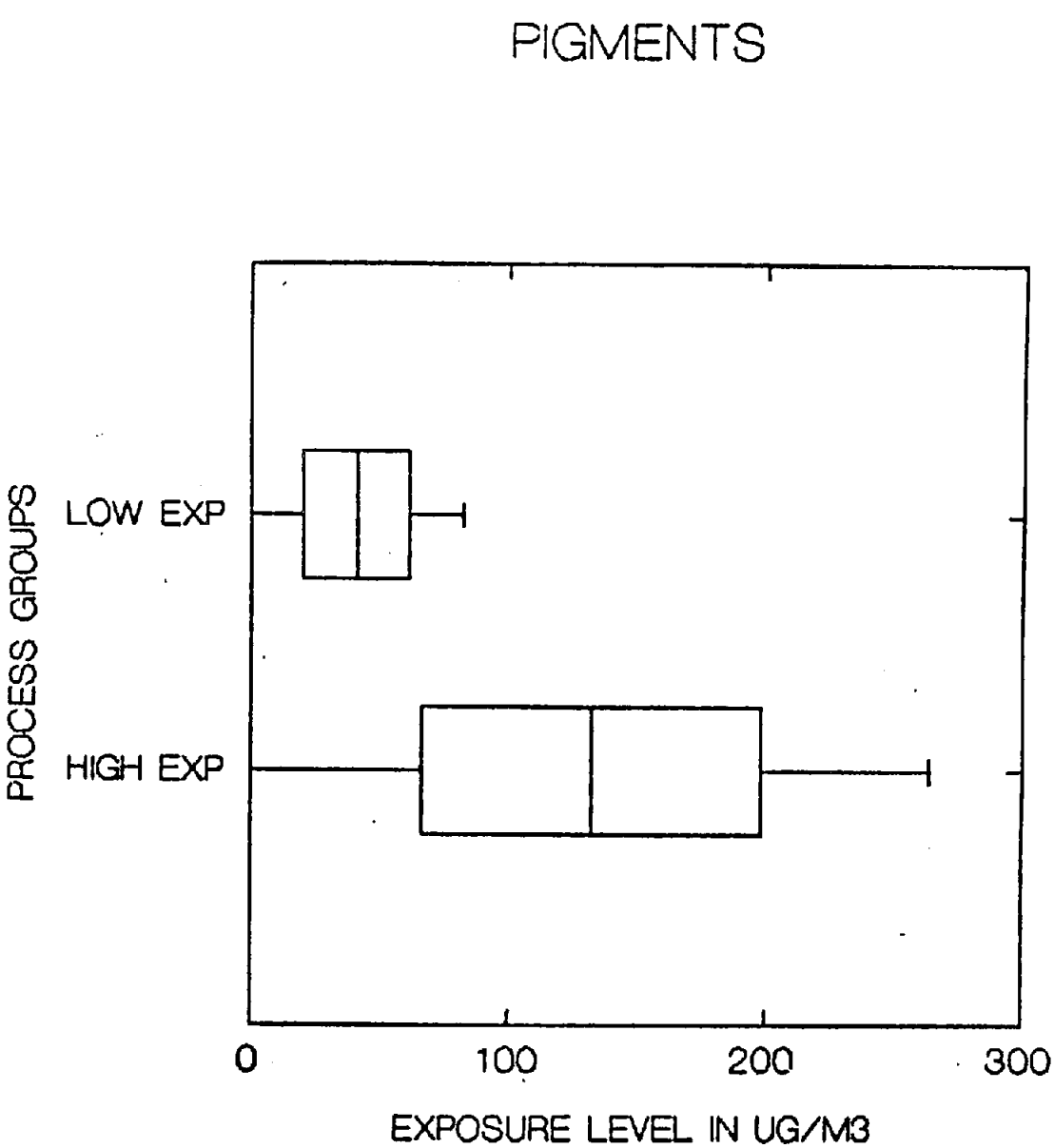
Mean exposure data for the two sets were as follows:

	High group	Low group
Number of observations	13	12
Mean	129.6	23.4
Standard deviation	100.3	23.1

To verify that the two groups within this industry were distinct, a *t* test was performed on the difference in the means. The null hypothesis that the means of the exposure data were equal, was rejected and the conclusion that they were drawn from separate statistical distribution, was accepted

BILLING CODE 4510-26-M

FIGURE VIII-C12



After the statistical difference between high and low exposure groups was verified, the data were analyzed separately. Separate process mean exposure values were drawn from each available data source. All exposure values in each set were "fitted" to a straight line using ordinary lease square formula. The result is shown in Figures VIII–C13 and VIII–C14.

A model was developed in order to identify the appropriate SECAL level for each exposure group. Current exposures for each group were reduced based upon alternative engineering control efficiency levels of 80, 60, 40, and 20 percent. The higher the efficiency level, the lower the projected exposure level and the closer it came to the vertical axis. Figures VIII–C15 and VIII–C16 show the reductions and shift in the distribution of exposures for the high and low groups in pigments manufacture.

The selection of an appropriate efficiency reduction factor was based on assessments of the anticipated ability to control cadmium exposures in this industry as provided by JACA, PACE, and industry sources. JACA projected that a reduction in exposure levels of 90–95 percent was achievable through additional ventilation and improvements in housekeeping and work practices [2, p. 4–12]. According to PACE, 80 percent reductions in exposure levels would be achievable but would require major capital expenditures and new production systems which were considered infeasible by industry sources. The economic feasibility of the control strategy was an important consideration in this sector since total sector profits were only $1.5 million.

BILLING CODE 4510-26-M

FIGURE VIII-C13

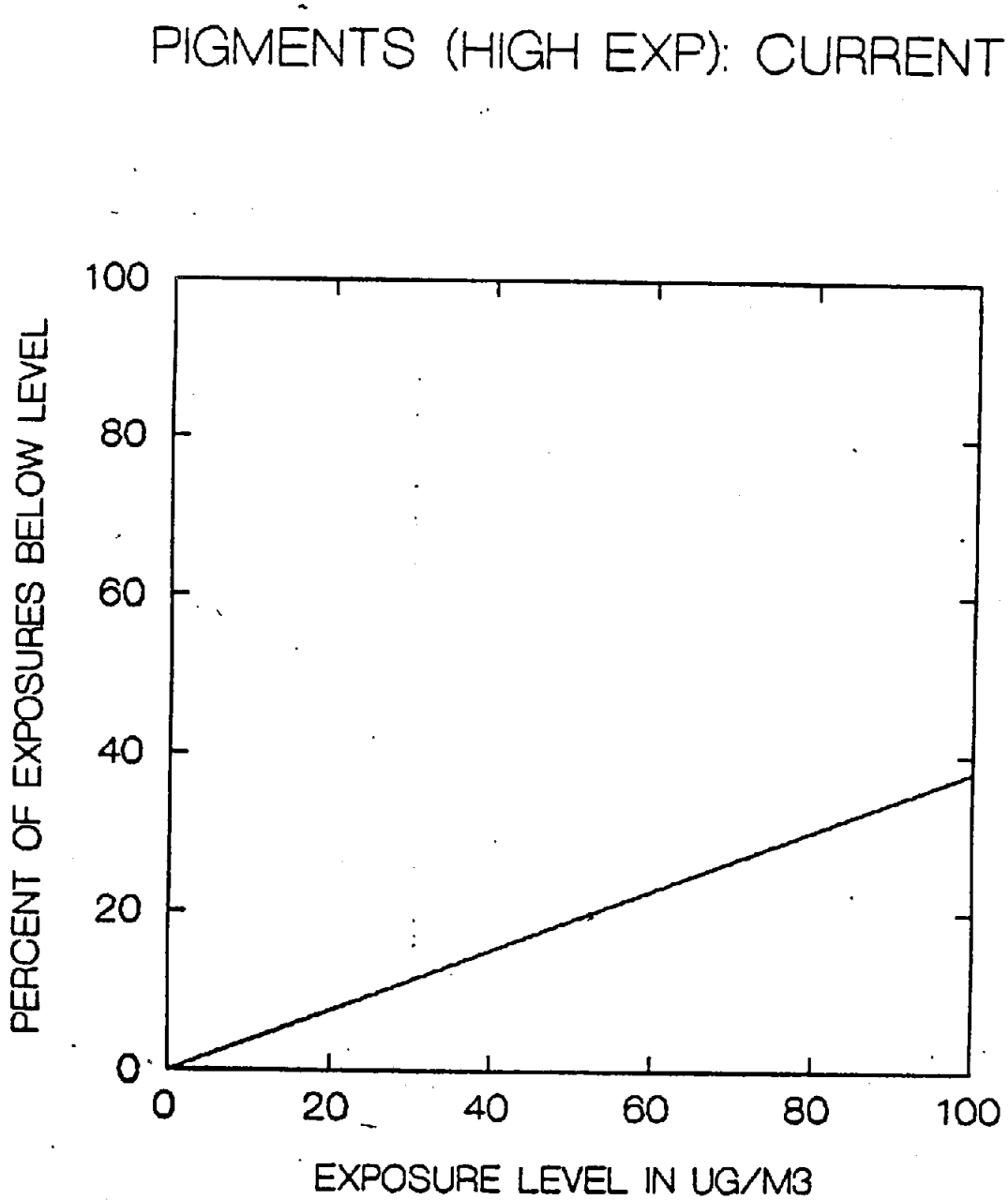


FIGURE VIII-C14

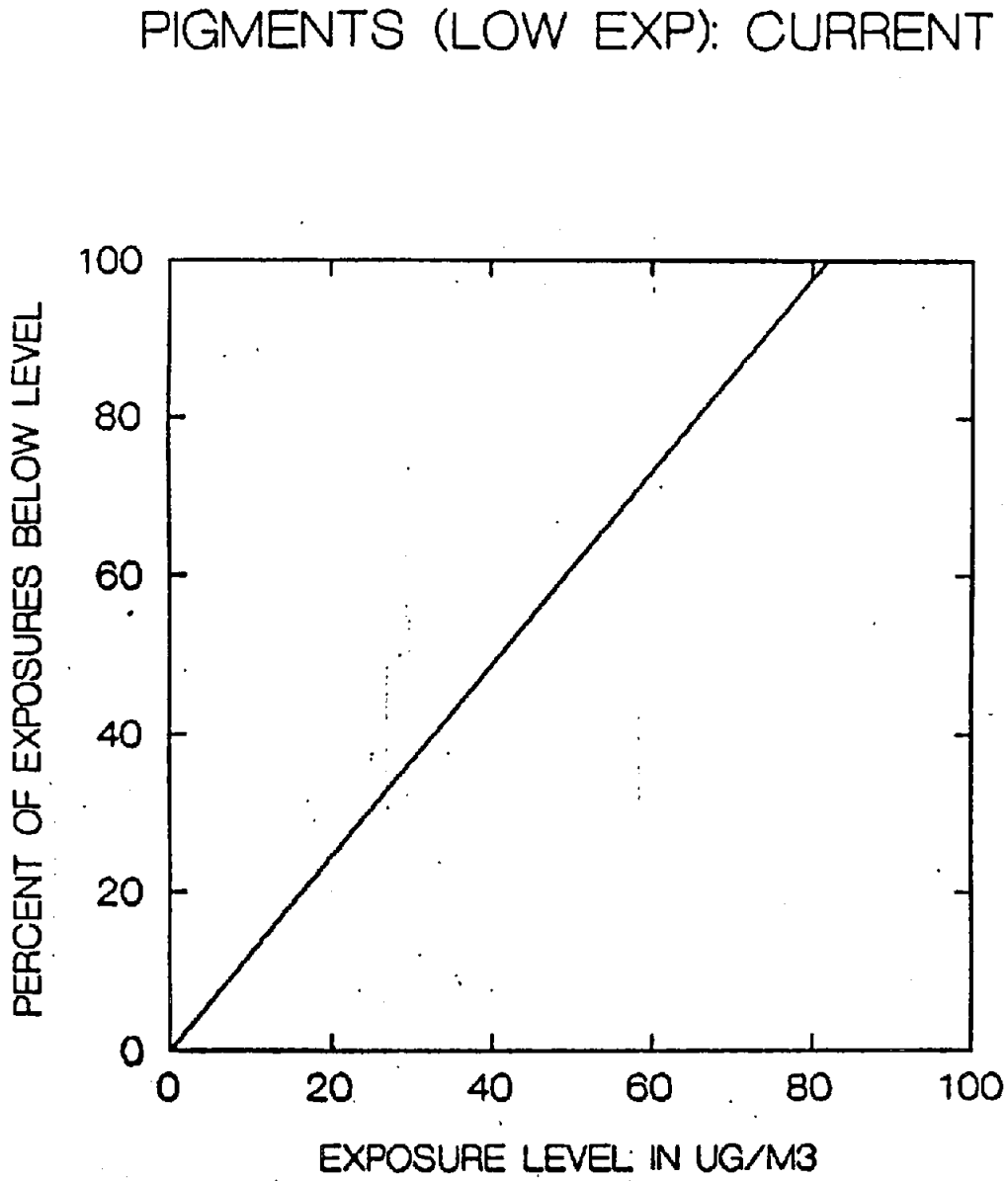


FIGURE VIII-C15

PIGMENTS (HIGH EXP.): CONTROLLED 80%-20%

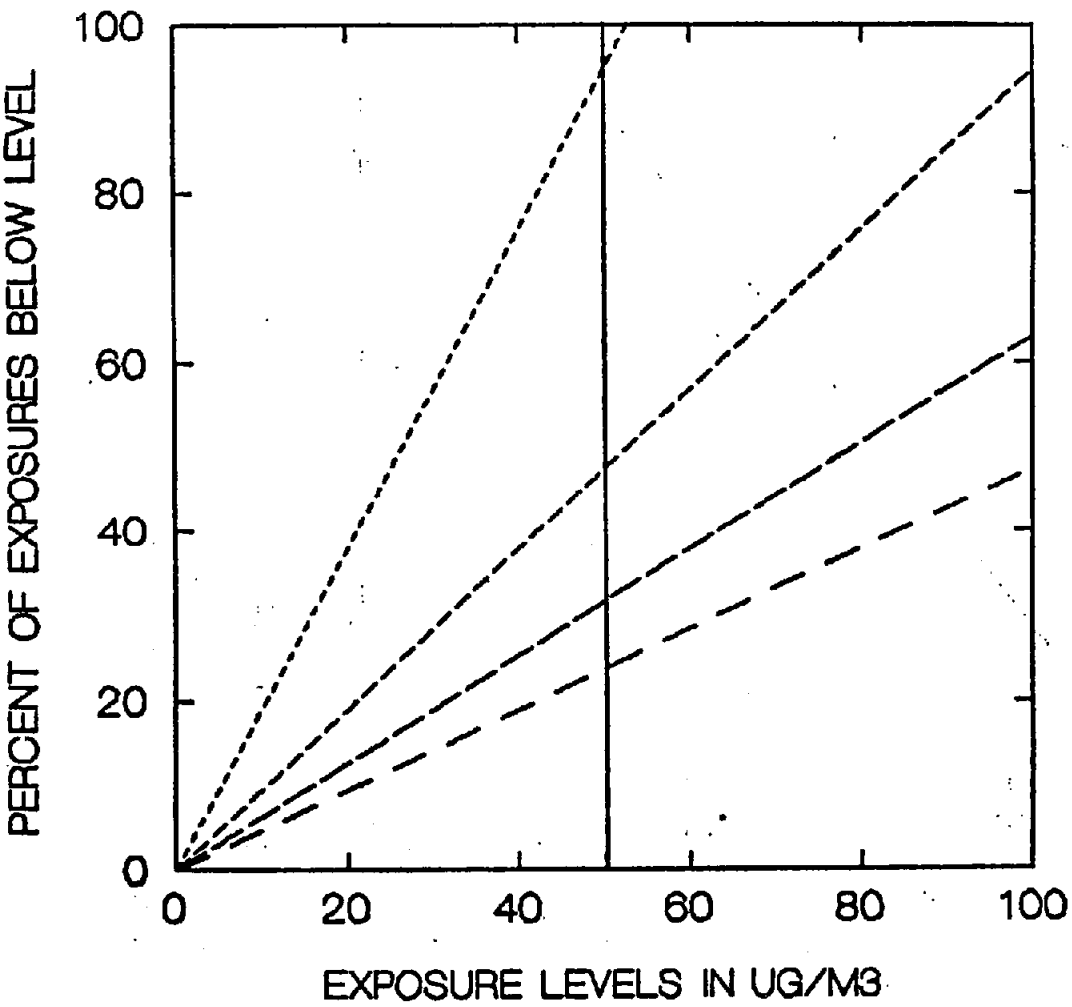
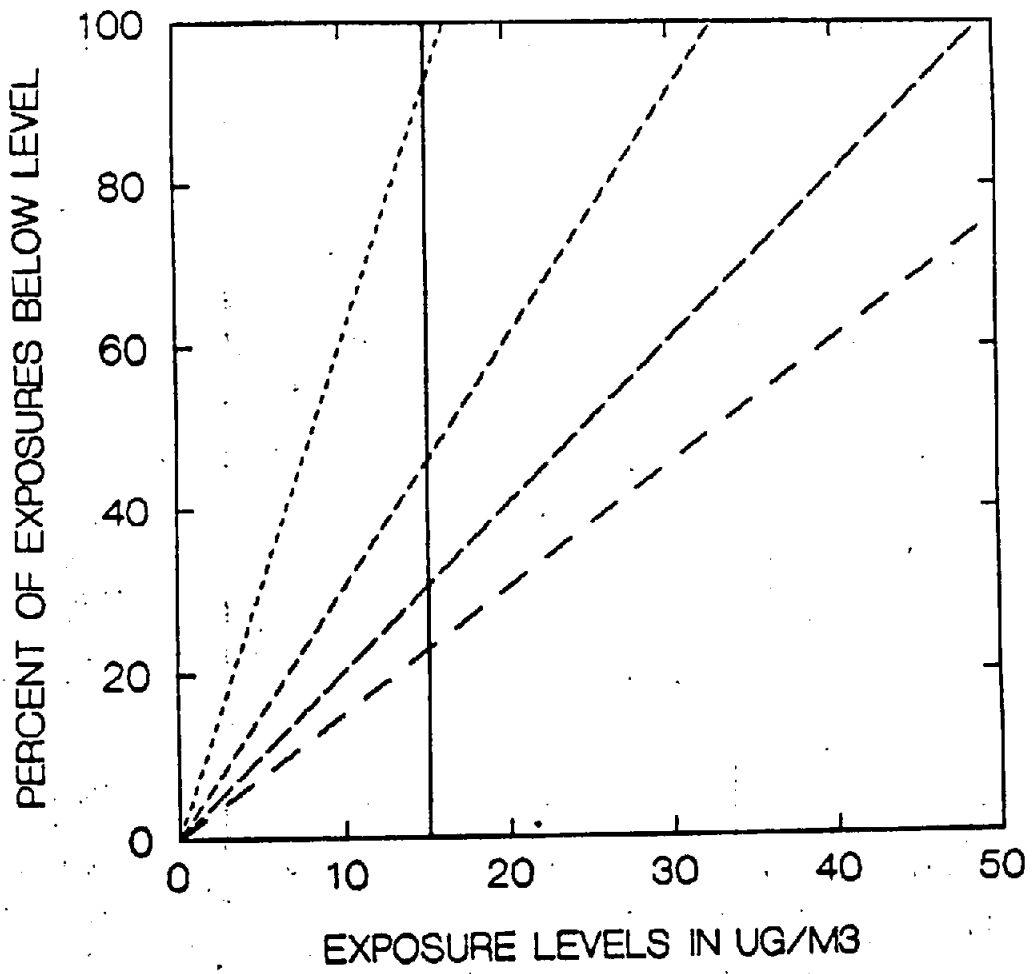


FIGURE VIII-C16

PIGMENTS (LOW EXP.) CONTROLLED 80%-20%



BILLING CODE 4510-26-C

In the final analysis it was determined that feasibility constraints may prevent establishments in this sector from achieving an exposure reduction level of over 80 percent. A reduction factor range of 60–80 percent was selected based on the expected effectiveness of the additional engineering controls that can be implemented in these establishments. OSHA believes this reduction range is both technologically and economically feasible for this industry.

Following selection of the efficiency factor range, the appropriate SECALs for each exposure group were identified at the level achievable for about 60–80 percent of the exposure observations. For the high exposure operations a SECAL of 50 $\mu g/m^3$ was identified, and for the low exposure operations a SECAL of 15 $\mu g/m^3$ was identified.

The cadmium standard authorizes supplemental reliance on respirators after all feasible engineering controls have been implemented. When exposure levels are not sufficiently reduced through engineering controls alone, compliance with the standard can be achieved in this industry through the use of respiratory protection.

Costs of compliance with 50–15 $\mu g/m^3$ SECALs and 5 $^m g/m^3$ PEL. The costs of compliance include costs for additional engineering controls, increased respirator use, more comprehensive exposure monitoring programs, medical surveillance requirements, hygiene provisions, and training and recordkeeping requirements. The estimated compliance costs represent the incremental costs necessary for achieving compliance with the final rule from a baseline of current practices; these costs do not include current or past expenditures.

JACA provided estimates of the costs of installing new or improved local exhaust ventilation systems. In current dollars, the costs of these systems range from $51,000 to $112,000. [2, Table 6–1]. Annual operating and maintenance costs were estimated to be 10 percent of the capital cost. JACA projected that new or improved ventilation systems could be installed at four work stations per plant.

PACE provided cost estimates for several types of controls in its analysis of the cadmium production industry [3]. Controls for the attack tanks included enclosure and back-draft exhaust ventilation, with a capital cost of about $30,000 and an annual cost of about $1,500. Controls at the strike tanks included improved ventilation and increased wash down of surfaces to prevent contaminant accumulation; the capital cost would be $25,000 and the annual cost would be $4,000. Controls suggested by PACE for other operations would require building modifications and the establishment of dedicated production lines. OSHA does not require major capital expenditure for plants in this industry based on economic feasibility considerations.

Details of an exposure reduction program recently completed was submitted to the record by one pigment manufacturing plant [4, section D–2]. The program included an improved ventilation system with additional local ventilation systems in three areas, two central vacuum systems, new pneumatic transfer systems, two steam-heated make-up air units, replacement of six mechanical scales with six digital scales, new larger blenders, portable wet vacuum units, and a complete upgrade of the electrical system.

The project involved $1.1 million in capital costs and about $140,000 in annual costs for maintenance and power. It appears, however, that these costs were not entirely dedicated to hazard reduction. Part of this cost involved the purchase of new and more efficient equipment which should not be attributed to compliance costs. Adjustment for this factor would result in cost estimates consistent with those from JACA and PACE. (JACA's total costs of compliance were lower because fewer controls were recommended; PACE's total costs were higher due to large costs for dedicated lines and building modifications.)

The other three plants in the industry appear not to have implemented extensive exposure control programs. These plants would be required to install additional engineering controls but would not be required to redesign production systems or invest in new buildings.

Pigment manufacturers emphasized that each plant was different and required different control solutions. OSHA recognizes that each plant would develop engineering controls based on individual circumstances and that the combination of controls appropriate at one plant may differ from that at another. OSHA assumes that the costs of the controls identified below would approximate the actual costs for the industry.

The combined work force at the four plants is about 100 workers. Most of these workers would probably need respiratory protection to meet the PEL of 5 $\mu g/m^3$ regardless of the number of controls installed.

Table VIII–C24 presents the estimated numbers of additional controls that plants may need to implement, the unit costs of the controls, and the total cost of engineering controls for the industry. OSHA estimates that on average each plant would install three new local exhaust ventilation systems, provide enclosures for three operations, and install one additional central vacuum cleaning system, or use a different combination of controls with an equivalent cost. The total annualized cost of additional engineering controls for the industry is estimated to be $312,000.

In addition to engineering controls, compliance with the revised standard would require respirator use, exposure monitoring, medical surveillance, hygiene facilities, information and training programs, and recordkeeping. The pigment manufacturing industry generally already provides extensive programs in these areas, but the revised standard may require some of these programs to be expanded. The estimated costs of compliance represent the incremental expenditure necessary to meet the requirements and do not include costs of current programs.

Testimony from the industry indicated that companies currently provide medical exams for every employee annually or every two years, conduct biological monitoring and exposure monitoring annually or more frequently and that some respirator use occurs among the entire workforce [5].

TABLE VIII–C24.—ESTIMATED COSTS OF ADDITIONAL CONTROLS IN THE PIGMENT MANUFACTURING INDUSTRY

Type of control	Controls per plant	Total industry controls	Cost per control [$thousands]			Industry costs [$thousands]				Total annualized industry cost [$thousands]
			Capital	Annual power and maintenance	Annual labor	Capital	Annualized capital	Annual power and maintenance	Annual labor	
Local Exhaust Ventilation	3	12	80	8	0	960	156	96	0	252
Central Vacuum Systems	1	4	15	1	7	60	10	4	28	42
Enclosure	3	12	9	0	0	108	18	0	0	18
Total		28				1,128	184	100	28	312

[1] Based on four plants needing additional controls.
Note: Totals may not add due to rounding.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

For purposes of calculating the costs of compliance for the industry, OSHA estimates that 80 percent of the 100 exposed employees would have to wear a respirator, and that about half of this respirator use is currently occurring. Thus, additional respiratory protection would be needed for about 40 employees. With an average annual cost per employee of $300 for providing a respirator, HEPA filter changes, and a fit test, the annual cost for the industry would be $12,000.

The revised standard requires exposure monitoring semi-annually for "each shift for each job classification in each work area." On average, six job categories over three shifts in four plants would require 144 samples to be taken annually in the industry. If one quarter of this sampling is already done, the laboratory cost of analyzing each sample is $40, and the average cost per plant to perform the sampling is $1,500 annually, then the additional annual cost to the industry for this provision would be about $10,300.

Compliance with the medical surveillance provisions of the revised standard appears to be partially met by pigment producers [5]. However, OSHA believes that some employees may not be provided with all of the required exams and tests. More frequent exams and tests are required for employees under certain conditions and for employees who may be medically removed.

Expanding the medical surveillance programs in this industry to meet the requirements of the revised standard may involve 30 additional physicals annually and an additional 100 of each of the three biological monitoring tests. Physicals are estimated to cost $250 each, lab analysis for a β_2-microglobulin sample is estimated to cost $80, lab analyses for cadmium in blood and urine are estimated to cost $60 each, and the cost of collecting biological monitoring samples is estimated to be $5 per sample. Incremental costs for medical exams and testing for the industry are thus estimated to be $29,000 annually (30 * $250 + 100 * $215).

Requirements for medical removal may involve compliance costs in addition to those for more frequent medical exams and monitoring estimated above. The criteria for mandatory removal would affect employees with the most extreme biological monitoring levels. The criteria for removal also allow for considerable physician's discretion. An estimated 6 percent of the exposed workforce may be removed initially on the basis of these criteria and the discretion of physicians.

Compliance with the new PEL for cadmium and other requirements of the final cadmium standard should prevent a continuing need to remove employees. The number of employees with relatively high past exposures who would be more likely to be removed should decline through attrition. However, as the criteria for removal become broader in future years (lower levels of cadmium in blood and urine triggering mandatory removal), additional employees may be subject to removal. The costs associated with the medical removal provisions are approximated by assuming that on average, 6 percent of the exposed workforce may be removed every 5 years.

The number of employees removed should be small enough to enable establishments to provide removed employees with alternative positions. Costs to the employer would include paying possible wage subsidies to removed workers, and hiring and training new employees. The average cost per removed employee would be an estimated $5,000. An estimated 6 employees may be removed every five years on average in the cadmium pigment industry, and the average annual cost for the industry would be $6,000.

The total annual cost for the medical surveillance and medical removal provisions is thus an estimated $35,000.

Achieving compliance with the hygiene provisions of the revised standard may involve additional costs at some establishments. PACE estimated that the necessary expansion of showering facilities would cost about $90,000 per establishment, which is an annualized cost of about $14,650. In addition, the estimated annual cost per employee associated with showering is $900 and would apply to an estimated 50 additional employees. The total annual industry cost associated with the hygiene provisions is thus estimated to be $103,600.

Incremental costs for recordkeeping are estimated to be about $5 per employee annually. Up to 100 employees may be affected by these requirements which would result in an annual compliance cost of about $500. The training requirements and other information-related requirements are not expected to involve additional compliance costs.

The total annualized costs of compliance with the cadmium standard for this industry are estimated to be $473,400. These costs are summarized by provision in Table VIII–C25.

Economic feasibility of 50–15 $\mu g/m^3$ SECALs and 5 $\mu g/m^3$ PEL. The economic feasibility of the revised cadmium standard for the cadmium pigments industry was analyzed on the basis of the technological feasibility analysis and the projected costs of compliance presented above. The batch production process used to manufacture cadmium pigments limits the applicability of some types of engineering controls. The use of respirators is authorized by the final rule where engineering controls have been implemented to the extent feasible and worker exposures remain above 5 $\mu g/m^3$.

The determination of economic feasibility is based on an analysis of the financial and economic impacts of compliance with the revised cadmium standard. The main focus involves impacts on prices and profitability, including an assessment of the elasticity of demand for the industry's product. In addition, consideration is given to effects on competition, employment, capital requirements, industry output, and international trade.

The most important determinant of a regulated industry's pricing flexibility is demand elasticity. The extent to which regulated firms can pass through compliance costs to their customers by increasing prices depends largely on the elasticity of demand. Compliance costs that cannot be recovered through price increases would have to be absorbed from profits. A relatively inelastic demand increases the ability of producers to increase prices without losing sales.

TABLE VIII–C25.—ESTIMATED COSTS OF COMPLIANCE WITH THE REVISED CADMIUM STANDARD FOR THE PIGMENT PRODUCTION INDUSTRY

Provision	Annualized cost [$thousands]
Exposure control	312.0
Respirator use	12.0
Exposure monitoring	10.3
Medical surveillance	35.0
Hygiene facilities/practices	103.6
Recordkeeping and information	0.5
Total	473.4

Note: Costs do not include current expenditures.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

Factors that influence demand elasticity include the availability of substitutes for the product, the importance of the product in customers' budgets, the degree of technological or contractual dependence of customers, and the importance of price versus non-price attributes of the product.

The typical U.S. cadmium pigment producer earns about $7.5 million in revenues annually [8, p. 4–7]. Profits are estimated to be about 5 percent of revenues [2, p. 7–8], or $375,000 annually. According to industry sources, "U.S. producers utilize facilities with similar processes and scale economies so that compliance with the standard is not likely to result in differences in costs among U.S. producers." [8, p. 4–7].

In order to evaluate the potential impact of compliance with the revised cadmium standard, the maximum effect on prices and profits was determined. Under conditions of inelastic demand, compliance costs could be passed on to customers through higher prices. A price increase of less than 1.6 percent would be sufficient to fully offset the compliance costs. If none of the compliance costs could be recovered by raising prices, then the costs would result in a reduction of profits of 31 percent. The actual result would probably involve a combination of a small rise in prices and a reduction in profits.

The overall demand for cadmium pigments appears to be relatively inelastic due to their superior coloring features and chemical properties. Cadmium pigments inhibit aging, prevent embrittlement, resist migration and interaction with other chemicals, and withstand processing temperatures of up to 600 degrees Celsius. The sum of these properties allows cadmium pigments to be used for coloring all types of plastics and is unattainable by any other class of colorants.

Cadmium pigments are also more expensive than other types of pigments. In some applications, such as the production of low-density polyethylene, the properties of cadmium pigments are not required and less expensive substitutes can be used. Environmental regulations in the U.S. and abroad have also provided incentives to substitute away from cadmium pigments. Where their unique properties are not essential, the use of cadmium pigments has been declining.

The plastics industry is currently the main consumer of cadmium pigments, using about 80 to 90 percent of total consumption. Other applications can be found in the paints, ceramics, and enamel industries. On the whole, the limits of substitution appear to have been reached [4, Part D4, p. 1]. Growth in the overall demand for cadmium pigments should be limited to those applications requiring their use. The total demand is likely to remain relatively inelastic under current technological conditions.

Pigments account for only small percentage of the cost of final products. For example, only about 1.5 percent of plastic by weight is attributable to cadmium pigments. Since plastic resins are relatively expensive, the cost of cadmium pigments contained in the resins amounts to less than 1 percent of the cost of the final product.

Although the total demand for the industry is inelastic on a global scale, the demand for the product of individual firm or a subset of firms would be more elastic due to competitive forces of the market. Since the revised rule affects all firms in the U.S., the total demand for these firms should be evaluated in the context of the presence of foreign competition.

Currently each domestic producer has a market share of over 15 percent [8, p. 2–21]. (A major U.S. production facility producing 5.5 million pounds per year recently closed, allowing competitors to increase market shares and revenues [ibid.].) Industry sources indicate that imports account for 20 to 30 percent of the U.S. market. The imported pigments reportedly sell for 15 to 30 percent less than domestically produced pigments [8, p. 4–7], signifying that domestic producers are able to maintain sales volumes through some form of product differentiation possibly involving customer service or product quality control. It is not clear whether the higher prices are associated with less efficient production systems, higher production costs, or larger profit margins.

The costs of compliance with the cadmium standard would increase production costs for U.S. producers. However, the magnitude of these costs are not likely to cause a significant impact on the domestic industry because of the relatively small changes in prices and profits that would result. These changes would be overshadowed by more fundamental and substantial developments in the industry, including price changes of raw materials and labor, restrictive environmental regulations in the U.S. and other countries, and changes in demand.

Compliance with the revised cadmium standard is considered to be economically feasible for the pigment manufacturing industry. One U.S. plant recently completed an exposure reduction project which involved over $1 million in capital costs. (The annualized cost is estimated to be about $320,000 [4, section D–2].) This investment indicates an expectation of profitability and a willingness to remain in the industry despite increased production costs.

Notes

1. Exhibit 19–40, Dry Color Manufacturers' Association, Comments "Re: Occupational Exposure to Cadmium," May 11, 1990.
2. Exhibit 13, "Economic Impact Analysis of the Proposed Revision to the Cadmium Standard," Final Report, JACA Corporation, March 15, 1988.
3. Exhibit 19–43, Attachment L, "Feasibility and Cost Study of Engineering Controls for Cadmium Exposure Standard," PACE Incorporated, April 30, 1990.
4. Exhibit 112, "Post-Hearing Documentary Evidence Submission by SCM Chemicals, Inc.", Cleary, Gottlieb, Steen, & Hamilton, September 18, 1990.
5. Hearing Transcript, p. 5–55, p. 5–56, p. 5–158, p. 5–214, p. 5–221; June 11, 1990.

6. Exhibit 106, Attachments.
7. Exhibit 112, Attachment E.
8. Exhibit 19-43, Attachment I, "Economic and Technological Feasibility of a 5 Microgram per Cubic Meter Workplace Standard for Airborne Cadmium," Putnam, Hayes, & Bartlett, Inc., April 30, 1990.

Stabilizer Production

Industry overview. Cadmium stabilizers are used primarily in the production of polyvinyl chloride (PVC). The stabilizers are available in solid and liquid forms and are added to plastic resins to provide heat stability and protection from ultraviolet light. The cadmium content of the stabilizers can range from 1 to 15 percent by weight, and the stabilizers constitute from 0.5 to 2.5 percent of the final PVC compound [1, p. 2-18].

Cadmium stabilizers are currently supplied by four companies operating five plants in the United States [2, Attachment I, p. 3; and 1, p. 4-6], and employing 200 workers with cadmium exposure. The scale of production is similar in the five plants. Three of the four manufacturers are large and diverse chemical companies, and cadmium stabilizers represent a "very small percentage" of their total revenues. The consumption of cadmium in this industry has remained fairly constant since 1978, ranging from about 500 to 650 metric tons per year [1, p. 2-18 and 4-6].

Production processes. The production of cadmium stabilizers involves several steps. The first step is referred to as the reaction step. Cadmium oxide is added to a reaction vessel with one or more organic acids. Other compounds may be added depending on the specific product chemistry desired.

For powdered stabilizers, the reaction step is followed by drying, flaking, and regrinding. Liquid stabilizers are filtered and pumped to blending tanks. Both types of stabilizers may be blended with other substances before being packaged in bulk containers [3, p. 8-1].

Employee exposures. The exposure profile in the preliminary analysis was based on research conducted by JACA Corporation, using data from seven years of sampling results in OSHA's IMIS data base [4, Tables 3-4 and 3-5]. JACA developed separate exposure profiles for workers in the dry and wet processes and these are presented in Table VIII-C26. In the dry process, production workers have estimated mean exposures between 45 $\mu g/m^3$ and 65 $\mu g/m^3$; in the wet process, mean exposures for production workers are less than 50 $\mu g/m^3$. Supervisors and maintenance technicians during both processes are estimated to have mean exposures of less than 5 $\mu g/m^3$, but individual samples can vary widely.

The exposure profile developed by PACE [3, p. 8-2] is presented in Table VIII-C27. Seven job categories are listed for solids production, and six of these have estimated mean exposures over 40 $\mu g/m^3$. The job category listed for liquid production has an estimated mean exposure of 139 $\mu g/m^3$.

One stabilizer manufacturer submitted exposure monitoring data for dry and liquid processes [2, Attachment III]. The samples were collected in cadmium process areas with and without cadmium products running. In addition, the data are disaggregated into categories indicating exposure levels before and after the installation of additional engineering controls, such as improved ventilation and enclosure.

TABLE VIII-C26.—CADMIUM EXPOSURE DATA FOR CADMIUM STABILIZER PRODUCTION BASED ON JACA

Job category	Concentration in $\mu g/m^3$		
	Geometric mean	Median	Range
Dry Process:			
Solution operator	46.2	28.0	22.0-160.0
Dry solids operator	63.0	140.0	1.0-936.0
Process supervisor	1.1	1.1	0.1-7.0
Maintenance technician	3.5	3.0	0.1-1,560.0
Wet process:			
Solution operator	46.2	28.0	22.0-160.0
Maintenance technician	3.5	3.0	0.1-1,560.0

Source: Exhibit 13, JACA, Tables 3-4 and 3-5.

TABLE VIII-C27.—PROFILE OF OCCUPATIONAL EXPOSURES TO CADMIUM IN THE CADMIUM STABILIZER INDUSTRY BASED ON PACE INCORPORATED

Job Category	Geometric mean exposures ($\mu g/m^3$)
Solids Production:	
Cadmium oxide charging	126
Flaker discharge	10
Crusher	45
Grinder	85
Rotary dryer	224
Tote bin unloader	91
Blender and packager	214
Liquid Production:	
Cadmium oxide charging	139

Source: PACE Incorporated, Exhibit 19-43, Attachment L, Table A8-1.

TABLE VIII–C28.—CADMIUM EXPOSURE DATA FOR CADMIUM STABILIZER PRODUCTION BASED ON COMPANY DATA

Job category	Geometric mean concentrations in $\mu g/m^3$		
	Before controls	After controls	Without cadmium in process
Dry process operator	174.8		2.9
Dry process blending		38.6	7.0
Liquid process	117.4	24.4	1.2

Source: Exhibit 19–46, Attachment III, Synthetic Products Company.

Table VIII–C28 summarizes the data submitted. Mean exposure levels during both types of processes involving cadmium stabilizers are less than 40 $\mu g/m^3$ after upgrading controls. Mean exposure levels when cadmium products are not running are 7 $\mu g/m^3$ or less for the dry process and under 2 $\mu g/m^3$ for the liquid process.

Employee exposures during the production of cadmium stabilizers are generally associated with specific tasks which occur intermittently. The dry process involves batch production; on average exposures to cadmium occur one week per month. Potential exposures during the liquid process are more limited and occur about two hours per week per shift [2, Appendix I, p. 4].

Existing and feasible additional controls. OSHA's preliminary analysis, based on the JACA report [4], described existing controls at the blender and packaging areas of the dry process consisting of local exhaust ventilation hoods connected to a baghouse. Solution operators in the wet process had no controls.

For dry process stabilizer production, JACA recommended the installation of an additional local exhaust ventilation system with a baghouse for dissolver charging operations, and expanded and improved ventilation systems with a new baghouse for the blending and packaging areas. Enclosures and other measures to seal fugitive emissions were recommended for the charging, blending, and packaging areas. Improvements in housekeeping and work practices, including frequent vacuuming or damp mopping, were also recommended for each operation.

For wet process stabilizer production additional controls were recommended for the charging operation. These would include a close-fitting hood at the dissolving vessel connected to a baghouse, as well as improvements in housekeeping and work practices.

PACE Incorporated also provided descriptions of existing and feasible additional controls for both dry and wet process cadmium stabilizer production [3, p. 8–1 through 8–14]. For the dry process, PACE recommended that each reactor in the cadmium oxide charging operation be provided with an automated and enclosed drum-dumping station that would handle and charge the cadmium oxide and then automatically wash, rinse, and dry the empty drums. Existing local exhaust ventilation at this operation would be retained to ventilate the drum dump station and any waste water generated would be handled at existing treatment facilities. PACE noted possible difficulties in applying this technology in this industry and that the projected exposure reductions of over 85 percent "may not be achievable." [3, p. 8–4].

For the flaker operation, PACE recommended improved enclosure at the feed end and a ventilated drum enclosure to control the flaker discharge. Increased attention to housekeeping and work practices were also considered necessary to reduce exposure levels.

According to PACE, exposures could be reduced at the crusher operation by enclosing the feed table and providing backdraft ventilation, sealing fugitive emissions sources, and improving ventilation for the drum enclosure. The grinder operation was considered amenable to total enclosure in a negative pressure area using an additional exhaust ventilation system. Rotary dryer and tote bin unloading operations could be improved by sealing several fugitive emissions sources and by providing enclosures that would make ventilation systems more effective.

Exposure levels during blending and packaging operations could also be reduced. The drum filling station analyzed by PACE was described as "enclosed on three sides and provided with exhaust ventilation." [3, p. 8–9]. The average exposure at this station was estimated to be 214 $\mu g/m^3$, including contributions from other sources.

PACE presented recommendations of additional controls for this operation that included an automated drum dumping station with wash, rinse, and drying facilities, and a "completely revised" drum filling operation. These technologies "have been used successfully in other industries" [3, p. 8–4], are available at reasonable cost, and their implementation appears to be feasible in this industry.

In addition to operation-specific controls, PACE recommended other measures for reducing exposures during solids production. All interior surfaces of the building would be steam cleaned and painted to reduce the presence of residual materials. High-efficiency secondary filtration would be added to the exhaust discharges of all new and existing fabric filters to reduce cadmium emissions to the environment (and possibly intake concentrations). A clean production facility with a good housekeeping program can contribute to keeping exposures low.

One manufacturer submitted comments indicating that existing controls in the wet process include a recently upgraded ventilation system, standardized work practices, and the use of a central vacuum system. The company does "not envision that levels could be reduced much below" current exposure levels (below 25 $\mu g/m^3$) in the wet process. In the dry process the blending and packaging operations have recently been completely redesigned and include improved ventilation systems, screws for transfer of material, enclosed bag compactors, and the use of a central vacuum cleaner. [2, Appendix I, p. 7]. Testimony from a cadmium stabilizer producer indicated that lower exposures can be expected for the dry process operator as a result of further engineering controls [11].

Technological feasibility limit for a SECAL. Following the procedure outlined in section B above, OSHA separated exposures into high and low occupation/process exposure groups to facilitate analysis. Exposure data were divided such that the difference between the mean values for the two separated data sets, was maximized.

Data segregation resulted in the identification of a high occupation/process exposure group which included cadmium oxide charging, drying, crushing and blending operations (job categories in solids and liquids cadmium

stabilizer production). These operations involve about 25 percent of employee exposures, representing about 50 full-time equivalent (FTE) employees. All remaining occupations/processes in this sector, involving about 150 FTE workers, were in the low exposure category. Figure VIII–C17 presents the high and low exposure categories in a "box and whisker" graph.

Mean exposure data for the two sets were as follows:

	High group	Low group
Number of Observations	13	6
Mean	116.3	3.2
Standard Deviation	67.4	2.15

To verify that the two groups within this industry were distinct a *t* text was performed on the difference in the means. Even with the small sample and the large standard deviation for the high group the *t* statistic was 3.7. In this case, there was less than a six percent probability that the *t* statistic would be larger than 2.0 if the means were equal. Therefore, the null hypothesis that the means of the exposure data were equal was rejected, and the conclusion that they were drawn from separate statistical distribution was accepted.

After the statistical difference between high and low exposure groups was verified, the data were analyzed separately. In Figures VIII–C18 and VIII–C19 process mean exposure values were drawn from available data sources. The mean values for each group were "fitted" to a straight line using ordinary least squares methodology. For the high exposed cadmium group over one-half of the mean exposure values are above 100 $\mu g/m^3$ (Figure VIII–C18). All exposures in the low group are below 10 $\mu g/m^3$.

BILLING CODE 4510–26–M

FIGURE VIII-C17

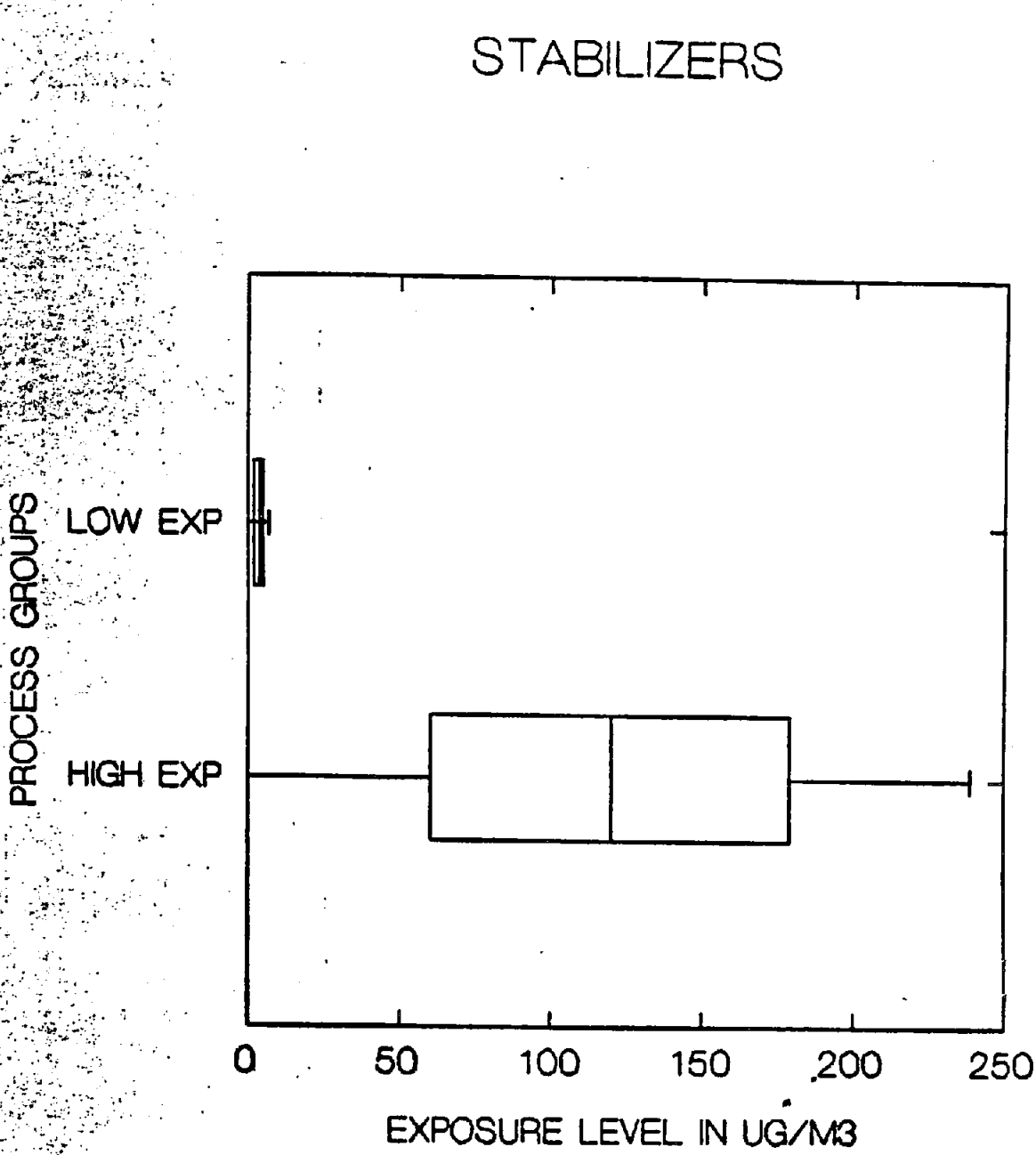


FIGURE VIII-C18

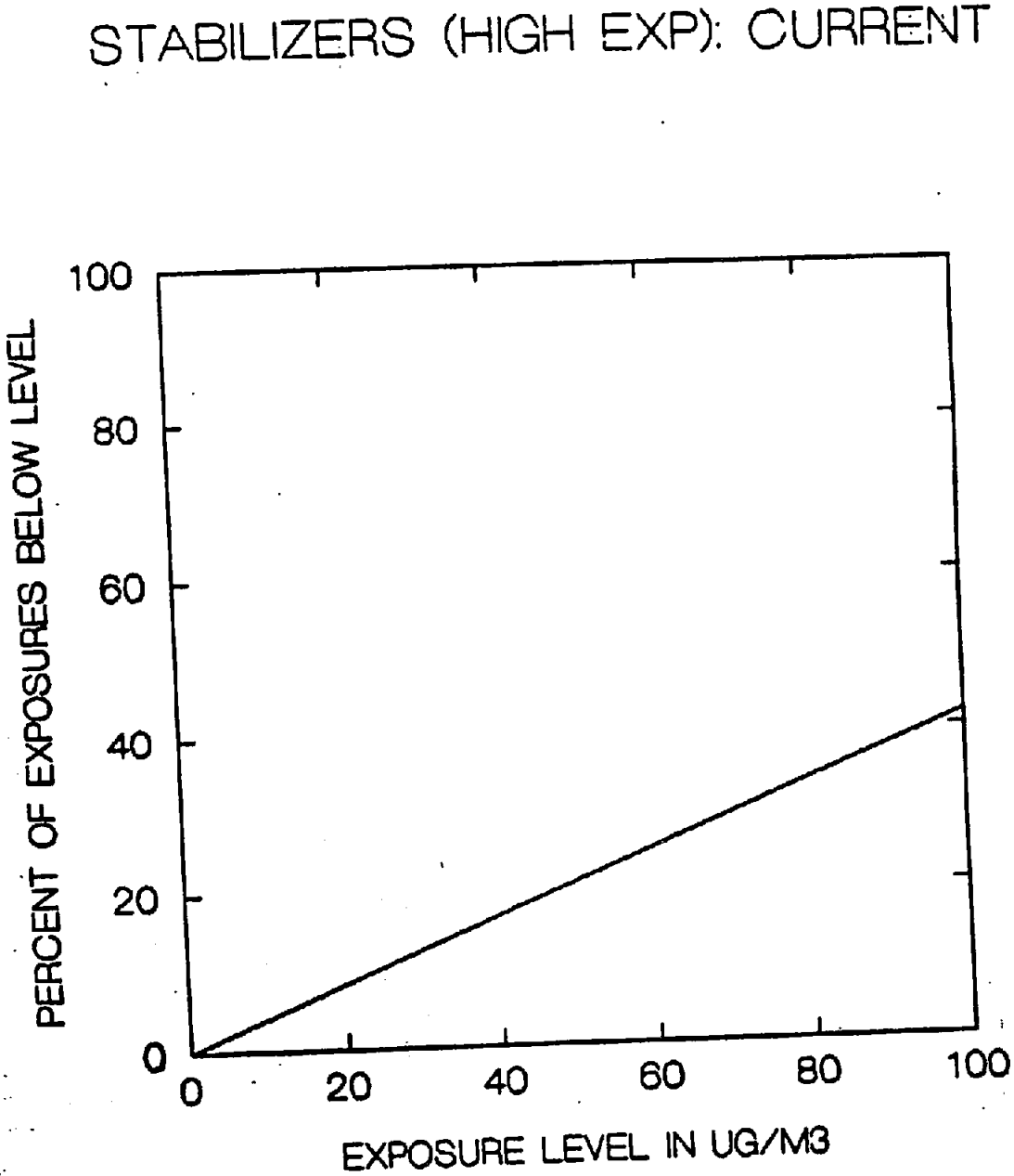
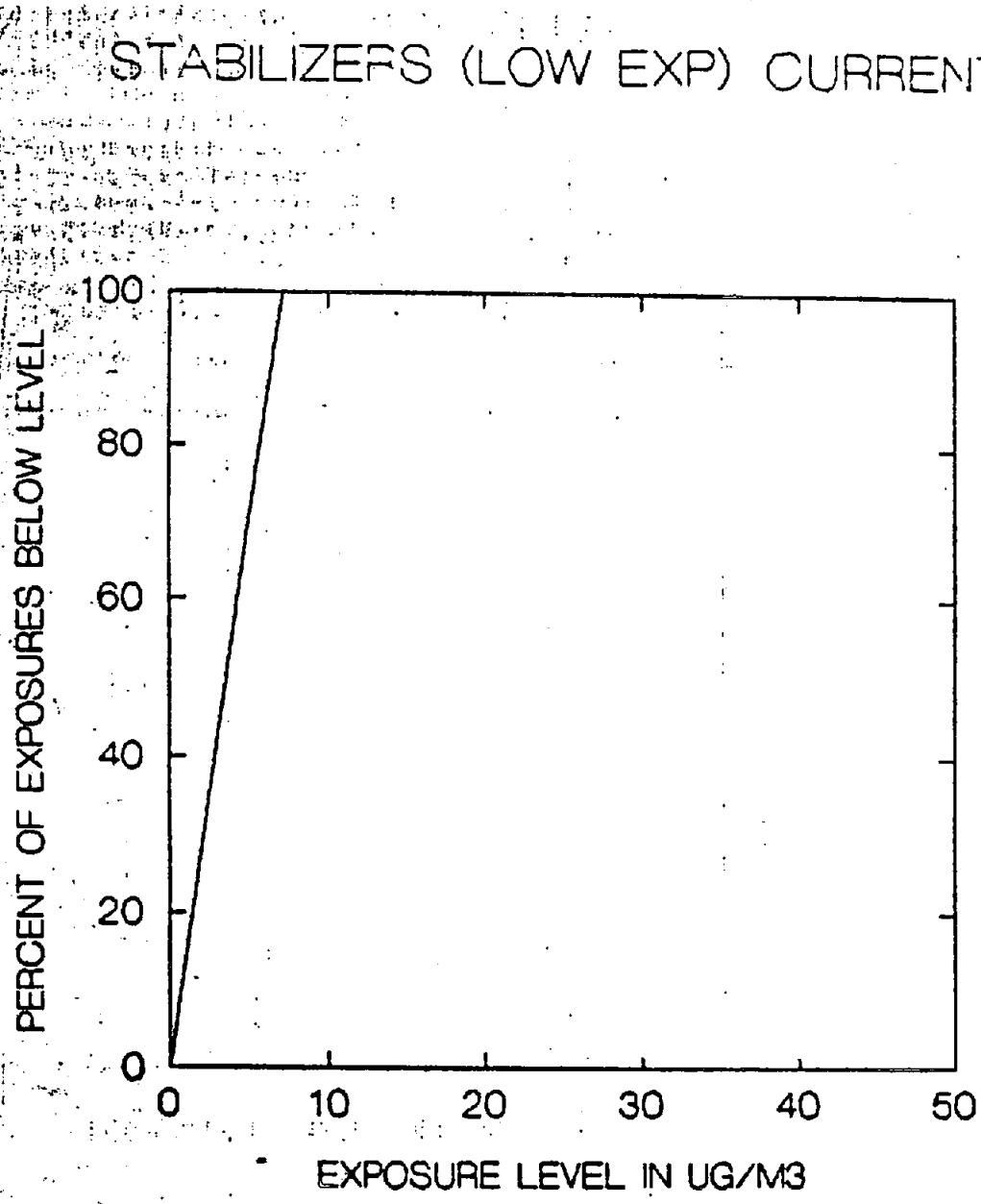


FIGURE VIII-C19



BILLING CODE 4510-26-C

Col

This se
contains
publishe
Rule, a
correctic
the Fec
correctic
docume
docume
issue.

DEPAR

48 CFR

Acquisi

Correct

In rul
on page
Wedne
followi

923.570-

1. On

a. In t
line, "si

b. In t
first line
lowerca

BILLING CI

For each group a model was developed to graphically show the effect on the exposure distribution after current exposures were reduced using alternative engineering control efficiency factors of 80 percent down to 20 percent, in 20 percent increments. The higher the efficiency level, the lower the projected exposure level and the closer the projected exposure line moves to the vertical axis. Figures VIII–C20 and VIII–C21 show the reduction and shift in the distribution of exposures for the high and low groups in stabilizer operations.

The selection of an appropriate engineering control reduction factor was based on evidence and testimony in the record and economic feasibility considerations.

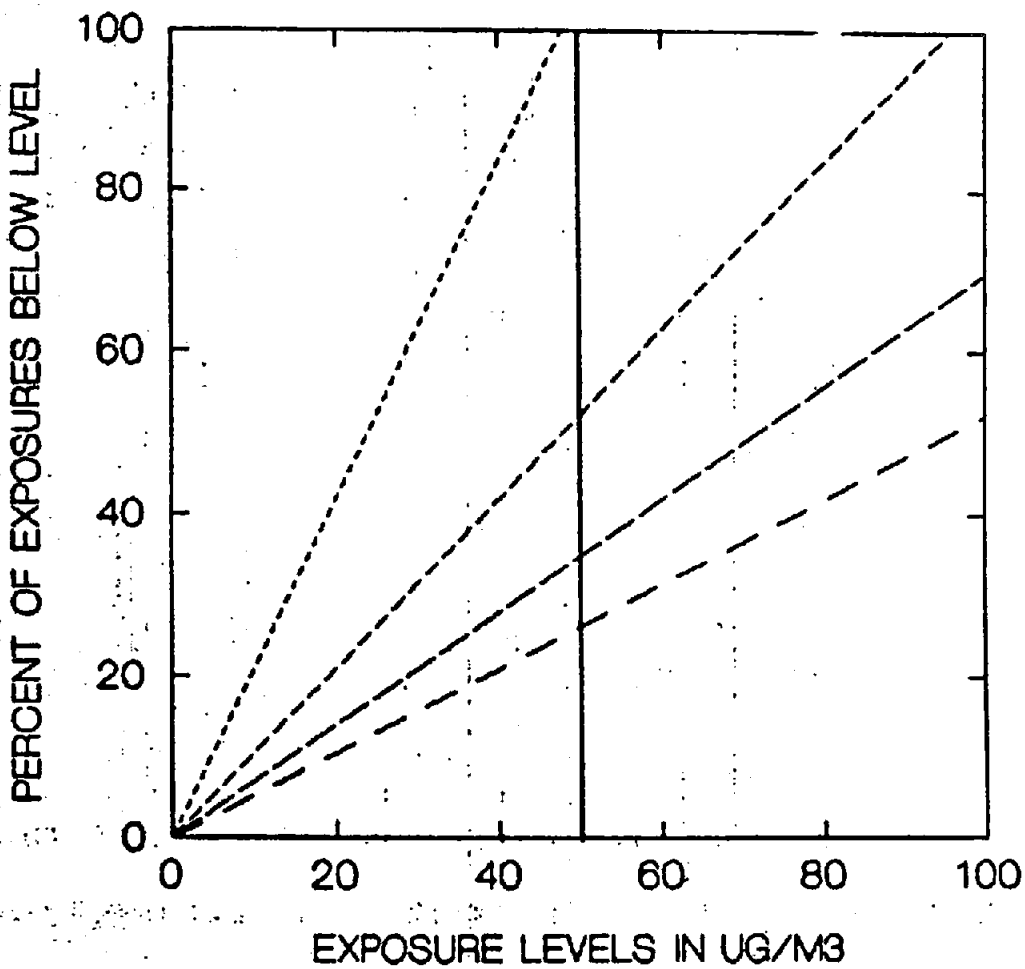
The evidence in the record substantiates the finding that additional feasible controls are available and can be implemented to further reduce exposure levels. The extent of current controls in place and the applicability of specific additional controls will vary depending on the individual plant, but the relevant comments in the record all basically agree that a multitude of control options exists to limit airbo cadmium concentrations. These ar generally conventional technologi are commonly known, readily ava and to some degree currently usec industry, as described above.

Analysis developed by JACA projected exposures of less than m^3 after the implementation of engineering controls in most liqui dry processes [4, pp. 3–13, 3–15, 4

BILLING CODE 45[illegible]

FIGURE VIII-C20

STABILIZERS (HIGH EXP.): CONTROLLED 80%-20%



41974–

Cori

This sect
contains
published
Rule, an
correction
the Fede
correction
document
document
issue.

DEPART

48 CFR I

Acquisit

Correcti

In rule
on page
Wednes
followin

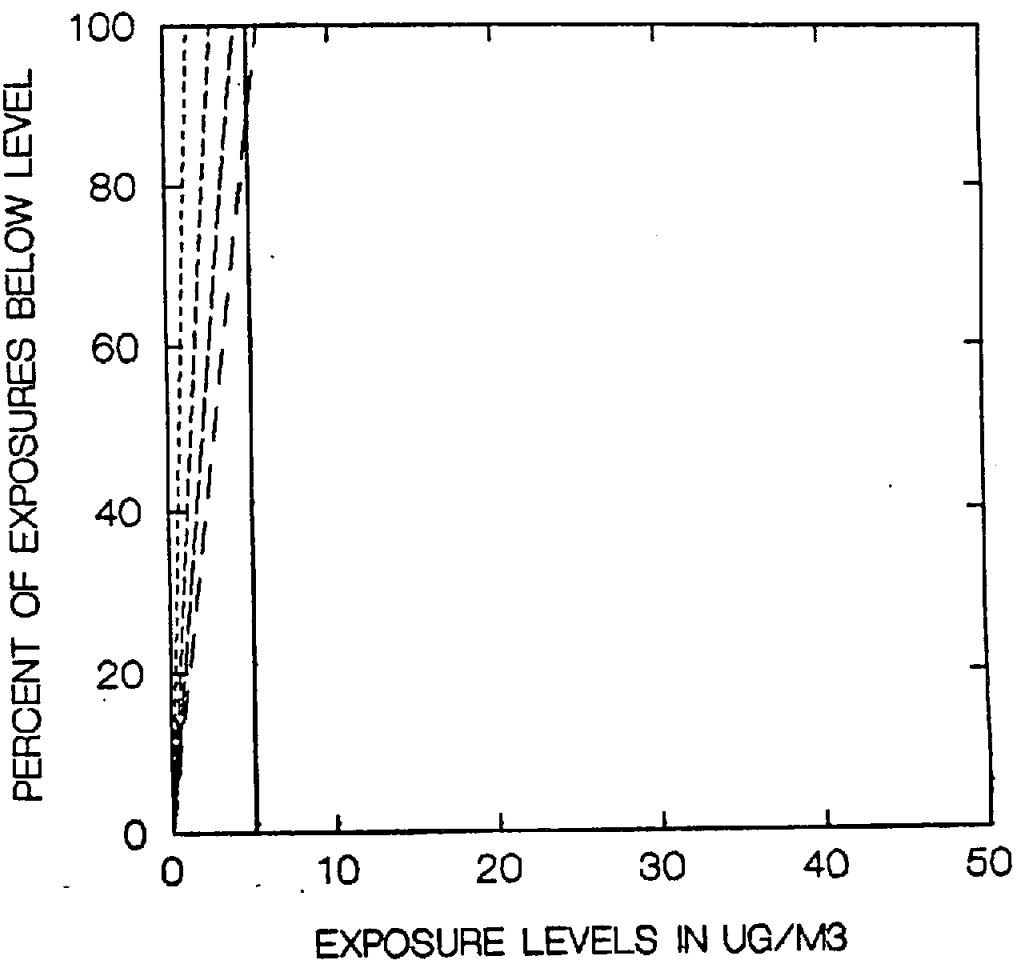
923.570-1

1. On
a. In s
line, "sit
b. In s
first line,
lowercas

BILLING CO

FIGURE VIII-C21

STABILIZERS (LOW EXP.): CONTROLLED 80%-2



VIII-C138

BILLING CODE 4510-26-C

NIOSH stated in their testimony that the production of liquid and solid formulations should be controllable to 5 $\mu g/m^3$ through engineering containment and ventilation [5, p. 10]. NIOSH draws upon decades of industrial hygiene experience and hundreds of exposure control studies in making such evaluations [6], and characterizes stabilizer manufacture as "a typical batch chemical manufacturing process" [5, p. 27]. Mean exposures projected by PACE are 10 $\mu g/m^3$ or less for six out of eight job categories identified [3, p. 8–2].

Air monitoring data recently submitted to the record by a cadmium stabilizer manufacturer using the dry process, show that two of the four samples for blending and packing operations taken while running cadmium products were less than 15 $\mu g/m^3$. The geometric mean of all personal samples taken during blending and packing was less than 14 $\mu g/m^3$, and if two outliers above 99 $\mu g/m^3$ are excluded the mean is less than 9 $\mu g/m^3$ [7, Attachment 3]. Mean exposures when cadmium products are not running are reported to be less than 8 $\mu g/m^3$ in all job categories [2, Attachment III]; these conditions would apply to about 75 percent of the workdays [2, Appendix I, p. 3].

Significant exposures were reported for one operation in the wet process (charging CdO) [7, Attachment 4]. This operation occurs for about two hours per week per shift or for about 5 percent of the total hours for one job category [2, Attachment I, p. 4]. The mean exposure during this periodic operation is less than 25 $\mu g/m^3$; mean exposures at other times and in other operations are less than 2 $\mu g/m^3$ [2, Attachment III].

Based on exposure control information supplied by one stabilizer company, reduction levels of 60–80 percent appear to be technologically feasible. For example, company results for liquid process controls reported in Table VIII–C28 showed a 79.2 percent reduction in cadmium (mean concentrations fell from 117.4 $\mu g/m^3$ to 24.4 $\mu g/m^3$ after controls were introduced).

Based on the evidence in the record, OSHA believes that an engineering control reduction level of 60–80 percent is reasonable for this industry segment and is economically feasible. The cost of engineering controls for this industry (discussed below) do not appear to represent a significant financial burden. Therefore, the engineering control reduction target of 60–80 percent is judged to be economically feasible.

Following the selection of this efficiency factor, the appropriate engineering control level for each exposure group was identified at the point achievable for 60–80 percent of the exposure observations. For the high processes including cadmium oxide charging, drying, crushing and blending operations, a SECAL of 50 $\mu g/m^3$ is identified. For all low exposed processes, OSHA believes that the PEL level of 5 $\mu g/m^3$ is achievable through engineering controls.

For the high exposure group, compliance with the PEL of 5 $\mu g/m^3$ with engineering controls and work practices is infeasible at this time and can only be achieved through the use of respirators. Respirators are readily available with a wide range of protection factors that can adequately protect workers from the potential exposures in this industry. Respiratory protection will be required for some production and maintenance employees full-time.

Costs of compliance with a 50 $\mu g/m^3$ SECAL and 5 $\mu g/m^3$ PEL. Compliance with the revised cadmium rule includes costs for additional engineering controls, increased respirator use, more comprehensive exposure monitoring and medical surveillance programs, hygiene provisions, information and training, and recordkeeping requirements. Estimated compliance costs are measured from a baseline of current practices and do not include current or past expenditures.

JACA estimated that the cost of installing new or improved local exhaust ventilation systems in this industry would range from $51,000 to $112,000. Annual operating and maintenance costs were estimated to be 10 percent of the capital cost. [4, Table 6–1]. JACA also estimated that a typical dry process plant would need to install two such systems and that a typical wet process plant would need to install one such system.

New ventilation systems recommended by PACE for this industry are estimated to cost between $20,000 and $60,000 each, and three such systems are recommended per dry process plant. Improvements in ventilation systems, costing about $10,000 or less, would be needed, on average, at three additional stations. Annual costs associated with ventilation systems are generally about 5 percent of the capital costs. Drum dumping stations are estimated to cost $90,000 each, with annual expenses for power, heat, maintenance, and labor of less than 10 percent of the capital cost. Four such stations were recommended for dry process plants and one was recommended for wet process plants. Enclosures, hoods, valves, and other recommended emission controls generally cost less than $5,000, but range up to $16,000 for the total enclosure of the grinder platform.

Comments received from one manufacturer supported the cost data used in OSHA's preliminary analysis (although the effectiveness of the controls in achieving levels below 5 $\mu g/m^3$ was contested). This company also stated that the "costs developed in the PACE report to attain cadmium in air levels of between 10 and 25 $\mu g/m^3$ have been reviewed by us and are considered to be adequate 'ball park' numbers." [2, Appendix I, p. 10.] The company noted that the "technologies given in the PACE report * * * are more sophisticated" than those implemented by the company and "yield only slightly lower estimated levels than we have attained but at a significantly larger investment." Thus, with the controls recommended by PACE, "we are in the realm of diminishing returns." [2, Appendix I, p. 10.] OSHA agrees with this assessment and believes that some expensive controls recommended by PACE may not achieve exposure reductions sufficient to justify their implementation.

In practice, each plant will be able to choose the combination of controls deemed necessary for compliance which is most cost-effective and best suited for its particular circumstances. However, in order to estimate the cost to cadmium stabilizer producers of installing additional engineering controls, the number of such controls for a typical plant was estimated. Controls used to estimate costs are based on evidence in the record indicating their effectiveness and feasibility for this industry.

Table VIII–C29 summarizes the costs of engineering controls estimated to be incurred by cadmium stabilizer producers. Two new ventilation systems at $80,000 each would be installed in dry process plants, and one would be installed in wet process plants. Some plants may spend an equivalent sum for new or improved ventilation systems at several exposure sources, as described in the PACE report. PACE identified additions or improvements in ventilation for at least five operations with a total cost of less than $150,000 [3, Table A8–4]. In addition, existing ventilation systems in this industry may be amenable to design improvements that would be "relatively minor in scope but would provide a significant improvement in dust control" (costing less than $1,500 and reducing emissions by 70 percent) according to PACE [3, p. 8–8 and Table A8–3].

Comments received from one manufacturer indicated that central vacuum systems were recently installed

and in use at both the dry and wet process plants operated by the company [2, Appendix I, p. 7]. The plant visited by PACE apparently did not have such a system in place, and PACE recommended a system costing over $30,000. OSHA estimates that on average plants would install one central vacuum system (or incur equivalent expenditures for housekeeping or other additional controls) with a unit cost comparable to that estimated previously.

TABLE VIII-C29.—ESTIMATED COSTS OF ENGINEERING CONTROLS FOR CADMIUM IN THE CADMIUM STABILIZER INDUSTRY

Type of control	Controls per plant by type of plant [1]			Total industry controls [2]	Cost per control (dollars in thousands)			Industry costs (dollars in thousands)				Total annualized industry cost (dollars in thousands)
	A	B	C		Capital	Annual power and maintenance	Annual labor	Capital	Annualized capital	Annual power and maintenance	Annual labor	
Local exhaust ventilation	3	1	2	10	80	8	0	800	130	80	0	210
Central vacuum systems	1	1	1	5	15	1	7	75	12	5	35	52
Enclosure	3	3	3	15	9	0	0	135	22	0	0	22
Material handling technology:												
Equipment	5	1	4	16	90	9	0	1,440	234	144	0	378
New drums	1	1	1	5	200	0	0	1,000	163	0	0	163
Total								3,450	561	229	35	825

[1] Type A plant: wet and dry processes; Type B plant: wet process only; Type C plant: dry process only.
[2] Based on two type A plants, two type B plants, and one type C plant.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

Improvements in enclosure and containment have been shown to be effective and feasible methods for reducing exposures from several sources in this industry [3, p. 8–4 through 8–14]. Most improvements cost less than $2,000; total enclosure of the grinder platform may cost over $16,000 and also require the use of a closed circuit monitoring system [3, Table A8–4]. OSHA estimates that on average each plant would incur costs of $27,000 for enclosures, valves, flanges, and similar improvements to reduce exposures.

About half of the total compliance costs estimated by PACE for this industry involve improvements in material handling technology, primarily with automatic drum dumping stations. Based on the evidence in the record, OSHA concludes that the adoption of such technology would generally be feasible for this industry (although not necessarily in every establishment). As outlined by PACE [3, p. 8–4 et seq.], the stations would cost $90,000 each. At the plant level, four stations would be used for each dry process and one station for each wet process. In addition, new drums would need to be purchased at a cost of about $200,000.

Total estimated costs for engineering controls, including ventilation and vacuum systems, enclosures, and automated material handling technology, would involve $3.45 million in capital costs and $264,000 annually for power, maintenance, and labor. The corresponding total annualized cost would be $825,000.

Additional costs of compliance for this industry are associated with expanded exposure monitoring, medical surveillance, and respirator programs, and with hygiene facilities and record keeping. Current efforts involving information and training programs should be sufficient for compliance with the revised standard.

Evidence in the record from two cadmium stabilizer plants (one dry process and one wet process) shows that all employees exposed to cadmium are currently using respiratory protection to supplement engineering controls [7, Attachments 3 & 4]. OSHA also recognizes that not all employees in the industry are likely to be wearing respirators for all exposures of 5 $\mu g/m^3$ or greater. Most employees in the industry will probably need respirators to comply with a PEL of 5 $\mu g/m^3$, and OSHA estimates that an additional 20 percent of the work force would need to be supplied with respiratory protection.

In the preliminary analysis OSHA estimated that about 200 employees were potentially exposed in this industry. One commenter pointed out that the subsequent reduction in the number of cadmium stabilizer suppliers from six to four "has reduced the number of exposed employees" [2, Attachment I, p. 2]. During the hearings it was suggested by one manufacturer that a total of 200 employees for the industry "might be a little bit low." [8]. Considering that employees producing cadmium stabilizers also produce non-cadmium products, 200 employees seems to provide a reasonable estimate of the number of exposed workers. Using a cost of $300 per employee per year [9, Attachment III, p. 1], the total annual cost of additional respiratory protection is estimated to be $12,000.

Exposure monitoring is required by the revised standard for every job category and every shift semi-annually. Data submitted to the record suggests that some monitoring is currently being performed and that additional monitoring would likely be necessary [7, Attachments 3 & 4]. OSHA estimates that on average each plant would have to monitor four job categories (including maintenance workers and supervisors) across three shifts [10] and that current monitoring accounts for about 20 percent of that required.

The costs of monitoring are estimated to be $40 per sample taken and $1,500 annually per plant for the services of an industrial hygienist or other competent person. The total cost of the additional monitoring required by the standard is thus estimated to be $11,340 [$40*4*3*2*5*0.8 + 5*$1500].

Evidence submitted to the record by the cadmium stabilizer industry consistently shows that employees are currently receiving medical exams and biological testing [2, p. 2; 7, Attachments 1 & 2; 12]. This evidence also indicates that biological testing would have to be performed more frequently to comply with the provisions of the revised standard.

OSHA estimates that an additional 100 samples each for cadmium in blood, cadmium in urine, and β_2-microglobulin in urine would need to be taken annually to meet the basic requirements for biological monitoring. Another 40 sets of these samples may be necessary to meet requirements for more frequent

testing of some employees. The lab analyses would cost $60, $80, and $80 per sample, respectively, and the estimated cost of collection is $5 per sample. The total additional annual cost of biological monitoring for the industry is estimated to be $30,100.

Requirements for medical removal may involve compliance costs in addition to those for more frequent medical exams and monitoring estimated above. The criteria for mandatory removal would affect employees with the most extreme biological monitoring levels. The criteria for removal also allow for considerable physician's discretion. An estimated 3 percent of the exposed workforce of 200 employees may be removed initially on the basis of these criteria and the discretion of physicians.

Compliance with the new PEL for cadmium and other requirements of the final cadmium standard should prevent a continuing need to remove employees. The number of employees with relatively high past exposures who would be more likely to be removed should also decline through attrition. However, as the criteria for removal become broader in future years (lower levels of cadmium in blood and urine triggering mandatory removal), additional employees may be subject to removal. The costs associated with the medical removal provisions are estimated based on 3 percent of the exposed workforce being removed every 5 years.

The number of employees removed should be small enough to enable establishments to provide removed employees with alternative positions. Costs to the employer would include paying possible wage differentials and hiring and training employees in new positions. The average cost per removed employee would be an estimated $5,000. An estimated 6 employees may be removed every five years on average in the cadmium stabilizer industry, and the average annual cost for the industry would be $6,000.

The total annual cost for the medical surveillance and medical removal provisions is estimated at $36,100.

Achieving compliance with the hygiene provisions of this standard may involve some additional costs for this industry. OSHA's preliminary conclusions regarding compliance with the proposed hygiene provisions were generally not challenged by industry. OSHA estimated that work clothing and appropriate shower and lunch facilities were already provided and that half of the affected workers currently do not shower after each shift. Under these assumptions, the cost of providing showers would be about $225 per employee per year (assuming employees are typically exposed for one week per month), or $22,500 annually for the industry.

PACE assigned over $16,000 in annual compliance costs for providing workers with daily changes of clean work clothes [3, p. 8–14], but did not add any costs for showering or for lunch rooms. A commenter from another industry stated that disposable work clothing could be provided for an annual cost of $104 per employee [9, Attachment III, p. 1].

OSHA concludes that the hygiene provisions are generally complied with in this industry but may not be consistently applied in all plants. On average each plant may incur an incremental cost of $10,000 to achieve full compliance with the revised standard. The total estimated annual cost for the industry would be $50,000.

Incremental recordkeeping costs imposed by the revised standard are estimated to be about $5 per employee annually. The estimated annual cost for the industry is $1,000.

Compliance costs for the stabilizer industry are summarized in Table VIII–C30. The total annualized cost of compliance is estimated to be $935,000.

Economic feasibility of a 50 $\mu g/m^3$ SECAL and 5 $\mu g/m^3$ PEL. The compliance costs estimated above are considered economically feasible for the cadmium stabilizer industry. Most of the costs should be able to be passed on to customers through slight price increases. Cadmium stabilizers are essential or preferred over other types of stabilizers in several applications; the lack of adequate substitutes with the qualities of cadmium stabilizers should ensure a continued demand for this product.

Plants producing cadmium stabilizers generally produce other products as well, including potential substitutes, and cadmium stabilizers may represent a small fraction of a manufacturer's revenues. For three of the four U.S. manufacturers "cadmium-based stabilizers represent a very small percentage of total revenues." [1, p. 4–6]. The remaining company "derives 35 percent of its revenues from sales of cadmium-based stabilizer products." [1, p. 4–6]. Although increased production costs resulting from compliance with the revised cadmium standard are not expected to be subsidized by unrelated operations within a corporation, most firms do have the ability to absorb the compliance costs as part of operating costs for producing "revenues that amount to hundreds of millions of dollars annually." [1, p. 2–19].

TABLE VIII–C30.—ESTIMATED COSTS OF COMPLIANCE WITH THE REVISED CADMIUM STANDARD FOR THE CADMIUM STABILIZER INDUSTRY

Provision	Annualized cost ($thousands)
Exposure control	825.0
Respirator use	12.0
Exposure monitoring	11.3
Medical surveillance	36.1
Hygiene provisions	50.0
Recordkeeping and information	1.0
Total	935.4

Note: Costs do not include current expenditures.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

An increase in the cost of producing cadmium stabilizers can also be compared to total revenues and profits derived from product lines manufactured with or closely related to cadmium stabilizers. The ability to offer a complete array of products attracts customers who prefer to deal with one supplier for all their needs. Manufacturers tend to assess the viability of producing a group of products together and would treat the compliance cost as an increase in operating costs for the whole group, especially when multiple products are made at the same plant.

Revenues from cadmium stabilizers alone are about $23 million for one company [1, p. 2–19]. All four U.S. firms have a similar scale of production [1, p. 4–6], and total industry revenues from cadmium stabilizers are estimated to be $92 million. Cadmium stabilizers represent about 36 percent of the stabilizer market [4, p. 2–54], which is estimated to be worth about $256 million annually.

Profits before taxes are estimated to be about 9 percent, consistent with the estimate used for the preliminary analysis. No comments were received disputing this figure, and no other profitability data for this industry were submitted to the record. Before-tax profits for the production of stabilizers are an estimated $23 million, of which $8.3 million are attributable to the production of cadmium stabilizers.

The estimated compliance costs represent less than 0.4 percent of stabilizer revenues (or about 1 percent of cadmium stabilizer revenues). The costs also represent about 4 percent of before-tax stabilizer profits (or about 11 percent of before-tax cadmium stabilizer profits). Actual effects on profits should be less than this depending upon the elasticity of demand for the industry's product.

The "dominant, almost exclusive market" for cadmium stabilizers is for the production of flexible PVC [13], and the stabilizers constitute between 0.5 and 2.5 percent of the final PVC compound [1, p. 2–18]. Because cadmium stabilizers make up a small fraction of PVC compounds, a small increase in cadmium stabilizer prices would have a minimal effect on the cost of manufacturing PVC products. This would tend to make the demand for cadmium stabilizers less elastic, improving the ability of stabilizer producers to recover compliance costs by increasing prices.

Imports currently constitute an "insignificant fraction" of total domestic supply, and distribution channels are "quite important" because the shelf life of cadmium stabilizers is limited. [1, p. 2–19]. This factor also contributes to an inelastic demand for cadmium stabilizers.

"At present no good substitutes exist" for most cadmium stabilizer applications, and "cadmium usage is expected to remain at current levels." [1, p. 2–18]. The lack of adequate substitutes provides strong evidence for the inelasticity of demand for these products.

OSHA concludes that manufacturers of cadmium stabilizers will be able to raise prices sufficiently to recoup compliance costs without major reductions in profits or sales volumes. The regulation does not threaten the financial viability or the competitive stability of the industry. Cost impacts from this regulation are not expected to result in any plant closures or produce any significant dislocation.

A study was conducted by an industry trade association on the economic impacts for this industry of compliance costs representing as much as 2 percent of revenues from stabilizer operations [1, p. 9, 10]. The study found that with "the lack of close substitutes, the lack of cost differentials among existing producers, and the relatively small share of these stabilizers in the cost of PVC resins, stabilizer producers should be able to pass costs through to PVC plastic manufacturers." [1, p. 4–6]. A cadmium stabilizer producer reported that they had reviewed this study and concurred with the findings [2, Appendix I, p. 10].

The cost increase due to this regulation would have a negligible effect on major investment decisions (such as relocating manufacturing operations), which are influenced by more significant factors of production cost.

Sources

1. Exhibit 19–43, Attachment I, "Economic and Technological Feasibility of a 5 Microgram per Cubic Meter Workplace Standard for Airborne Cadmium," Putnam, Hayes, & Bartlett, Inc., April 30, 1990.
2. Exhibit 19–46, Comments "RE: Occupational Exposure to Cadmium 29 CFR 1910," Synthetic Products Company, May 2, 1990.
3. Exhibit 19–43, Attachment L, "Feasibility and Cost Study of Engineering Controls for Cadmium Exposure Standard," PACE Incorporated, April 30, 1990.
4. Exhibit 13, "Economic Impact Analysis of the Proposed Revision to the Cadmium Standard," Final Report, JACA Corporation, March 15, 1988.
5. Exhibit 57, Testimony of NIOSH, July 17, 1990.
6. Hearing Transcript, July 17, 1990, p. 8–112 and 8–113.
7. Exhibit 102, Comments "RE: Occupational Exposure to Cadmium 29 CFR 1910," Synthetic Products Company, September 17, 1990.
8. Hearing Transcript, June 12, 1990, p. VI–81.
9. Exhibit 19–30, Big River Zinc Corporation, "Comments on OSHA Proposed Cadmium Regulation," May 10, 1990.
10. Hearing Transcript, June 12, 1990, p. VI–94 and VI–118.
11. Hearing Transcript, June 12, 1990, p. VI–119.
12. Hearing Transcript, June 12, 1990, p. VI–99.
13. Hearing Transcript, June 12, 1990, p. VI–97.

Lead Smelting and Refining

Industry Overview. Lead ore is recovered from underground and open pit mines around the world. The United States is one of the largest producers and consumers of the soft, heavy metal which has many important industrial uses. Lead ores are crushed and milled into lead concentrates before being sent to smelting operations.

Four lead smelters and/or refiners are currently operating in the United States. Two plants are both smelters and refiners, one plant is a smelter only, and one plant is a refiner only [1, p. 2–26 and 2, p. 3]. Two additional lead smelters were formerly active but have suspended operations. About 400 employees working in this industry sector are exposed to cadmium.

Production processes. Lead concentrates and other materials are received and transported with rail cars and cranes to provide the inputs necessary for producing lead. Multiple conveyors and storage bins are also used for materials handling throughout the plant. A preliminary step in the production process involves mixing and crushing raw materials in preparation for sintering. The sintering operation converts lead sulfides to agglomerated lead oxides. As the mixture is processed by the sintering machine, gases are produced which are used to make acids in another operation.

The sintered material is transferred to the blast furnace which is charged with coke, fluxes, and other materials. The blast furnace reduces the lead oxides to form lead bullion, which is further processed in the dross furnace to remove copper and other elements. The lead bullion produced by the dross furnace becomes the raw material for the lead refining process.

Lead refining involves several steps in which the lead bullion is processed through refining kettles to separate out other metals and remove any remaining impurities. Copper, silver, and zinc are removed and may be refined further in separate operations. The end product of the lead refining process is virtually pure lead which can be fed into a strip rolling mill or a straight line casting machine, depending on the type of product desired. The lead may also be combined with alloy materials before casting.

Employee exposures. Exposures to cadmium arise in the lead smelting and refining process because the lead concentrates received by plants contain small amounts of cadmium which exist naturally in the environment. Loose materials are transferred in large quantities and intense heat and rapid gas flows are used in the production process; emissions of lead and cadmium result in exposures in the work environment.

Employees may be exposed to cadmium in several job categories and operations. Material handlers are exposed to dusts generated by unloading railroad cars, operating cranes and conveyor systems, or loading and retrieving materials in stockpiles. Employees in the sinter plant are exposed to dusts generated by mixing and transferring materials. Employees in the furnace areas are exposed to emissions from conveyors, charging operations, tuyere punching (enabling air to enter a blast furnace to facilitate combustion), and filling ten ton pots with molten lead bullion. Fumes generated during refining and casting operations may also contain cadmium. Maintenance employees are exposed to dust and fume that may contain cadmium while working on equipment throughout the plant and on dust control systems including baghouse operations.

The exposure profile developed by JACA Corporation to represent a typical lead smelting and refining plant is presented in Table VIII–C31 [1, page 3–27]. Mean cadmium exposures for six of the seven job categories are less than 7

$\mu g/m^3$; all job categories have mean exposures less than 14 $\mu g/m^3$.

Exposure monitoring data were submitted for three lead smelting and/or refining plants by one company [2, Attachment I]. Data for a lead smelter are summarized in Table VIII–C32; data for a lead smelter and refiner are summarized in Table VIII–C33; and data for a lead refiner are summarized in Table VIII–C34. At each of these plants mean exposures for most workers are less 5 $\mu g/m^3$, and almost all exposures are less than 20 $\mu g/m^3$.

A study conducted for the Cadmium Council included an exposure profile for workers at a large lead smelting and refining facility [3, Tables IV–1 through IV–6]. These data are shown in Table VIII–C35. Thirty of the 47 job categories have current mean exposures less than 20 $\mu g/m^3$, and 37 have exposures less than 30 $\mu g/m^3$.

TABLE VIII–C31.—CADMIUM EXPOSURE DATA FOR LEAD SMELTING AND REFINING BASED ON JACA

Job category	Concentration in $\mu g/m^3$		
	Geometric mean	Median	Range
Furnace operator	4.5	5.8	0.1–223.0
Material handler	3.4	3.5	0.1–360.0
Maintenance technician	6.6	4.2	0.1–92.0
Supervisor	9.1	2.4	0.1–39.0
Sinter machine operator	13.1	9.0	0.8–174.0
Mixing room operator	6.2	4.6	0.1–453.0
Refinery operator	0.6	0.7	0.1–5.0

Source: Exhibit 13, JACA, Table 3–9.

TABLE VIII–C32.—CADMIUM EXPOSURE DATA FOR LEAD SMELTER BASED ON COMPANY DATA

Job category	Concentration in $\mu g/m^3$					
	Geometric mean	Number of samples				
		<1	1–5	5–20	20–50	>50
General:						
Assayer	<1	13	3	0	0	0
Instrument Man	2	2	13	1	0	0
Change House Attd	<1	19	5	1	0	0
Transport/Unloading:						
Foreman	1	7	3	1	0	0
Crane operator	3	3	8	3	0	1
Moisture sampler	1	3	5	0	0	0
Sampler	2	1	10	0	1	0
Bucker	<1	13	3	0	0	0
Mill tender	2	1	7	2	0	0
Crusherman	2	2	5	2	0	0
Plateman	<1	5	2	0	0	0
Backhoe operator	2	7	6	2	0	1
Loco crane helper	8	0	9	2	3	2
Car dumper	3	0	10	1	0	0
Beltman	5	0	2	3	0	0
Screen floor man	2	2	7	1	1	0
Car puller	3	1	9	4	0	0
Mechanical/Maintenance:						
Foreman	2	15	15	2	0	0
Machinist	2	16	16	7	2	1
Mechanic	<1	18	4	0	0	0
Blacksmith	2	2	6	1	0	0
Pipefitter	2	7	14	7	0	1
Carpenter	2	11	16	3	1	0
Painter	<1	5	2	0	0	0
Mason	2	3	9	2	1	0
Electrician	3	10	17	9	3	1
Welder	3	12	23	13	1	2
Oiler	11	0	3	4	1	1
Tool room man	<1	3	0	0	0	1
Insulator	<1	9	3	1	0	1
Blast Furnace Department:						
Foreman	4	2	14	6	2	0
Furnaceman	17	0	3	11	3	7
Loco engineer	3	4	30	9	3	1
Feed floor hoistman	20	1	8	2	8	8
Front end loader	3	7	10	7	0	0
Slag dumper	1	1	2	0	0	0
Slag Hauler	<1	3	0	0	0	0
Sinter Plant:						
Foreman	1	10	12	2	0	0
Crane man	3	2	13	8	1	0
Operator	7	4	3	11	3	2
Helper	12	1	1	6	3	1
Machineman	19	0	3	9	8	5
Feederman	9	1	9	8	2	4
Baghouse Man	10	0	6	1	2	2
Dross Reverb Department:						
Furnaceman	3	5	11	7	2	0
Furnace helper	3	3	15	4	1	1

TABLE VIII–C32.—CADMIUM EXPOSURE DATA FOR LEAD SMELTER BASED ON COMPANY DATA—Continued

Job category	Concentration in μg/m³					
	Geometric mean	Number of samples				
		<1	1–5	5–20	20–50	>50
Crane man	<1	15	8	1	0	0
Bullion man	4	1	16	5	1	2
Zinc Fuming Department:						
Crane man	<1	9	0	0	0	0
Furnaceman	<1	1	0	0	0	0
Ladle chaser	<1	8	1	0	0	0
Yard Department:						
Foreman	2	0	5	0	0	0
Front end loader	2	9	14	5	0	1
Power sweeper operator	2	6	5	0	1	0
Adobeman	2	0	8	0	0	0
Laborer	6	0	2	0	1	0
Janitor	7	1	3	3	1	1
Breaking floor labor	4	1	4	4	0	0
Break floor crane man	2	2	5	1	0	0
Water truck operator	<1	7	2	0	0	0
Acid Plant:						
Foreman	<1	6	2	0	0	0
Operator	<1	20	3	0	0	1
Assistant operator	<1	14	7	2	0	0
Cottrellman	6	0	4	3	1	0
Acid loader	<1	8	0	0	0	0
Dust loader	6	1	2	5	1	0
Sample Man	1	5	7	0	0	0

Source: Exhibit 19–32, Attachment I.

TABLE VIII–C33.—CADMIUM EXPOSURE DATA FOR LEAD SMELTER AND REFINER BASED ON COMPANY DATA

Job category	Concentration in μg/m³					
	Geometric mean	Number of samples				
		<1	1–5	5–20	20–50	>50
General:						
Administrative	<1	1	0	0	0	0
Laboratory	<1	1	0	0	0	0
Utility	<1	7	0	0	0	0
Warehouse	<1	8	0	0	0	0
Lead Refinery:						
Supervisor	<1	18	2	0	0	0
Foreman	<1	1	0	0	0	0
Craneman	<1	21	1	2	0	0
Kettleman	<1	22	4	0	0	0
Transport/Unloading:						
Supervisor	<1	7	0	0	0	0
Diesel engine operator	1	6	1	0	0	0
Switchman	<1	7	1	0	0	0
Moisture sampler	<1	7	0	0	0	0
Sampler	<1	9	1	0	0	0
Mechanical/Maintenance:						
Mechanical/maintenance	2	3	1	1	0	0
Supervisor	<1	8	2	0	1	0
Foreman	<1	1	0	0	0	0
Painter	<1	3	2	0	0	0
Electrician	1	7	4	2	0	0
Laborer	<1	1	0	0	0	0
Blast Furnace Department:						
Supervisor	3	8	4	3	6	0
Foreman	<1	1	0	0	0	0
Crane Man	3	3	15	5	0	0
Furnaceman	5	1	11	10	2	0
Charge car operator	6	3	7	9	4	1
Dross skimmer	7	1	9	12	0	3
Sinter Plant:						
Supervisor	1	15	9	1	0	1
Foreman	<1	2	0	0	0	0
Crane man	<1	19	5	0	0	0
Operator	1	11	12	1	0	0
Prop weigher	3	5	8	7	1	1
Helper	3	6	13	2	2	1
Baghouse:						
Supervisor	<1	1	0	0	0	0
Baghouseman	3	1	2	4	0	0
Helper	3	0	1	0	0	0

TABLE VIII–C33.—CADMIUM EXPOSURE DATA FOR LEAD SMELTER AND REFINER BASED ON COMPANY DATA—Continued

Job category	Concentration in µg/m³					
	Geometric mean	Number of samples				
		<1	1–5	5–20	20–50	>50
Molding Crew:						
Supervisor	<1	10	1	0	0	0
Molding Crew	<1	16	0	0	0	0
Mechanical/Maintenance	10	0	0	2	0	0

Source: Exhibit 19–32, Attachment I.

TABLE VIII–C34.—CADMIUM EXPOSURE DATA FOR LEAD REFINER BASED ON COMPANY DATA

Job category	Concentration in µg/m³					
	Geometric mean	Number of samples				
		<1	1–5	5–20	20–50	>50
General:						
Laboratory	<1	3	0	0	0	0
Assayer	<1	3	0	0	0	0
Utility	<1	3	0	0	0	0
Watchman	<1	3	0	0	0	0
Lead Refinery:						
Supervisor	<1	9	0	0	0	0
Crane man	<1	9	0	0	0	0
Softenerman	<1	9	0	0	0	0
Kettleman, desilver	<1	9	0	0	0	0
Kettleman, dezinc	<1	6	2	0	0	0
Floorman	<1	9	0	0	0	0
Mechanic	<1	3	0	0	0	0
Dockman	<1	3	0	0	0	0
Molder	<1	3	0	0	0	0
Salvage	<1	3	0	0	0	0
Transport/Unloading:						
Supervisor	<1	3	0	0	0	0
Leadman	<1	3	0	0	0	0
Crane operator	<1	3	0	0	0	0
Sampler	<1	2	0	0	0	0
Truck driver	<1	3	0	0	0	0
Fork lift driver	<1	3	0	0	0	0
Mechanical/Maintenance:						
Supervisor	<1	3	0	0	0	0
Machinist	<1	3	0	0	0	0
Mechanic	<1	3	0	0	0	0
Blacksmith	<1	5	0	0	0	0
Pipefitter	<1	4	0	0	0	0
Carpenter	<1	3	0	0	0	0
Mason	<1	3	0	0	0	0
Construction man	<1	3	2	0	0	0
Kettle welder	<1	4	1	0	0	0
Laborer	2	1	0	1	0	0
Power House:						
Supervisor	<1	3	0	0	0	0
Station tender	<1	8	1	0	0	0
Electrician	<1	2	1	0	0	0
Oiler	<1	3	0	0	0	0
Laborer	<1	2	0	0	0	0
Residue Department:						
Supervisor	<1	7	1	0	0	0
Crane man	<1	9	0	0	0	0
Baghouse man	<1	3	0	0	0	0
Furnaceman	<1	5	4	0	0	0
Kettleman	<1	5	0	0	0	0
Bismuth Department:						
Supervisor	<1	9	0	0	0	0
Cupelman	<1	9	0	0	0	0
Retortman	<1	9	0	0	0	0
Kettleman	<1	9	0	0	0	0
Mechanic	<1	3	0	0	0	0
Laborer	<1	4	0	0	0	0
Antimony Department:						
Supervisor	<1	3	0	0	0	0
Oxide operator	<1	9	0	0	0	0
Oxide packer	<1	9	0	0	0	0

Source: Exhibit 19–32, Attachment I.

TABLE VIII-C35.—PROFILE OF OCCUPATIONAL EXPOSURES TO CADMIUM IN THE LEAD SMELTING/REFINING INDUSTRY BASED ON PHB STUDY

Job category	Geometric mean exposures ($\mu g/m^3$)
Material Handling:	
Railroad engineer	2
Railroad conductor	5
Railroad switchman	27
Crane engineer	1
Crane laborer	1
Unloader 1	59
Unloader 2	52
Unloader helper	29
Service foreman	3
Yard pool trestle	19
Unloader 3	26
General foreman	1
Sinter Plant:	
Control room man	17
SP operator	180
SP helper	240
Mix room man	420
Mix room helper	116
South end man	135
Foreman	40
General foreman	1
Oiler	25
Feed floor operator	100
Blast Furnace:	
Trestle man	14
Feed floor man	12
Furnace helper	26
Head furnace operator	10
Furnace operator	14
Operator helper	19
Utility man	8
Crane operator	6
Foreman	5
General foreman	2
Dross Plant:	
Crane operator	4
DP operator	20
DP operator helper	17
Refinery:	
Fireman	1
Fireman helper	2
Refinery helper	1
Foreman	1
General foreman	1
Retort operator	3
Caster	1
Lead loader operator	1
Weigher	1
Foreman	1
Baghouse Area:	
Baghouse operator	41
Foreman	12

Source: Exhibit 19-43, Attachment J, Putnam, Hayes & Bartlett, Inc., Tables IV-1 through IV-6.

Exposures to cadmium in the lead smelting and refining industry were also evaluated by the Bureau of Mines of the United States Department of the Interior [4, p. 7]. These data indicate that for over 80 percent of the workforce mean exposure levels are less than 25 $\mu g/m^3$.

Existing and feasible additional controls. JACA concluded in their study that due to the requirements of the OSHA lead standard, the lead smelting industry is already employing engineering controls to the extent feasible to control lead and cadmium exposures [1, p. 4-6]. A company operating two lead smelters confirmed that assessment. [2, Attachment G, p. 3]. The company also emphasized that the controls do not necessarily achieve the PEL for lead or the proposed PEL for cadmium and that the potential impacts of other provisions in the proposed cadmium standard should not be dismissed. In response to OSHA's request in the preamble for information on the extent of existing engineering controls, this company stated that with regard to lead plants, "all feasible engineering controls and housekeeping methods are utilized for control of exposure to arsenic and lead." [2, p. 4]. Exposures to cadmium in this industry occur concomitantly with exposures to lead and/or arsenic.

The study by Putnam, Hayes & Bartlett (PHB) described exposure sources and possibilities for additional controls for a large lead smelter and refiner [3, Chapter III]. However, some suggested controls are not adequately specified, hindering an evaluation of their feasibility, and PHB does not provide any cost estimates for the controls.

PHB found that improvements in the railroad yard could reduce exposures during unloading by over 80 percent. In the sinter plant improvements in enclosure and ventilation were projected to reduce exposures by 50 to 75 percent. According to PHB, new and improved ventilation, enclosure, and automation in the blast furnace area could reduce average exposures by about 50 percent. Improvements in the dross plant could achieve minor reductions in exposures, and exposures in refining operations generally cannot be reduced significantly. Exposures during baghouse operations were expected to remain near current levels.

It should be noted that the PHB submission was based on a site visit to one plant at which employee exposure readings were considerably higher than those reported at other plants. The high reduction factors noted in the PHB submission (50 to 80 percent) may be achievable for one plant but not for other plants in this sector.

Technological feasible limit for a SECAL. Following the procedure outlined in section B above, OSHA separated exposures into high and low occupation/process exposure groups to facilitate the technological feasibility analysis. Data were divided at a breakpoint which maximized the difference between the mean values for the two separated data sets.

The data segregation resulted in the identification of a "high" occupation/process exposure group which included sinter plant, blast furnace and yard area operations involving 60 workers. All other plant operations including zinc fuming, dross furnace, acid plant, lead refining, etc., were included in the "low" exposure group involving about 340 employees. Figure VIII-C22 graphically represents the segregated data. The vertical line within each box depicts the median value for the distribution.

Mean exposure data for the two sets were as follows:

	High group	Low group
Number of observation	21	21
Mean	43	3.6
Standard deviation	27	3.2

To verify that the two groups within this industry were distinct, a t test was performed on the difference in the means. The null hypothesis that the means of the exposure data were equal was rejected, and the conclusion that they were drawn from separate statistical distributions, was accepted.

After the statistical difference between high and low exposure groups was verified, the data were analyzed separately. In Figures VIII-C23 and VIII-C24 process mean exposure values drawn from each available data source are presented. All process data were "fitted" to a straight line using ordinary least squares methodology.

For each group a model was developed to graphically depict the effect on the exposure distribution after current exposures were reduced using alternative engineering control efficiency factors from 80 down to 20 percent, in 20 percent increments.

BILLING CODE 4510-26-M

FIGURE VIII-C22

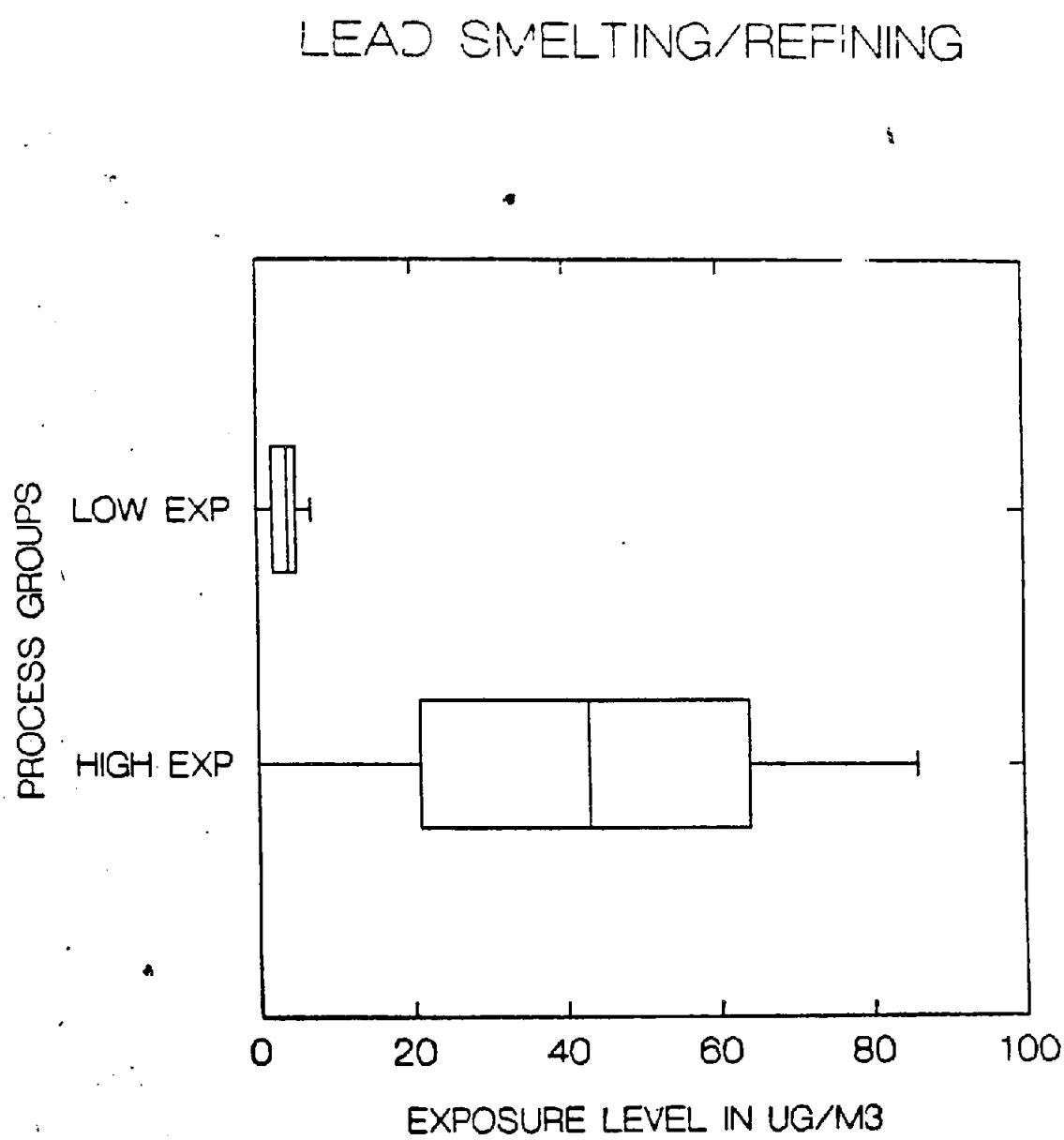


FIGURE VIII-C23

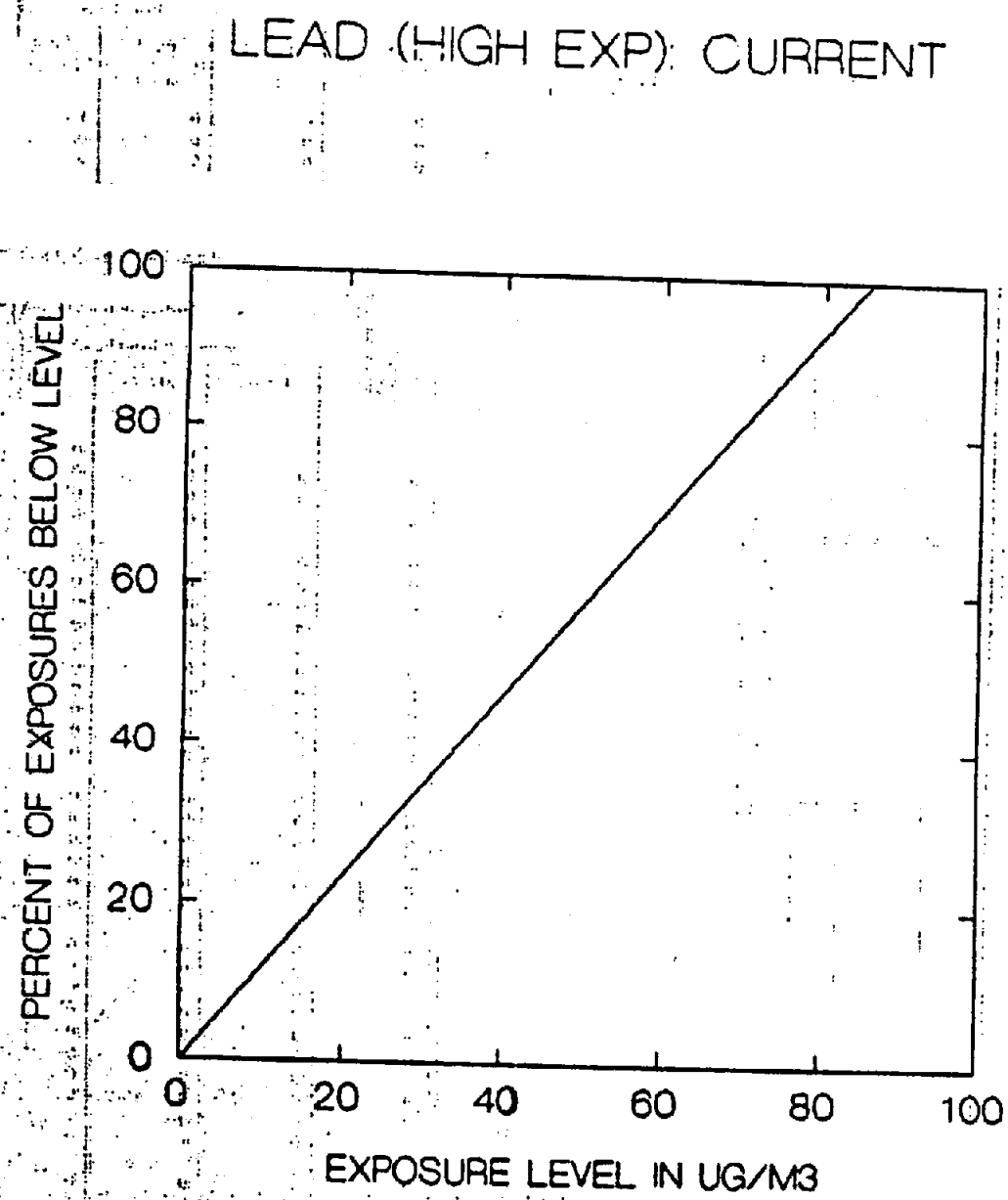
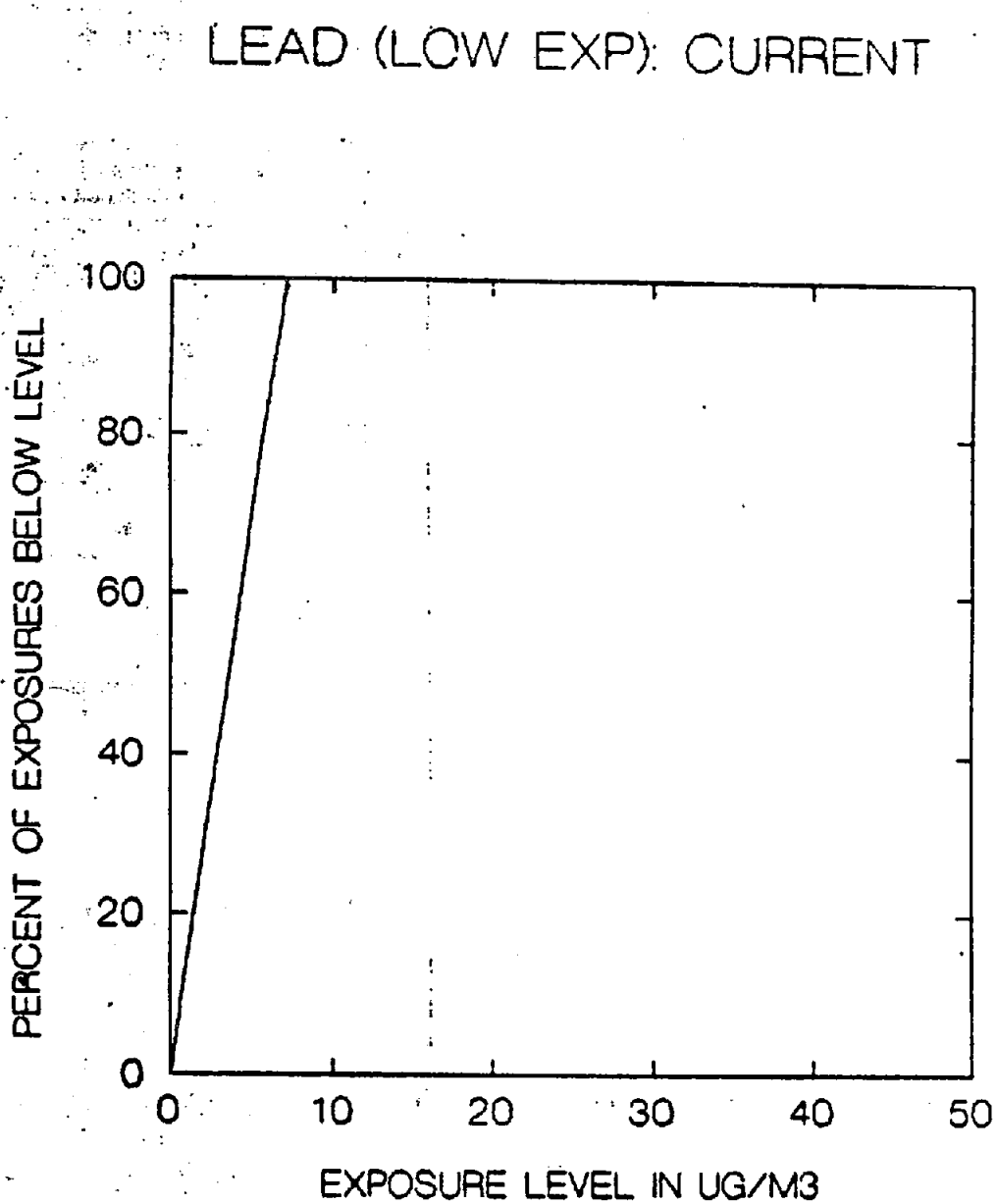


FIGURE VIII-C24



BILLING CODE 4510-26-C

The lower the projected efficiency the smaller the exposure change from current levels. Figures VIII–C25 and VIII–C26 show the effect of such reductions and the shift in the distribution of exposures for the high and low groups in lead smelting operations.

It is very unlikely that requirements for additional engineering controls will have very much success in further reducing cadmium exposure levels, since most sites are already required to introduce engineering controls to the extent feasible in order to reduce lead and arsenic exposures. (OSHA enforcement experience suggests that some plants may not be in full compliance with existing standards.) Improved housekeeping and work practices could further reduce exposures at some of these plants.

Most exposure monitoring data indicated that exposures are generally at or below 5 $\mu g/m^3$ for employees in low exposure occupations. Data from PHB differ from the other sources and indicate higher exposures for some categories. The PHB data indicate that about 20 percent of all job categories have mean exposures above 30 $\mu g/m^3$. However, PHB acknowledged that exposures can be reduced for most workers.

In order to combine the different reduction expectations between the PHB submission and all other industry data, the 80 percent reduction level projected for the one PHB site was averaged with a zero reduction expectation for the remaining three plants making up this industry subsector. The resulting 20 percent reduction is acknowledged to be concentrated within only one plant in this subsector

BILLING CODE 4510-26-M

FIGURE VIII-C25

LEAD (HIGH EXP): CONTROLLED 80%-20%

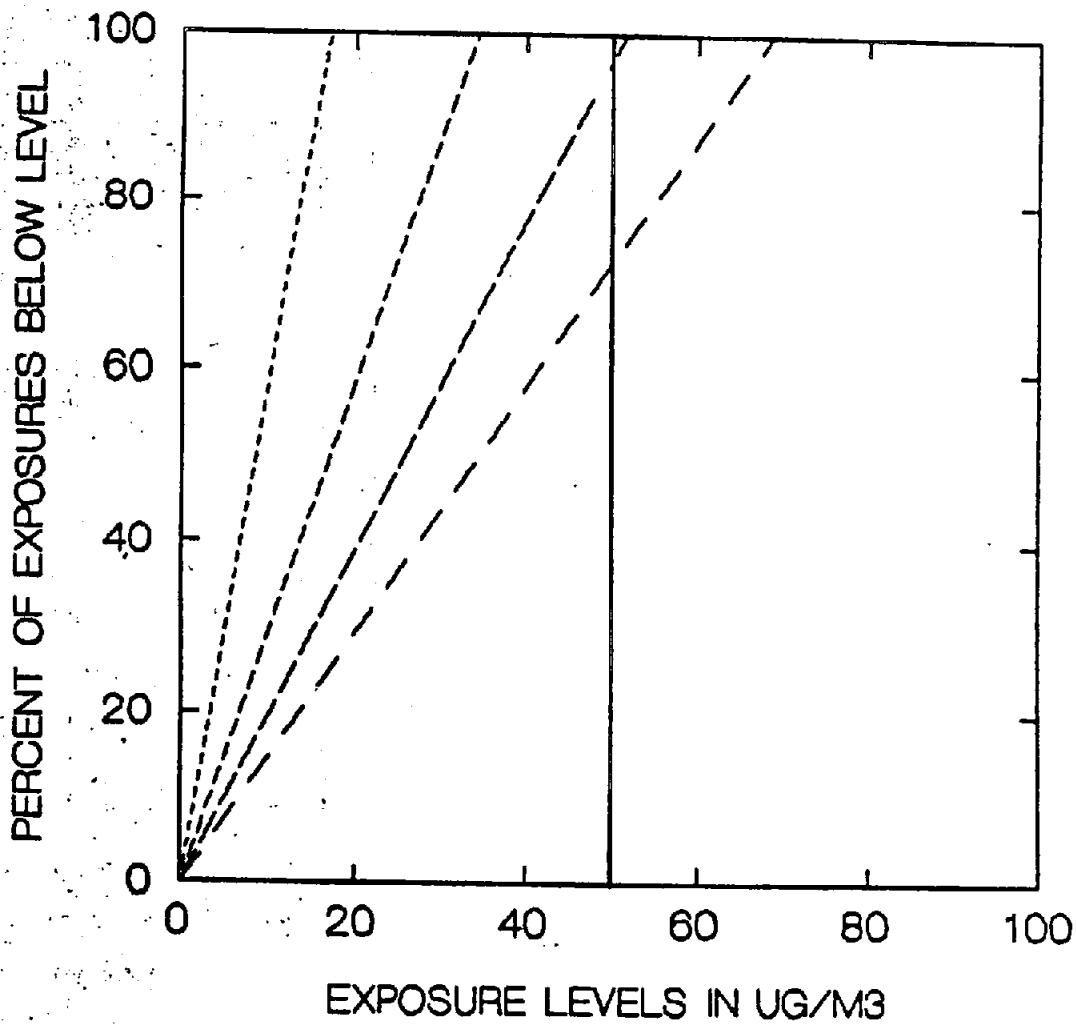
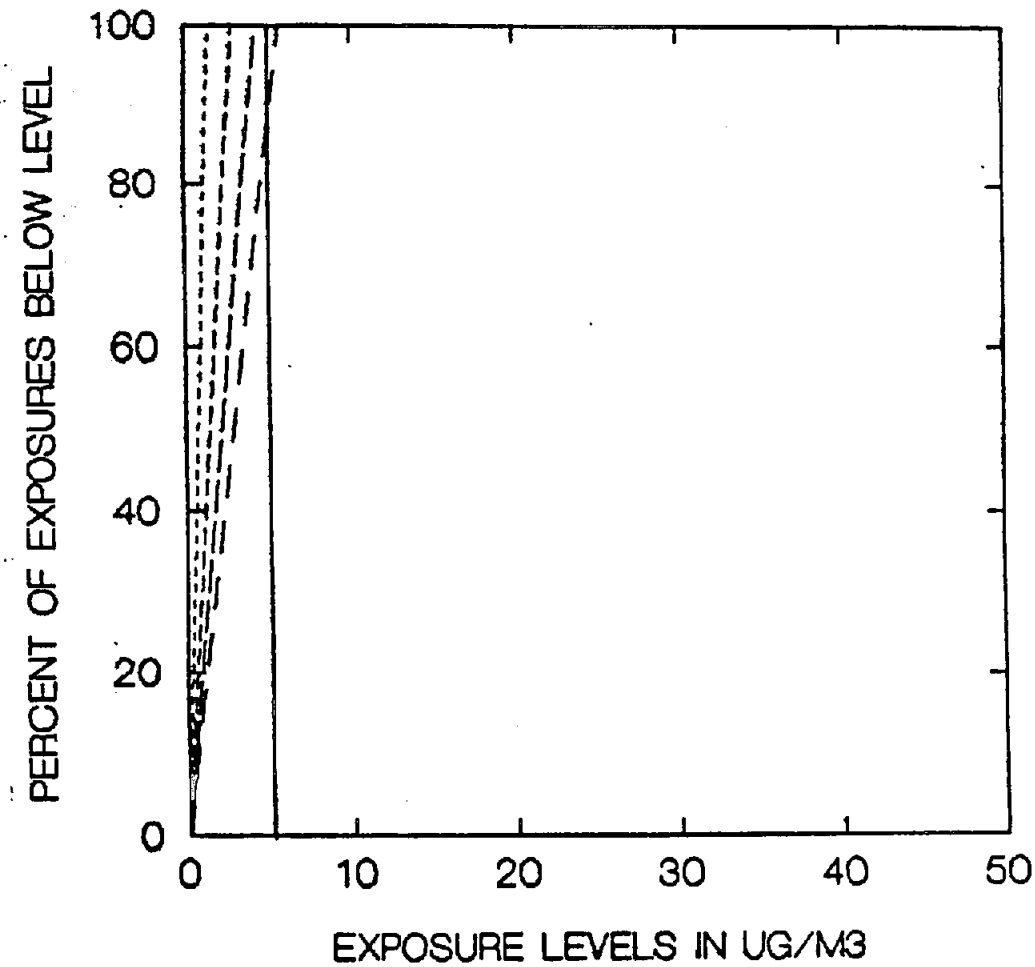


FIGURE VIII-C26

LEAD (LOW EXP.): CONTROLLED 80%-20%



BILLING CODE 4510-26-C

Based on the evidence in the record, OSHA concludes that a 50 $\mu g/m^3$ SECAL for 60 employees in high exposed occupations/processes is technologically feasible and the PEL of 5 $\mu g/m^3$ is feasible for all other employees (340) in this industry. Selection of these levels was based on a 20 percent expected exposure reduction resulting from improved conditions within one affected plant. There were no economic feasibility concerns at this efficiency level.

Costs of compliance with a 50 $\mu g/m^3$ SECAL and 5 $\mu g/m^3$ PEL. The evidence and comments in the record generally confirm OSHA's preliminary finding that lead smelters and refiners have already installed feasible controls to reduce cadmium exposures [1, 2, 3, 4]. Current exposure monitoring data demonstrate the feasibility of compliance with the revised standard for low exposure processes. On the basis of these data, OSHA believes that additional engineering controls will be installed in one plant in this industry to achieve compliance with the revised cadmium standard.

The engineering controls necessary to comply with a SECAL of 50 $\mu g/m^3$ would be less extensive than those listed in the PHB report, which was based on an attempt to meet a PEL of 5 $\mu g/m^3$ in all operations. Furthermore, some additional controls recommended by PHB may be required by existing OSHA standards, and thus the costs for these controls should not be attributable to this cadmium rulemaking.

According to the PHB data, current exposures in most of the job classifications in the high exposure areas are already below the SECAL, and current exposures in most low exposure job classifications are below the PEL. Engineering controls identified by PHB primarily involved enclosures and ventilation systems. Since PHB did not provide cost estimates, OSHA used standard unit cost figures for such systems from industries with similar operations (such as zinc refining and cadmium refining). A typical ventilation system would cost an estimated $80,000 in capital costs and $8,000 in annual costs, and enclosure of an operation would cost about $9,000 on average.

The costs of compliance with the final cadmium standard for engineering controls were approximated by calculating the cost of installing an additional enclosure and ventilation system (or other controls with equivalent cost) in each of the five production areas identified (material handling, sinter plant, blast furnace, dross plant, and refinery). The estimated capital cost would be $445,000, the annual cost would be $40,000, and the total annualized cost would be an estimated $112,000.

Employees in lead smelters and refiners use respiratory protection for lead and arsenic exposure, and cadmium exposure sources generally coincide with lead and arsenic exposure sources. Evidence from the industry confirmed that employees in lead plants are provided with respirators [2, p. 9], and the record does not demonstrate the existence of any sources of cadmium exposure independent of lead or arsenic exposure sources. Most employees exposed above the revised PEL for cadmium should already be using respiratory protection.

Based on a visit to a lead smelter and refiner and on other research in the industry, JACA concluded that all employees with significant exposure to cadmium in this industry were provided with respiratory protection [1, p. 6–17]. Comments from one company representing three lead smelters/refiners indicated that the revised PEL for cadmium would affect a total of 285 employees at these plants [2, p. 3]; however, the extent of current respirator usage among these employees was not specifically addressed.

OSHA recognizes that situations may arise for which compliance with the revised cadmium standard may involve costs that would not be required by standards for lead and arsenic. OSHA estimates that 200 employees in the industry would need to be provided with additional respiratory protection (assuming that about half of all affected employees are already protected). At a cost of $300 per employee per year the total estimated annual cost for the industry would be $60,000.

JACA concluded on the basis of site visit data and survey responses that exposure monitoring for cadmium was conducted in lead smelters every six months on average. Comments from the industry regarding three lead facilities indicated that exposure monitoring for cadmium was conducted quarterly for each job category and each shift affected by the lead and arsenic standards [2, p. 3]. Another section of these comments refers to "additional employees" affected by a revised cadmium PEL, but the table cited shows the number of employees potentially exposed to cadmium, including those exposed to arsenic and lead [2, p. 9].

Monitoring data submitted by the industry suggest that the exposure monitoring for cadmium already being done in some plants covers all job categories with potential cadmium exposure [2, attachment I]. However, it seems likely that some additional monitoring may be necessary for the industry to achieve full compliance with the revised cadmium standard.

The extent of monitoring required by the standard depends in part on the number of job categories that are identified. JACA grouped workers into seven job categories; PHB distributed workers into over 45 classifications. OSHA believes the PHB data could be collapsed to conform with the JACA classifications. Assuming that current monitoring represents from 60 to 90 percent of that required under the new rule, OSHA estimates that, on average, additional monitoring will be required for three job categories per plant.

Monitoring would be conducted every six months for each of three shifts. A typical plant would have 18 additional samples analyzed for cadmium annually. These samples are already collected and analyzed for lead and/or arsenic, and thus no additional collection costs would be imposed by the cadmium standard. At a cost of $40 per sample for the lab analysis, the annual cost to the industry would be about $2,900.

Employees in this industry generally receive medical surveillance and quarterly biological monitoring [1, p. 6–20 and 2, p. 9]. Additional analyses would be needed for an estimated 400 exposed employees for cadmium in blood ($60 per sample), cadmium in urine ($60 per sample), and β_2-microglobulin in urine ($80 per sample). About 500 of each of these analyses are estimated to be needed annually for full compliance (including more frequent testing of some employees), resulting in a total annual industry cost of $100,000.

Requirements for medical removal may involve compliance costs in addition to those for more frequent monitoring estimated above. The criteria for mandatory removal would affect employees with the most extreme biological monitoring levels. The criteria for removal also allow for considerable physician's discretion. An estimated 1.5 percent of the exposed workforce may be removed initially on the basis of these criteria and the discretion of physicians.

Compliance with the new PEL for cadmium and other requirements of the final cadmium standard should prevent a continuing need to remove employees. The number of employees with relatively high past exposures who would be more likely to be removed should also decline through attrition. However, as the criteria for removal become broader in future years (lower levels of cadmium in blood and urine triggering mandatory removal),

additional employees may be subject to removal. The costs associated with the medical removal provisions are approximated by assuming that on average, 1.5 percent of the exposed workforce may be removed every 5 years.

The number of employees removed should be small enough to enable establishments to provide removed employees with alternative positions. Costs to the employer would include paying wage differentials over eighteen months and hiring and training new employees. The average cost per removed employee is estimated to be $5,000. An estimated 6 employees may be removed every five years, on average, in the lead refining industry, and the average annual cost for the industry would be $6,000.

The total annual cost for medical surveillance and medical removal provisions is estimated to be $106,000.

Employees at lead smelters and refiners are currently provided with "the full gambit of hygiene facilities, protective clothing," etc. for lead and/or arsenic exposure [2, p. 9]. This statement from industry generally confirms JACA's conclusion that additional costs would not be imposed by related provisions in the cadmium standard.

The revised cadmium standard may impose additional costs for recordkeeping. These costs are estimated to be $5 per employee per year or about $2,000 annually for the industry.

The estimated costs of compliance for the lead smelting and refining industry are presented in Table VIII–C36. The estimated total annual cost is $282,900, representing about $42,725 per plant for three plants and $154,725 for one plant in which additional engineering controls appear to be feasible.

TABLE VIII–C36.—ESTIMATED COSTS OF COMPLIANCE WITH THE REVISED CADMIUM STANDARD FOR THE LEAD SMELTING/REFINING INDUSTRY

Provision	Annualized cost ($thousands)
Exposure control	112.0
Respirator use	60.0
Exposure monitoring	2.9
Medical surveillance	106.0
Hygiene provisions	0.0
Recordkeeping and information	2.0
Total	282.9

Note: Costs do not include current expenditures.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

Economic feasibility of a 50 μg/m³ SECAL and 5 μg/m³ PEL. Compliance with the revised cadmium standard is considered economically feasible for the lead smelting and refining industry. The compliance cost imposed by the standard represents an incremental increase in exposure control costs and a marginal expansion of employee protection programs already instituted and widely applied in this industry. Many of the requirements of the revised cadmium standard overlap existing requirements and do not create new burdens.

JACA estimated that the average revenues of lead smelters and refiners were about $44 million, ranging from $30 million for a small facility to over $70 million for a large facility [1, p. 7–7]. Additional information was not provided to the record. The lead smelting and refining plants would typically have estimated compliance costs of less than 0.1 percent of revenues. For one plant in which additional controls may be feasible, the compliance costs would represent less than 0.4 percent of revenues. Costs impacts of this magnitude are consistent with the general conclusion of economic feasibility for this industry sector.

Lead prices are dictated by worldwide market factors. When prices are low, smelters and refiners will be unable to pass compliance costs on to customers. When price levels are high, large increases in profits are possible. JACA estimated that an increase in the price of lead of 6 cents per pound (as occurred recently within one year) should increase industry profits by $16.7 million annually. The estimated compliance cost would represent less than 0.6 percent of these profits.

Lead smelters and refiners should be able to absorb the estimated compliance costs into operating costs. The typical cost increase per plant approximates the labor costs for one additional employee, and the typical facility has over 100 employees. Costs of this magnitude should not have a significant effect on the viability of the operation or influence major production or investment decisions.

Finally, it may be the case that some engineering control costs identified in this rule should already have been put in place in order to comply with existing rules for lead and arsenic.

Notes

1. Exhibit 13, "Economic Impact Analysis of the Proposed Revision to the Cadmium Standard," Final Report, JACA Corporation, March 15, 1988.
2. Exhibit 19–32, "Comments of ASARCO Incorporated," ASARCO Inc., May 9, 1990.
3. Exhibit 19–43, Attachment J, "Technological Feasibility of a Workplace Standard for Airborne Cadmium at the Herculaneum Lead Smelter," Putnam, Hayes & Bartlett, Inc., November 2, 1989.
4. Exhibit 105, "The Cost of Engineering Controls for Reducing Workplace Exposure to Cadmium at Primary Producers," Bureau of Mines, U.S. Department of the Interior, September 18, 1990.

Plating

Industry overview. Plating involves coating one material with another in order to impart the characteristics of the plating material. Surfaces commonly plated include parts made of steel, brass, aluminum, and iron; common plating materials include zinc, chromium, copper, nickel, and cadmium.

Plating is most often used to protect surfaces from corrosion, but can also increase electrical conductivity and improve appearance. Plated parts are used in many manufacturing industries; the heaviest use is in the automotive, electronics, industrial hardware, and aerospace industries. The military frequently specifies cadmium-plated parts because of their superior performance under extreme conditions.

The electronics industry uses cadmium to plate chassis hardware, connectors, and fasteners. Cadmium-plated parts possess high conductivity, excellent solderability, and are easily bonded.

The aerospace industry specifies cadmium for plating to reduce corrosion between high tensile steel fasteners and aluminum alloys. Plated parts include bolts, major structural members, and landing gear parts. Cadmium provides excellent lubricity and performs well under extreme temperatures and in salty environments.

Automotive applications include plating nuts and bolts for suspension bars, brass and steel springs, and brake line connectors. Cadmium properties of importance to auto makers include lubricity and adhesion. Cadmium can be applied in thin coats which makes it an excellent plating material for small parts.

Cadmium plating is done with one of two basic plating methods. Electroplating is the most common and involves coating materials through electrodeposition by submerging them in a liquid mixture with the plating compound. Mechanical plating is a dry operation in which parts are coated with a powder in a tumbling process.

Cadmium plating is performed at approximately 350 to 400 facilities in the United States [4, p. 1]. Electroplating is the most common method of plating with cadmium, and only about 20 facilities currently use mechanical plating [8, p. 5–122]. At mechanical plating facilities, less than 10 percent of

This se
contain
publishe
Rule, a
correcti
the Fed
correcti
documer
documer
issue.

DEPAR

48 CFR

Acquisi

Correcti

In rule
on page
Wednes
followin

923.570-

1. On
a. In se
line, "sit
b. In se
first line,
lowercas

BILLING COI

additional employees may be subject to removal. The costs associated with the medical removal provisions are approximated by assuming that on average, 1.5 percent of the exposed workforce may be removed every 5 years.

The number of employees removed should be small enough to enable establishments to provide removed employees with alternative positions. Costs to the employer would include paying wage differentials over eighteen months and hiring and training new employees. The average cost per removed employee is estimated to be $5,000. An estimated 6 employees may be removed every five years, on average, in the lead refining industry, and the average annual cost for the industry would be $6,000.

The total annual cost for medical surveillance and medical removal provisions is estimated to be $106,000.

Employees at lead smelters and refiners are currently provided with "the full gambit of hygiene facilities, protective clothing," etc. for lead and/or arsenic exposure [2, p. 9]. This statement from industry generally confirms JACA's conclusion that additional costs would not be imposed by related provisions in the cadmium standard.

The revised cadmium standard may impose additional costs for recordkeeping. These costs are estimated to be $5 per employee per year or about $2,000 annually for the industry.

The estimated costs of compliance for the lead smelting and refining industry are presented in Table VIII–C36. The estimated total annual cost is $282,900, representing about $42,725 per plant for three plants and $154,725 for one plant in which additional engineering controls appear to be feasible.

TABLE VIII–C36.—ESTIMATED COSTS OF COMPLIANCE WITH THE REVISED CADMIUM STANDARD FOR THE LEAD SMELTING/REFINING INDUSTRY

Provision	Annualized cost ($thousands)
Exposure control	112.0
Respirator use	60.0
Exposure monitoring	2.9
Medical surveillance	106.0
Hygiene provisions	0.0
Recordkeeping and information	2.0
Total	282.9

Note: Costs do not include current expenditures.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

Economic feasibility of a 50 μg/m³ SECAL and 5 μg/m³ PEL. Compliance with the revised cadmium standard is considered economically feasible for the lead smelting and refining industry. The compliance cost imposed by the standard represents an incremental increase in exposure control costs and a marginal expansion of employee protection programs already instituted and widely applied in this industry. Many of the requirements of the revised cadmium standard overlap existing requirements and do not create new burdens.

JACA estimated that the average revenues of lead smelters and refiners were about $11 million, ranging from $30 million for a small facility to over $70 million for a large facility [1, p. 7–7]. Additional information was not provided to the record. The lead smelting and refining plants would typically have estimated compliance costs of less than 0.1 percent of revenues. For one plant in which additional controls may be feasible, the compliance costs would represent less than 0.4 percent of revenues. Costs impacts of this magnitude are consistent with the general conclusion of economic feasibility for this industry sector.

Lead prices are dictated by worldwide market factors. When prices are low, smelters and refiners will be unable to pass compliance costs on to customers. When price levels are high, large increases in profits are possible. JACA estimated that an increase in the price of lead of 6 cents per pound (as occurred recently within one year) should increase industry profits by $16.7 million annually. The estimated compliance cost would represent less than 0.6 percent of these profits.

Lead smelters and refiners should be able to absorb the estimated compliance costs into operating costs. The typical cost increase per plant approximates the labor costs for one additional employee, and the typical facility has over 100 employees. Costs of this magnitude should not have a significant effect on the viability of the operation or influence major production or investment decisions.

Finally, it may be the case that some engineering control costs identified in this rule should already have been put in place in order to comply with existing rules for lead and arsenic.

Notes

1. Exhibit 13, "Economic Impact Analysis of the Proposed Revision to the Cadmium Standard," Final Report, JACA Corporation, March 15, 1988.
2. Exhibit 19–32, "Comments of ASARCO Incorporated," ASARCO Inc., May 9, 1990.
3. Exhibit 19–43, Attachment], "Technological Feasibility of a Workplace Standard for Airborne Cadmium at the Herculaneum Lead Smelter," Putnam, & Bartlett, Inc., November 2, 1989.
4. Exhibit 105, "The Cost of Engine Controls for Reducing Workplace Ex to Cadmium at Primary Producers," B Mines, U.S. Department of the Interio September 18, 1990.

Plating

Industry overview. Plating inv coating one material with anoth order to impart the characteristi plating material. Surfaces comm plated include parts made of ste brass, aluminum, and iron; comm plating materials include zinc, chromium, copper, nickel, and c

Plating is most often used to p surfaces from corrosion, but can increase electrical conductivity improve appearance. Plated pa used in many manufacturing in the heaviest use is in the auton electronics, industrial hardwar aerospace industries. The milit frequently specifies cadmium-p parts because of their superior performance under extreme co

The electronics industry use cadmium to plate chassis hard connectors, and fasteners. Ca plated parts possess high con excellent solderability, and a bonded.

The aerospace industry sp cadmium for plating to reduc between high tensile steel fa aluminum alloys. Plated part bolts, major structural memb landing gear parts. Cadmium excellent lubricity and perfo under extreme temperatures environments.

Automotive applications plating nuts and bolts for st bars, brass and steel spring line connectors. Cadmium importance to auto makers lubricity and adhesion. Ca applied in thin coats which excellent plating material parts.

Cadmium plating is don two basic plating methods Electroplating is the most involves coating material electrodeposition by subm a liquid mixture with the compound. Mechanical p operation in which parts a powder in a tumbling p

Cadmium plating is pe approximately 350 to 400 United States [4, p. 1]. El the most common metho with cadmium, and only facilities currently use m plating [8, p. 5–122]. At m plating facilities, less th

the work involves cadmium [8, p. VI-134]. An estimated 1,200 employees are exposed to cadmium in plating establishments.

Cadmium plating can be done by independent plating companies and also by other companies as part of multi-faceted manufacturing operations. The analysis of the plating industry includes only those establishments engaged in plating as a primary business. Potential cadmium exposures and regulatory impacts at other establishments are analyzed in the sections for their respective industries.

Production processes. Electroplating with cadmium is usually conducted in a cyanide bath. The solution is prepared from cadmium oxide and sodium cyanide. Cadmium or cadmium oxide powder is weighed out and then dissolved in a salt solution which is added to the electroplating tank. As a current is passed through the solution, the positively charged cadmium metal ions are attracted to the part to be plated, thereby creating a cadmium coating.

Mechanical plating involves tumbling the parts to be plated in a barrel with a mixture of cadmium powder, glass beads, acid, and other chemicals. The cadmium powder is initially weighed out into paper bags, which are placed in the barrel intact and disintegrated by the acid. After the tumbling process is complete the parts are discharged onto a table provided with water sprays, where they are washed and separated.

Employee exposures. JACA identified two job categories with potential exposure to cadmium during electroplating operations, the operator and the maintenance technician. Based on exposure data representing over seven years of OSHA monitoring, JACA concluded that the geometric mean exposure for the workers was less than 0.2 $\mu g/m^3$ [1, p. 3-21].

An in-depth health hazard survey report of an electroplating facility was provided by NIOSH [2, Attachment 14]. Exposure monitoring results reported for cadmium did not include any quantifiable concentrations. A second in-depth health hazard survey report of another electroplating facility also failed to reveal any quantifiable concentrations of cadmium [2, Attachment 15]. NIOSH concluded in their testimony that sampling results in electroplating operations were generally at or below 2 $\mu g/m^3$ (the limit of analytical detection in the study) [3, p. 15].

The National Association of Metal Finishers (NAMF) cited a NIOSH technical report which evaluated cadmium exposures during electroplating "using an absolute worst case method." Samples were taken inches above the plating solution on hand operated tanks. The highest potential concentrations of cadmium ranged from 2 $\mu g/m^3$ to 15 $\mu g/m^3$. Monitoring conducted by the New York State Department of Labor indicated concentrations of less than 2 $\mu g/m^3$ above the operating tanks. [4, p. 2]. These results refer to area samples and do not represent personal eight-hour time-weighted average exposure levels.

Exposures during mechanical plating are higher than electroplating. One plant conducting mechanical plating with cadmium reported that during the past three years exposure levels ranged from 8 $\mu g/m^3$ to 38 $\mu g/m^3$ [5, p. 9]. The result of a single eight-hour sample taken during mechanical plating with cadmium was submitted by another plant as 33 $\mu g/m^3$ [8, Exhibit A, p. 10]. However, this sample "does not represent the normal range of exposures" because the monitoring was done during a "worst possible case scenario" created specifically to evaluate the highest potential exposure to cadmium [6, Exhibit B, p. 1].

A study conducted by the Cadmium Council estimated exposures separately for different work stations during mechanical plating [7, Table A6-1]. Exposures during weighing were estimated to be 92 $\mu g/m^3$, exposures while operating the barrel were estimated to be 60 $\mu g/m^3$, and exposures during other operations were estimated to be 16 $\mu g/m^3$. The study conceded that "the entire cadmium plating process is frequently done by one person" [7, p. 6-1] but did not provide information on the number of samples taken, the duration of the sample(s), or what actual exposures might be based on personal monitoring over a full shift. Weighing and barrel operations involving cadmium represent short duration, infrequent activities at mechanical plating plants [5, p. 4].

Existing and feasible additional controls. JACA described existing controls at electroplating facilities that included local exhaust ventilation and hoods over the material handling areas. JACA suggested that if further controls were needed, respirators should be used [1, p. 3-18 and 4-10]. Testimony from an electroplating facility confirmed that ventilation systems and glove boxes were already being used, and that other chemicals contribute to exposure problems during electroplating [8, p. VI-135 and p. VI-146].

NIOSH provided descriptions of two electroplating facilities. Ventilation systems were generally implemented as necessary, and NIOSH recommended some possible minor improvements [2, Attachments 14 and 15]. NIOSH concluded in their testimony that exposures for cadmium electroplating are "generally at or below 2 $\mu g/m^3$" [3, p. 15] and are "controllable to 1 $\mu g/m^3$ using available engineering controls" [3, p. 26].

A consultation report developed by the Michigan Department of Public Health described controls at a mechanical plating facility [6, exhibit A]. Ventilation systems were used for the weighing operation and for the mechanical plating area. The systems were considered adequate, but some changes in hood designs were recommended to improve their effectiveness.

Comments regarding existing controls were also provided by another mechanical plating facility [5, p. 9]. The company stated that local exhaust ventilation was provided at the plater barrel.

Technologically feasible limit for a SECAL. Data for mechanical plating operations were analyzed separately from electroplating since all available data indicated that mechanical operators were exposed to significantly higher levels of cadmium. Figure VIII-C27 graphically shows the different exposure profile for the 120 employees in the high exposure mechanical plating process versus the 1,080 employees in the low exposure electroplating category. Consistent with the methodology used for other industries, a *t* test was performed on the data and verified that the means of the two exposed populations were drawn from separate statistical distributions.

In Figures VIII-C28 and VIII-C29, all available exposure data for each data set were "fitted" to a straight line (OLS methodology). Currently, all exposures in the low exposure electroplating operations fall below 5 $\mu g/m^3$.

For each group, graphs were developed to model the effect of exposure reductions, based on engineering control solutions with efficiency ratings from a high of 80 down to 20 percent. Figures VIII-C30 and VIII-C31 show the projected reductions for both groups (the high efficiency 80 percent factor is closest to the "y" axis).

BILLING CODE 4510-26-M

FIGURE VIII-C27

PLATING

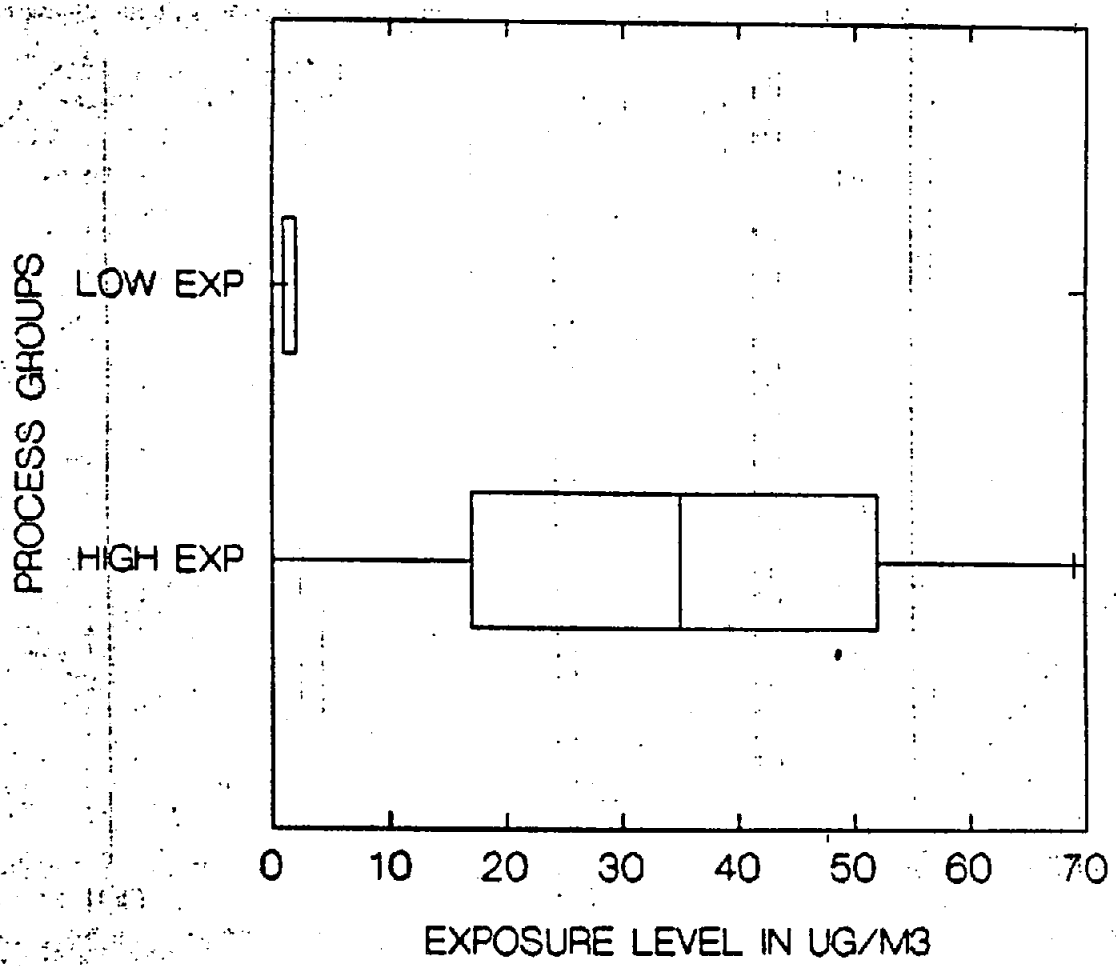


FIGURE VIII-C28

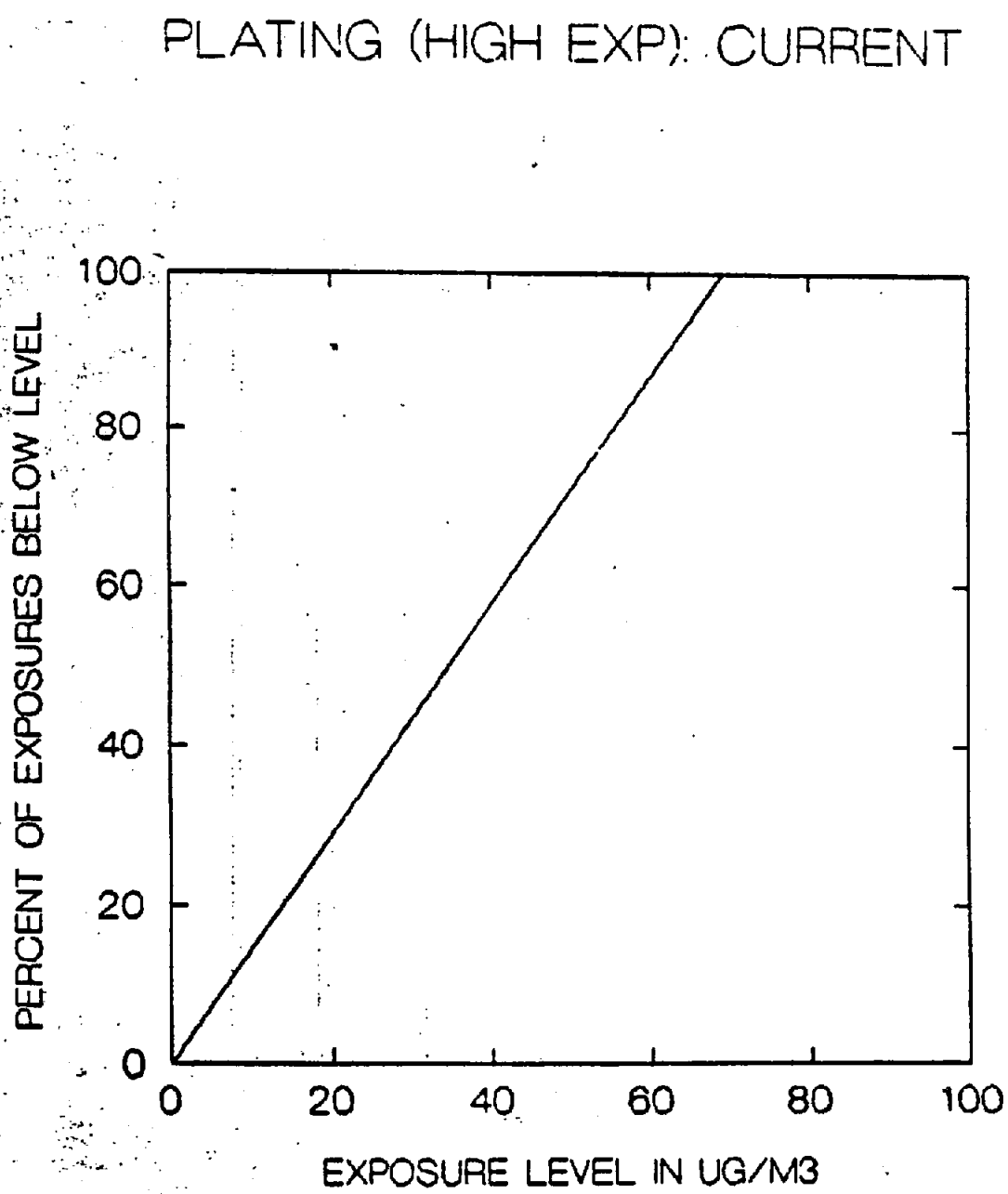


FIGURE VIII-C29

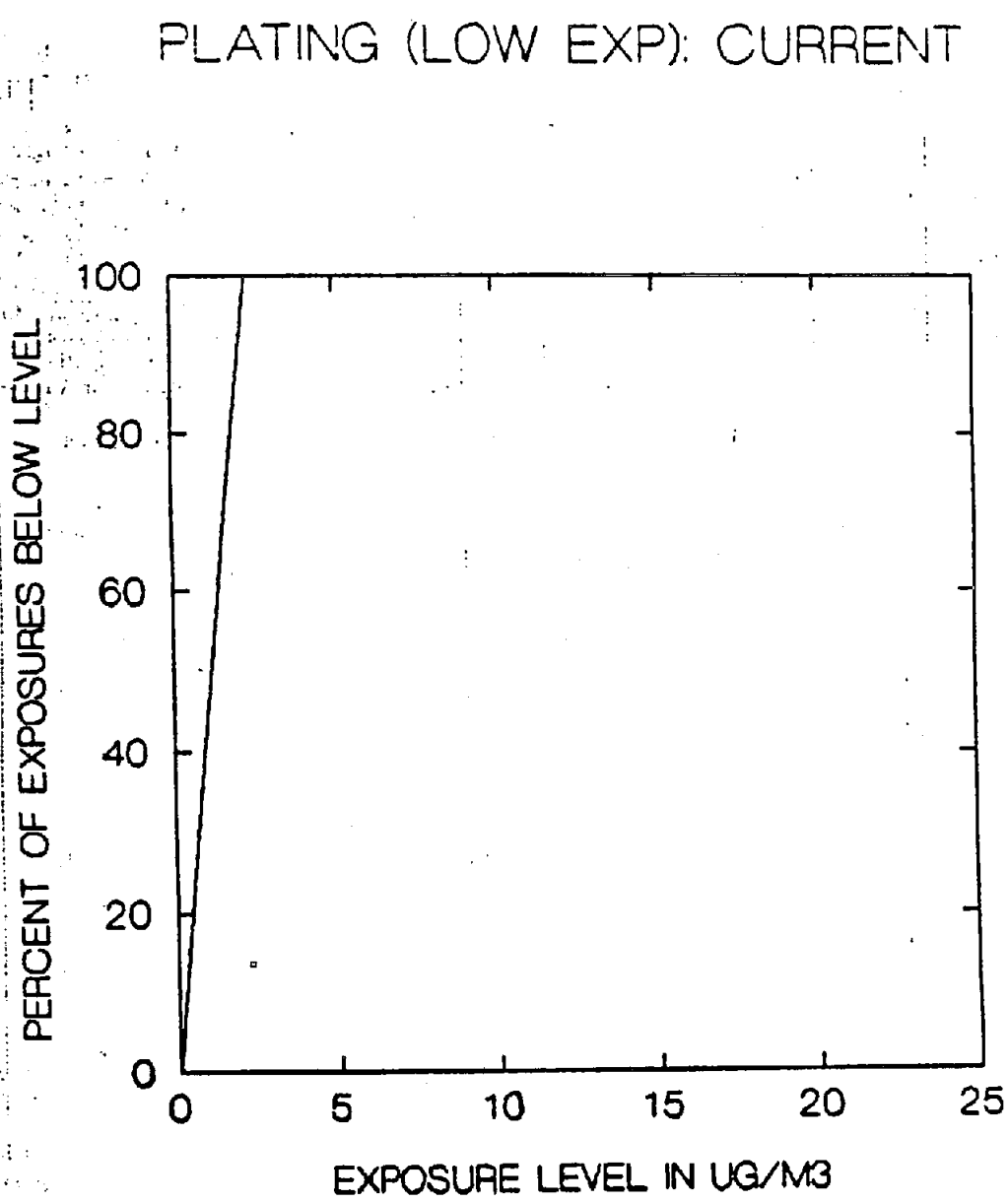


FIGURE VIII-C30

PLATING (HIGH EXP.): CONTROLLED 80%-2C

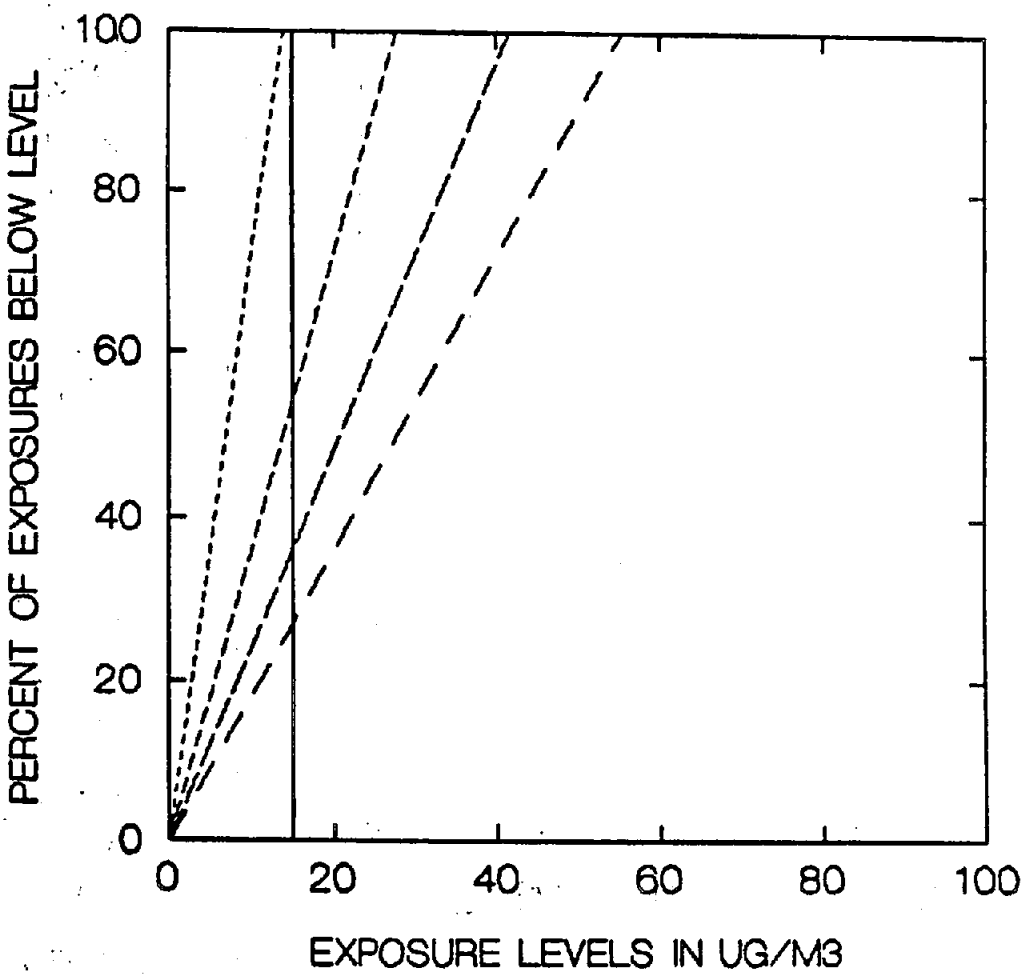
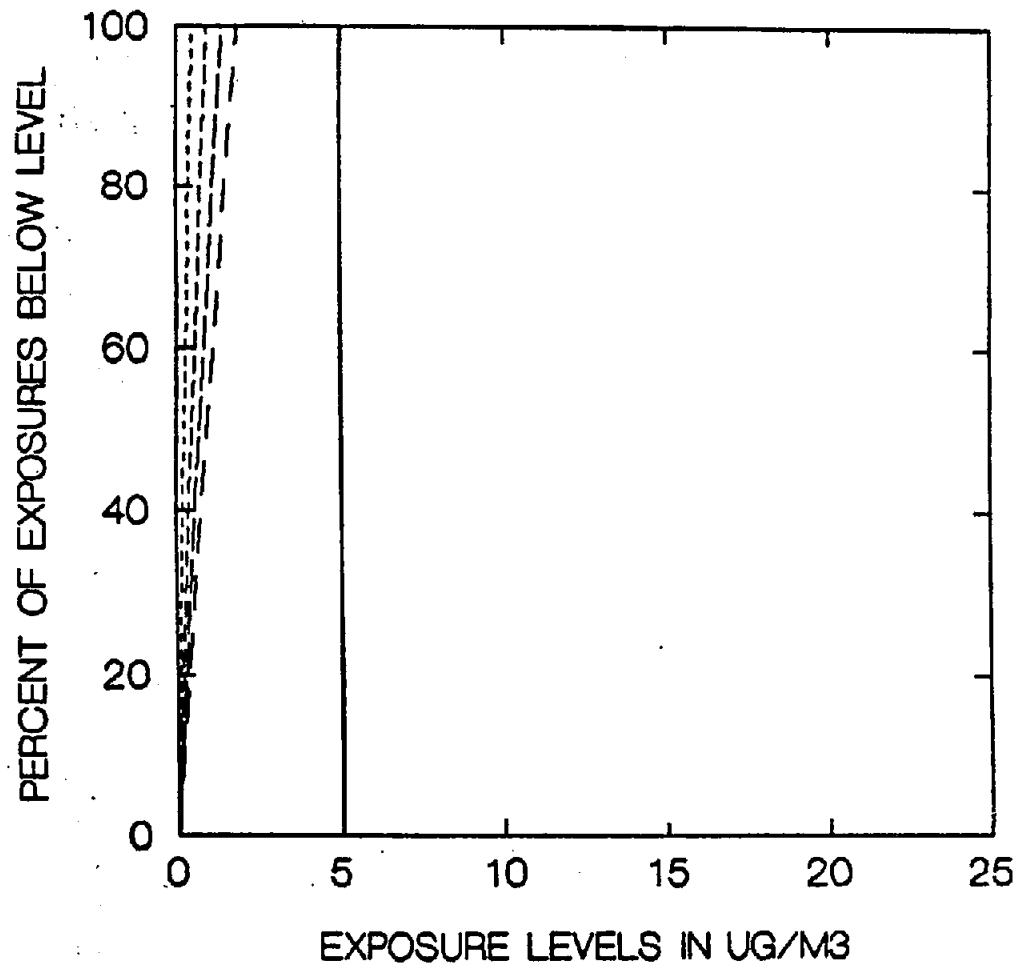


FIGURE VIII-C31

PLATING (LOW EXP.): CONTROLLED 80%-20%



BILLING CODE 4510-26-C

The selection of an appropriate engineering control factor was based on evidence and testimony in the record and economic feasibility considerations.

PACE evaluated a typical mechanical plating facility and reported that a ventilated sandblast booth ("a simplified type of glove box") was used for weighing operations [7, p. 6–1]. PACE recommended that a "much higher quality glove box" should be used in conjunction with better work practices and housekeeping procedures. These improvements could reduce exposures by over 90 percent during this operation. PACE also recommended the installation of a ventilation system and partial enclosure to control sources of cadmium-bearing mist during the barrel operation. Exposures were projected to be reduced by 85 percent as a result. PACE concluded that exposures could be reduced by up to 75 percent in other operations. Exposures from handling finished mechanically plated parts are considered insignificant because a process change recently introduced removes potential sources of dust before the parts are washed and dried.

The use of pre-bagged cadmium was suggested as a possible control option [3, p. 17], but this approach does not appear to be feasible in this industry [5, p. 4 and 6, p. 5].

Based on this review, a 60–80 percent reduction in exposure levels should be achievable for mechanical plating facilities. This reduction factor translates into a SECAL of 15 $\mu g/m^3$ for the mechanical plating operations. The PEL of 5 $\mu g/m^3$ is technologically feasible for electroplating operations, and most exposure levels for this group are already below this level.

For mechanical plating operations there are no apparent economic feasible constraints preventing them from achieving the 15 $\mu g/m^3$ SECAL.

OSHA concludes that a PEL of 5 $\mu g/m^3$ is technologically feasible for electroplating operations. Respiratory protection will be necessary during some mechanical cadmium plating operations.

Costs of compliance with a 15 $\mu g/m^3$ SECAL and 5 $\mu g/m^3$ PEL. Based on the evidence in the record, OSHA believes that electroplating facilities consistently maintain employee exposures below 5 $\mu g/m^3$ and would generally not need to install additional engineering controls.

Establishments performing mechanical plating with cadmium would be required to install engineering controls to the extent feasible. Testimony from a mechanical plating facility indicated that all feasible controls have already been implemented [8, p. 5–134]. As described above, mechanical plating facilities already use glove boxes, local exhaust ventilation, and other controls to reduce cadmium exposures. Nevertheless, some establishments will find it necessary to improve engineering controls to achieve compliance with the revised standard.

A pass-through airlock glove box, providing "a much higher quality" than conventional glove boxes [7, p. 6–4], would cost about $5,000 [7, Table A6–4]. The installation and use of a vacuum system is estimated to cost $15,000 initially and $8,000 annually for operating costs. A complete ventilation system with two hoods, make-up air, and clean air islands could be provided at a barrel operation without existing controls for about $60,000 plus $6,000 in annual costs.

Some mechanical plating facilities may not require any additional controls, some may only require minor improvements, and a few may need new controls. OSHA estimates that about two thirds of the facilities would incur costs for engineering controls, and that on average these facilities would need half of the engineering controls listed above or the equivalent. About 14 of 20 mechanical plating establishments would have an average annualized cost for engineering controls of approximately $13,500, and the annualized cost for the industry would be $189,000.

Shower facilities with a double-sided locker room could be provided for employees in mechanical plating operations for $35,000 in capital costs and $9,000 in annual costs [7, Table A6–4]. All facilities performing mechanical plating with cadmium need shower and locker facilities for their employees to comply with the revised standard. The annualized cost would be $14,700 per plant or $294,000 for the industry.

The National Association of Metal Finishers stated that the "use of protective clothing and respirators where required is standard practice within the industry." [4, p. 4]. However, it is likely that additional respirator use would be required by the revised standard during some mechanical plating operations. Plating facilities are estimated to have an average of three employees per plant [1, p. D–4], and employees in mechanical plating spend less than 10 percent of the time working with cadmium [8, p. VI–134]. The cost of providing respiratory protection for an average of one full-time employee per plant would be $300 per plant annually, and the total annual cost for the industry would be $6,000.

Exposure monitoring and medical surveillance programs are generally not implemented at plating facilities. However, most electroplating facilities should be able to keep exposures below the action level and avoid most of these requirements.

OSHA estimates that the plating industry consists of 400 establishments with 1,200 employees and two job categories per plant [4, p. 1 and 1, p. D–4]. Regular exposure monitoring may be required at 100 plants. At a cost of $40 per sample and $1,500 annually for collection, each of the affected plants would have an annual cost of $1,660. The annual cost for the industry would be $166,000, of which about $33,000 would apply to mechanical platers.

Medical surveillance is estimated to cost $250 for a medical examination and $215 for the collection and analysis of the required biological monitoring samples. Compliance with the revised standard is expected to involve 150 medical examinations and 300 biological monitoring samples annually. Employees in this industry are not expected to be affected by the medical removal requirements since occupational exposures are relatively low and intermittent. The total annual cost for the industry for medical surveillance requirements would be $102,000, of which about $22,000 would apply to mechanical platers.

Information, training, and recordkeeping requirements may involve incremental costs for plating establishments. These requirements would include provisions for establishing regulated areas, using warning labels, developing a compliance program, and providing information to employees and physicians. Some of these costs would already be required by existing standards or be included in current practices; requirements may not apply to establishments with exposures consistently below the action level. Additional costs are estimated to average $100 per employee per year for about 25 percent of plating establishments. The total annual cost for the industry would be $30,000, of which about $6,000 may be borne by mechanical platers.

Compliance costs for the plating industry are summarized in Table VIII–C37. The total estimated cost is $787,000 annually, of which $237,000 is for electroplating and $550,000 is for mechanical plating.

Economic feasibility of a 15 $\mu g/m^3$ SECAL and 5 $\mu g/m^3$ PEL. The revised cadmium standard with a SECAL of 15 $\mu g/m^3$ is considered economically feasible for the cadmium plating industry.

Average annual revenues from cadmium plating are estimated to be

$500,000 per facility, and the average pre-tax profit margin is 4.4 percent, resulting in average estimated annual profits of $22,000 [9, p. VI–16]. Almost all facilities that plate with cadmium also plate with other materials [1, p. 7–10], and thus total revenues and profits per plant would be higher.

TABLE VIII–C37.—ESTIMATED COSTS OF COMPLIANCE WITH THE REVISED CADMIUM STANDARD FOR THE CADMIUM PLATING INDUSTRY

Provision	Annualized cost ($thousands)		
	Electroplating	Mechanical plating	Total
Exposure control	0	189.0	189.0
Respirator use	0	6.0	6.0
Exposure monitoring	133.0	33.0	166.0
Medical surveillance	80.0	22.0	102.0
Hygiene provisions	0	294.0	294.0
Recordkeeping/ information	24.0	6.0	30.0
Total	237.0	550.0	787.0

Note: Costs do not include current expenditures.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

Over 90 percent of the establishments in this industry are electroplaters. These establishments generally have sufficiently low exposures so that compliance with the standard can be achieved at minimal or no additional expense. If exposures at an electroplating facility are such that medical surveillance and exposure monitoring of employees would be required, the additional cost would typically be less than $3,000 per year. Electroplating facilities providing cadmium plating should be able to offset compliance costs with an average price increase of less than 0.5 percent.

Mechanical platers will face higher compliance costs than electroplaters. The total annual compliance cost may reach $30,000 at facilities that have not implemented adequate controls but would be less for establishments with existing controls. Mechanical platers would not be competitively disadvantaged in comparison to electroplaters. Mechanical plating costs more than electroplating, and customers do not use it unless they have to; the two methods of plating are not interchangeable [6, p. 4 and 8, p. VI–143].

A representative mechanical plater has "revenues of about $1 million * * * Revenues from mechanical plating account for about 35 percent of the total, or about $350,000." [10, p. 4–4]. An increase in the price of mechanical cadmium plating of less than 10 percent would offset the estimated compliance costs for these establishments.

The cost of plating components generally comprises a small fraction of the cost of final products such as automobiles, and the estimated increase in plating costs would translate into negligible increases in prices for products with cadmium plated components. Where properties of cadmium plating are essential, such as in some military applications, the cost increase could be passed through to customers. The automobile industry and the military together account for over 80 percent of the demand for mechanically plated components [10, p. 4–4].

The costs associated with cadmium plating may be less than those estimated above to the extent that market forces lead to a more efficient solution for the industry. Some facilities may discontinue cadmium plating operations or make production schedule changes to take advantage of the 30 day exclusion provision in the rule. Other facilities may increase cadmium plating and be able to spread compliance costs over a greater percentage of production.

Such shifts in production would not constitute a major structural change in the industry. The percent of revenues derived from cadmium plating varies among plating establishments and for many firms only small adjustments would be necessary to eliminate or concentrate on cadmium related business. Recent environmental regulations, including water pollution standards, are already causing such a trend towards specialization throughout the industry [8, p. VI–147]. Also, "most platers appear sufficiently flexible to respond relatively easily to new specifications for plating different metals." [10, p. 4–5].

The average increase in prices associated with the estimated compliance costs would not threaten the viability of the industry or cause any significant contraction. Compliance costs for over 90 percent of the establishments would be minimal. Costs are primarily concentrated in mechanical plating; demand for this more expensive and specialized service is relatively inelastic and should not be significantly impacted.

The trade association for the plating industry emphasized that most of the affected establishments were small businesses for whom the implementation of the standard would cause "major problems." [4, p. 5]. The association recommended that the standard be coupled with a technical assistance program funded by the government for small businesses.

OSHA recognizes that some establishments may need assistance in complying with safety or health regulations. The Office of Compliance Assistance and representatives of regional and area offices are available for answering questions and offering advice to small businesses. In addition, small businesses may take advantage of OSHA's consultation program which conducts a comprehensive assessment of facilities, provides guidance, and makes recommendations.

Notes

1. Exhibit 13, "Economic Impact Analysis of the Proposed Revision to the Cadmium Standard," Final Report, JACA Corporation, March 15, 1988.

2. Exhibit 19–26, "Comments of the National Institute for Occupational Safety and Health on the Occupational Safety and Health Administration's Proposed Rule on Occupational Exposure to Cadmium," U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, May 7, 1990.

3. Submitted Testimony of NIOSH on OSHA's Proposed Cadmium Rule, Draft 2, July 6, 1990.

4. Exhibit 5, "NAMF Comments Occupational Exposure to Cadmium," National Association of Metal Finishers, May 1, 1990.

5. Exhibit 99, "Additional Comments Filed on Behalf of the Cadmium Council," Prather, Seeger, Doolittle & Farmer, September 18, 1990.

6. Exhibit 100, "NAMF Amended Comments Regarding Occupational Exposure to Cadmium," Reilly Plating Company, September 14, 1990.

7. Exhibit 19–43, Attachment L, "Feasibility and Cost Study of Engineering Controls for Cadmium Exposure Standard," PACE Incorporated, April 30, 1990.

8. Hearing Transcript, June 11 and 12, 1990.

9. Exhibit 15A, "Preliminary Regulatory Impact and Regulatory Flexibility Analysis for the Proposed 5 $\mu g/m^3$ Cadmium Standard," Office of Regulatory Analysis, OSHA, U.S. Department of Labor, January 22, 1990.

10. Exhibit 19–43, Attachment I, "Economic and Technological Feasibility of a 5 Microgram per Cubic Meter Workplace Standard for Airborne Cadmium," Putnam, Hayes & Bartlett, Inc., April 30, 1990.

Dry Color Formulators

Industry Overview. Cadmium pigments are purchased by companies in several industries for applications in the manufacture of plastics, ceramics, specialty coatings, and other products. Some companies purchase cadmium pigments directly from the manufacturers; many companies rely on intermediate compounders to formulate custom color concentrates and resin concentrates. The compounders are referred to by the industry as dry color formulators.

The Dry Color Manufacturers' Association (DCMA) estimates that the market of pigment users consists of "hundreds of companies and thousands of employees" [1, p.5], and that formulators of plastic resins constitute "a very large market" for cadmium pigments [3, p. 44]. The Society of the Plastics Industry stated in its comments that over 100 member companies are involved in the compounding business (including concentrate producers and resin producers) [4, p. 7]. A representative of the Cadmium Pigments Committee of DCMA testified during the hearings that 1,000 direct customers of manufacturing members were identified (including formulators and firms in other industries), and that the firms involved in compounding "are by and large very, very small companies" [5]. OSHA estimates that there are approximately 700 separate dry color formulators using cadmium pigments and that these plants employ on average, 10 workers each. These estimates are consistent with the numbers used in the preliminary analysis (which were not directly challenged or refuted by interested parties), with other evidence in the record, including data from JACA [2, p. C-4] and trade associations [4, p. 1 and p. 7; 1, p. 5], and with information presented at the public hearings [5].

Production processes. Dry color formulators compound cadmium pigment material into colored concentrates. The products are considered to be "very customized" [5], virtually made to order in a batch production process. The formulators purchase pigments in dry bulk form. The raw pigment is measured and mixed into a matrix with other materials. The matrix may contain as much as 50 percent cadmium pigment.

The pigment mixture is blended and then compounded, extruded, or dispersed into a shape suitable for further processing. Often the colored resin concentrates must be ground to a powder for further blending or made into pellets. Plastic resin pellets are packaged and sold as the final product.

The pellets in turn are used by molders in making plastic products and by other firms using cadmium pigment concentrates. Subsequent employee exposures to cadmium during the production of plastics and during other manufacturing processes using products made by formulators are likely to be minimal or nonexistent because the cadmium pigment has in effect been encapsulated or made part of a solution [6].

Employee exposures. Formulators create specific color formulations that span the full spectrum of colors. As many as 4,000 different variations of colors may be produced from the relatively limited color palette provided by the pigment manufacturers. The quantity of each blend produced can range from five pounds to five thousand pounds, depending on the customer order [7].

Cadmium pigments are not used to produce all color combinations and may not be used at all on some days [7]. Operators "in the pigment using sector may only be exposed to cadmium pigments in one batch operation for a short period of time. * * * these short term exposures may only last a few minutes a week" [3, p. 75]. Occupational exposure to cadmium in the dry color formulator sector of the pigments industry is thus considered to be intermittent.

The airborne concentrations of cadmium created during the production of a batch of concentrate involving cadmium pigments are characterized by several sources in the record. JACA Corporation developed a preliminary occupational exposure profile for cadmium which categorized employees into cross-industry occupations [2]. This approach reflected the belief that exposures were more likely to be similar for certain types of work across industries. The JACA report included a full breakdown by industry of the employees in each occupational category; employees of formulators were included in the occupational category of chemical mixing and milling.

The exposure data presented by JACA for formulators are based on over 200 samples. The data have a range of 0.05 $\mu g/m^3$ to 710 $\mu g/m^3$, a geometric mean of 3 $\mu g/m^3$, and a median of 5 $\mu g/m^3$.

Well-documented exposure data on pigment users was submitted to the record by NIOSH in two health hazard evaluations [8]. At one facility, all exposures were less than 10 $\mu g/m^3$ on an eight-hour time-weighted average (TWA8) basis. Exposures occurred during short term material handling operations. NIOSH noted that better industrial hygiene practices could be implemented at the plant, such as vacuuming or damp mopping instead of dry sweeping. The second study found exposures ranging from 5 $\mu g/m^3$ to 25 $\mu g/m^3$ while adding pigments and during color changes.

Exposure data were also submitted to the record by a company with two plants using cadmium pigments to formulate custom colored plastics [9]. At one plant the weighted mean exposure level for the job categories with cadmium exposure was 4.4 $\mu g/m^3$. Of the 101 employees exposed, the highest mean exposure level occurred among sixteen blending operators at 7.5 $\mu g/m^3$. Data from the second plant indicate that there were approximately 60 employees exposed at an average of 10 $\mu g/m^3$ TWA8.

The higher exposures occurred during cleaning and other periodic tasks, which occur whenever a color blend has been completed and the next blend must be prepared. These activities cause intermittent exposure, and the duration and frequency of the exposure are not predictable [9]. "The variability of exposure is very large, with individual handling styles affecting exposure levels greatly." [12].

Current employee exposures in this industry appear to be generally below 20 $\mu g/m^3$.

Existing and feasible additional controls. The operations involving employee exposures to cadmium in pigment-using establishments can be controlled in a variety of ways. Standard technologies for controlling exposures in such operations have been developed and implemented in this and other industries. Feasible controls include local exhaust ventilation, general ventilation, and good housekeeping practices such as vacuuming and damp mopping. Appropriate work practices can also help reduce exposures by minimizing airborne dust.

The batch operations involved in the process cause intermittent, variable exposures and require frequent clean-outs. With a PEL of 5 $\mu g/m^3$, respiratory protection would probably be necessary during these activities even after the implementation of feasible engineering controls. Comments provided by one pigment user indicate that exposures above 5 $\mu g/m^3$ occur with local exhaust ventilation present at all points of exposure [9]. Some commenters claimed that achieving levels below 5 $\mu g/m^3$ with engineering controls and work practices was infeasible [1,3,4,10,11].

Comments regarding operations at two formulating facilities included details on the feasibility of additional controls. At one facility exposures could be reduced by installing ventilated work stations with downdraft airflow, adding a dust collection system for the pigment blender, making improvements in the blender to prevent dust from escaping, and modifying material handling systems to reduce the amount of handling. Exposure reduction at the other facility would involve the installation of dust collectors and ventilation systems in two major areas, the replacement of pigment blenders, the installation of a masterbatch feeder, and the use of portable HEPA vacuums [12].

A PEL of 5 $\mu g/m^3$ was asserted to be technologically feasible at these facilities [9, p. 3], but would "threaten the viability" of the custom-colored plastics business [9, p. 1]. Exposures above 5 $\mu g/m^3$ tend to occur during cleaning and maintenance activities and other intermittent activities such as weighing out pigments, even when conducted under a dust collecting hood. Respirators would provide an appropriate form of protection during such activities after engineering controls have been implemented to the extent feasible.

Technologically feasible limit for a SECAL or PEL. OSHA could not distinguish high and low exposure groups for this industry segment. All available data indicated that current exposure levels were below 20 $\mu g/m^3$ with means near 10 $\mu g/m^3$. Figures VIII–C32 and VIII–C33 graphically present the available exposure data and Figure VIII–C34 shows projected exposures with 80, 60, 40, and 20 percent efficiency factors.

Evidence on the availability and effectiveness of engineering controls to lower exposure levels in this industry was referenced above.

BILLING CODE 4510-26-M

FIGURE VIII-C32

DRY COLOR FORMULATORS

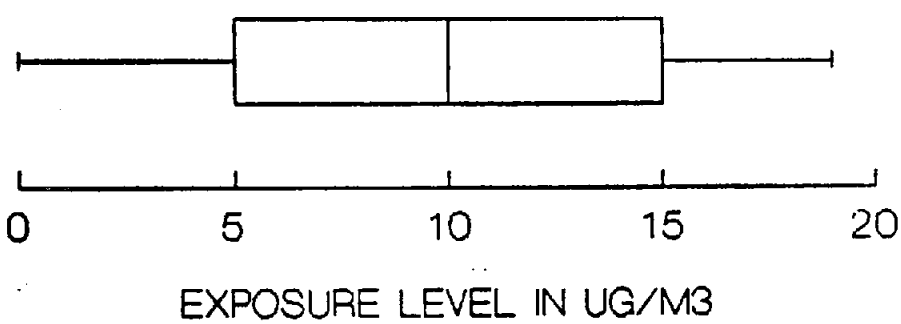


FIGURE VIII-C33

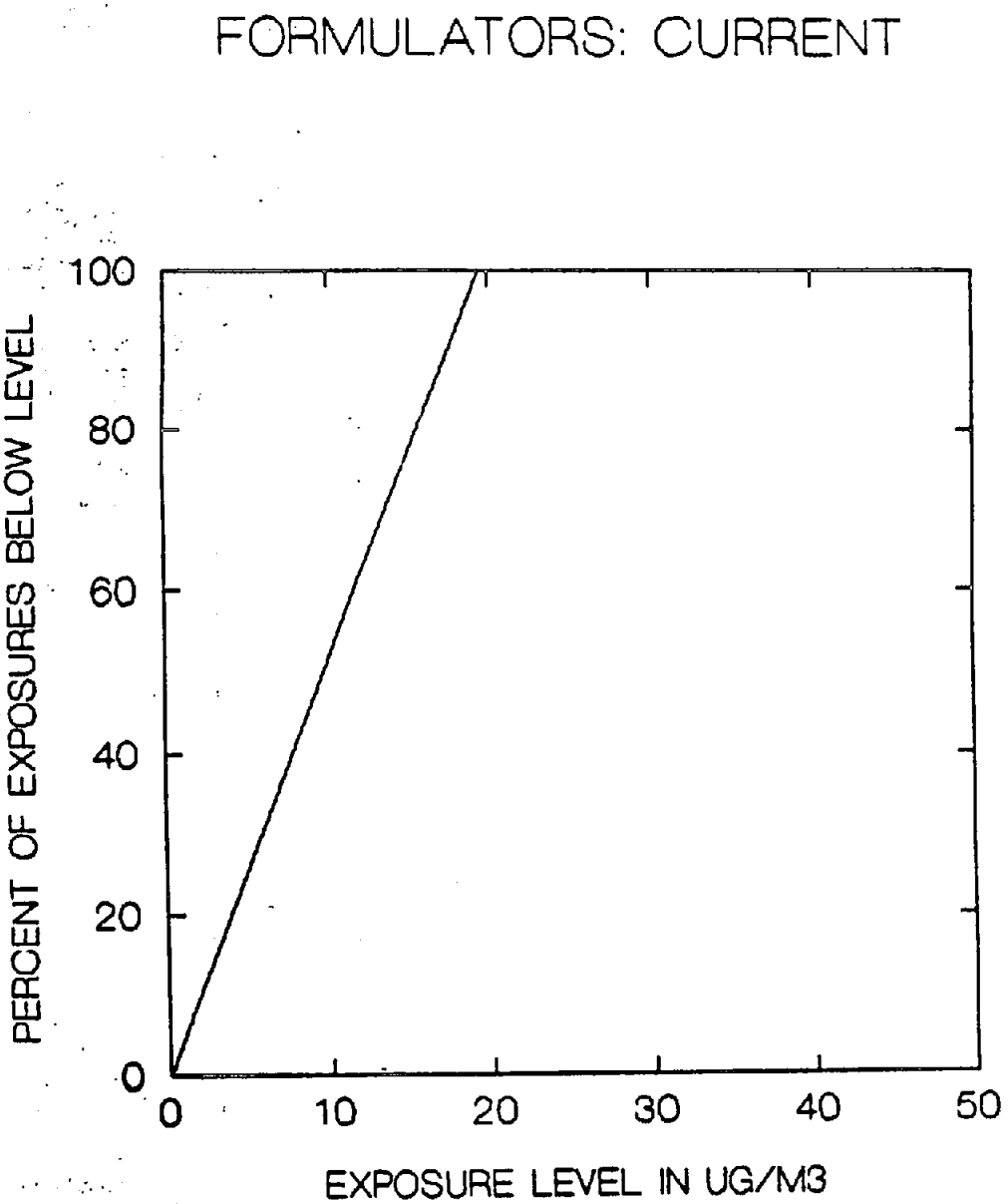
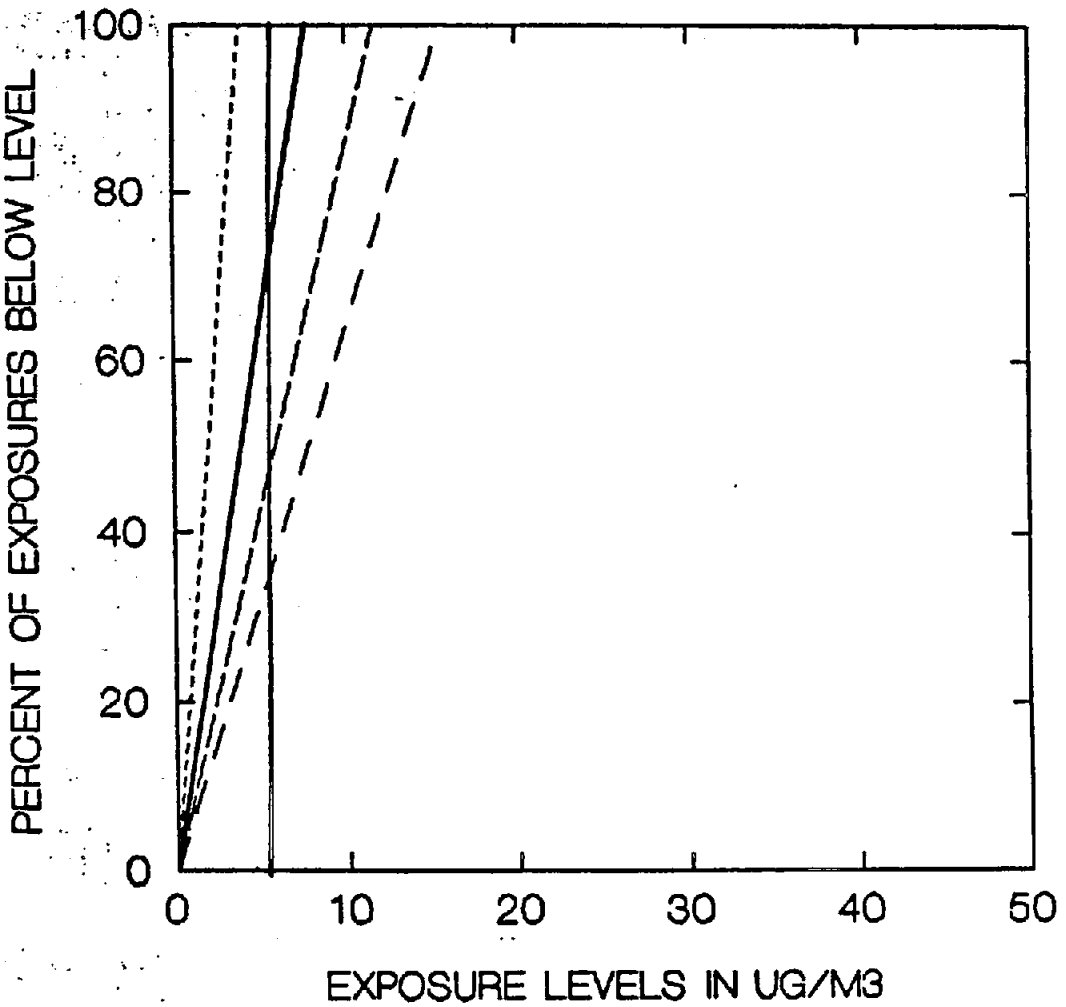


FIGURE VIII-C34

FORMULATORS: CONTROLLED 80%-20%



BILLING CODE 4510-26-C

Technology found to be successful includes standard control solutions such as local exhaust ventilation, general ventilation, and dust collection systems.

Based on the record evidence, it appears that more can be done within many plants to further reduce cadmium exposure levels, but that the targeted level of 5 $\mu g/m^3$ will be difficult to achieve for many plants in this sector. Other data in the record confirm that some firms are already below the PEL level.

On balance, OSHA believes that the PEL of 5 $\mu g/m^3$ is technologically feasible for this industry.

This determination reflects several considerations:

- A minority of plants in this sector have already achieved the PEL level for 8 hour TWA exposures.
- The thirty day exclusion provides the option for many formulators to regulate their intermittent use of cadmium, such that workers are exposed no more than 30 days per year. If successful, such firms will have no obligation to introduce additional engineering controls.
- The record supports the finding that additional engineering control technology and improved work practices can further reduce exposure levels in this subsector.

These controls are moderate in price and can reduce exposures by 60–80 percent. OSHA estimates that 20 percent of all firms in this industry could lower existing exposure levels through the introduction of additional engineering controls; in addition, improved housekeeping in all affected firms are expected to further reduce exposure levels.

Figure VIII–C34 illustrates that at the 60 percent efficiency level about 80 percent of employees in this sector would be at or below the PEL level of 5 $\mu g/m^3$.

Compliance with the PEL of 5 $\mu g/m^3$ may require the use of respirators during operations where cadmium pigments are used. Such respirator use would be intermittent following the introduction of feasible engineering controls and improved work practices.

Costs of compliance with a 5 $\mu g/m^3$ PEL. The costs of compliance include costs for additional engineering controls, increased respirator use, more comprehensive exposure monitoring programs, medical surveillance requirements, hygiene provisions, information and training, and recordkeeping requirements. The estimated compliance costs represent the incremental costs necessary for achieving compliance with the final rule from a baseline of current practices; these costs do not include current or past expenditures.

JACA provided estimates of the costs of installing new or improved local exhaust ventilation systems. In current dollars, the costs of these systems range from $51,000 to $112,000. Annual operating and maintenance costs were estimated to be 10 percent of the capital cost. [2, table 6–1]. JACA projected that new or improved ventilation systems could be installed for most employees in the occupational category of chemical mixer.

PACE provided cost estimates for several types of controls in its analysis of other industries that would be applicable to reducing exposures for formulators [10]. Controls included enclosure and back-draft exhaust ventilation, with a capital cost of about $30,000 and an annual cost of about $1,500. Controls at another operation included improved ventilation and increased wash down of surfaces to prevent contaminant accumulation; the capital cost would be $25,000 and the annual cost would be $4,000.

Details of an exposure reduction program recently completed by a formulator were submitted to the record by a trade association representing the industry [4, p. 8]. The program included improved ventilation systems with dust pick-up booths or dust pick-up systems at six locations, ranging in cost from $1,200 to $7,000, and a central vacuum system costing $18,000. The cost of the program also included new batch mixing vessels costing $500,000. While no evidence was provided indicating the effectiveness of such vessels in reducing exposures, it was noted that "virtually all the plant workers would have to be placed in respirators" after new batch mixing vessels were installed in order to achieve compliance with a PEL of 5 $\mu g/m^3$ [4, p. 8]. Since new mixing vessels only provide a marginal reduction in exposures and may produce significant economic impacts for many firms, this measure was judged to be impractical and not vital to controlling the problem.

Estimated costs of controls for two other formulator establishments were provided to the record in public comments. At one establishment, the installation of ventilated work stations incorporating downdraft airflow was estimated to cost $50,000; the cost of a pigment blender dust collection system was estimated to be $11,000; improvements to prevent dust escaping while blending would cost an estimated $2,000; a new pigment storage/retrieval system would cost $100,000; and the installation of a feeder on an extruder would cost $18,000. At the second establishment, the installation of dust collector and ventilation systems in two major areas would cost an estimated $1 million; the replacement of pigment blenders would cost $1.2 million; a masterbatch feeder would cost $125,000; pressurization of the control rooms would cost $50,000; and ventilation of the color lab would cost $50,000 [12].

OSHA believes that compliance with the 5 $\mu g/m^3$ PEL can be achieved without the significant capital expenditures for engineering controls, noted above by the second establishment.

Descriptive information on existing controls for formulators using cadmium pigments was available for three facilities. Each of the facilities relied on local exhaust ventilation to reduce exposure levels [4, p. 9 and 9, p. 5]. Personal protective equipment and other elements of a comprehensive industrial hygiene program were also utilized. On the basis of these comments it is apparent that dry color formulators can implement engineering controls. No other comments to the record indicated the extent to which formulators have implemented engineering controls.

OSHA believes that opportunities for implementing additional feasible controls exist at many establishments. The preliminary analysis included an assessment of existing and feasible additional controls for workers in this industry. Commenters expressed concern about the impact of the rule in this industry. They did not challenge the cost estimates presented in the preliminary analysis, but emphasized that the costs should be isolated and carefully evaluated for this industry [3, 4, 13].

The total potential cost of additional engineering controls for the industry is based on an estimate that 20 percent of the firms lack appropriate controls. These plants will need new or improved ventilation systems, more sophisticated enclosures, or better dust control programs including vacuums. The prices for these controls would be comparable to those estimated for other industries [4, 12].

On average, a complete local exhaust ventilation system will cost an estimated $80,000 plus $8,000 in annual costs; a central vacuum system will cost an estimated $15,000 plus $8,000 in annual operating costs; and process enclosures or material handling modifications are estimated to cost $9,000. The actual controls implemented would vary depending on the particular circumstances in each plant; these estimates are intended to provide a general gauge of the costs involved.

Since plants in this sector are typically small, one of each type of control referenced above, will be

needed. The annualized cost for the combination would be approximately $33,000. Assuming 80 percent of existing plants currently have this combination in place, controls are costed only for the balance. The annualized cost of additional controls for the industry is estimated to be $4.62 million. For all plants in this sector, work practice changes involving more care when handling cadmium can be made at no cost.

According to comments provided by one company for two formulating facilities, employees are currently provided with respiratory protection when working in areas with cadmium exposure [9, p. 5]. As discussed above, some of the workers in this industry would probably need to wear respirators to comply with the 5 $\mu g/m^3$ PEL. In order to estimate the cost of compliance with the revised standard, OSHA assumes that 25 percent of the employees do not wear respirators and would need to be provided with one. Using a cost of $300 per employee per year [14, Attachment III, p. 1], the total annual cost for the industry would be $525,000.

Establishments in this industry would be required to conduct exposure monitoring for every job category semi-annually. A large facility with over 100 employees identified three job categories affected [9, p. 5]; smaller plants also have three job categories. Comments about exposure levels in this industry indicate that some monitoring is currently being done [9, p. 5 and 4, p. 9], but not to the extent required by the revised standard. OSHA estimates that about 25 percent of the required monitoring is currently being conducted.

The costs of exposure monitoring are estimated to be $40 per sample taken and $1,500 annually per plant for the services of an industrial hygienist or other competent person. The total cost of the additional monitoring required by the standard is estimated to be $913,500 [($1500+$40*3*2) *700*0.75].

Compliance with the medical surveillance requirements would require additional costs. In the preliminary analysis, it was estimated that workers in this industry are being provided with annual medical exams, and the evidence in the record does not dispute this conclusion. Since medical exams would only be required every two years by the revised standard, this requirement should not involve added costs.

Employers would also have to provide biological monitoring at least annually for exposed employees. The lab analyses for cadmium in blood and urine samples are estimated to cost $60 per sample; lab analyses would cost about $80 per sample for β_2-microglobulin tests; and the estimated costs of collection are $5 per sample. Such monitoring may be necessary for an estimated 75 percent of the employees. The cost of providing the basic biological monitoring was increased by 10 percent to include additional medical surveillance that may be required for some employees. The total annual cost of biological monitoring would thus be about $1.242 million [($65+$85+$85)*7000*0.75*1.1].

Provisions for medical removal are not expected to have significant compliance costs in this industry. Occupational exposures in this industry are relatively low and intermittent, and no employees are expected to meet the criteria for mandatory removal. To allow for the possibility that some employees may be removed on the basis of a physician's determination, OSHA assumed that on average 0.1 percent of the exposed employees would be removed annually. With an average cost per removal of $5,000 associated with removal benefits and hiring and training costs, the total annual cost to the industry would be about $35,000.

The total annual cost of compliance with the medical surveillance provisions for this industry is estimated at $1.277 million.

The revised provisions for hygiene facilities, work clothing, and information and training appear to be complied with in this industry [9, p. 5]. Additional recordkeeping requirements are estimated to cost about $5 per employee or $35,000 for the industry.

Table VIII–C38 summarizes the costs of compliance for the dry color formulator industry. The total annualized cost is an estimated $7.371 million.

Economic feasibility of a 5 $\mu g/m^3$ PEL. Compliance with the revised cadmium standard is economically feasible for this industry. The analyses of technological feasibility and costs presented above show that the changes required by the revised rule would not involve significant adverse impacts for most establishments.

The total estimated cost of compliance represents a small percent of industry revenues. One company estimated that revenues associated with the color business at two formulating facilities with a combined workforce of over 180 employees were $25 million [9, p. 13]. In order to compare revenues with costs on an industry-wide basis, the revenues per employee at this company were applied to the total estimated number of workers in the industry.

TABLE VIII–C38.—ESTIMATED COSTS OF COMPLIANCE WITH THE REVISED CADMIUM STANDARD FOR THE DRY COLOR FORMULATOR INDUSTRY

Provision	Annualized cost ($thousands)
Exposure Control	4,620.0
Respirator Use	525.0
Exposure Monitoring	913.5
Medical Surveillance	1,277.0
Recordkeeping and Information	35.0
Total	7,370.5

Note: Costs do not include current expenditures.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

Total revenues are thus estimated to be over $900 million, and the estimated compliance costs would represent less than 0.82 percent of revenues.

Cadmium pigments are essential in many applications. Where substitution is possible, a reduction in quality is likely to result. Purchasers of custom formulated colors are likely to value the proximity of suppliers. The cost of pigment products generally constitutes a minor fraction of the cost of final products. Under these circumstances, the formulator industry should be able to recoup compliance costs through very small increases in prices.

The slight increase in prices required to offset compliance costs should not threaten the viability of the formulator industry or produce any significant adverse impacts in other industries. Costs of compliance will vary among establishments; effects on individual firms will depend on the type of technology used and the extent of existing exposure controls.

As in most industries, competition may limit the ability of some producers to raise prices to fully offset increases in production costs. As a result, some firms may experience a reduction in profits. Since the compliance costs are relatively modest on average, the standard is not expected to result in plant closures.

Establishments for which information is available in the record [4, 8, 9, 12] appear to need only minimal changes to achieve compliance with the revised standard. Some additional ventilation can be provided at emission sources, dust containment and collection equipment can be introduced or upgraded, and workers can be provided with personal protective equipment including respirators with HEPA filters, rubber gloves, and laundered uniforms. OSHA concludes that workers in this industry can feasibly be protected from exposure to 5 $\mu g/m^3$ levels of cadmium

with an appropriate industrial hygiene program that includes the intermittent use of respirators.

Sources

1. Exhibit 19–40, Dry Color Manufacturers' Association, Comments "Re: Occupational Exposure to Cadmium," May 11, 1990.
2. Exhibit 13, "Economic Impact Analysis of the Proposed Revision to the Cadmium Standard," Final Report, JACA Corporation, March 15, 1988.
3. Exhibit 120, Dry Color Manufacturers' Association, "Post-Hearing Comments," October 18, 1990.
4. Exhibit 19–41, Society of the Plastics Industry, Inc., "Comments of the Society of the Plastics Industry, Inc.," May 11, 1990.
5. Hearing transcript, p. 5–45, 5–46, and 5–47, June 11, 1990.
6. Hearing transcript, p. 5–41 and 5–46, June 11, 1990.
7. Hearing transcript, p. 5–42 to 5–44, June 11, 1990.
8. Exhibit 19–26, Attachments to NIOSH Comments, HETA 84–230–1528 (1984), and HETA 82–223–1340 (1983).
9. Exhibit 19–24, Comments from Hoechst Celanese Corporation, May 7, 1990.
10. Exhibit 19–43, Attachment L, "Feasibility and Cost Study of Engineering Controls for Cadmium Exposure Standard," PACE Incorporated, April 30, 1990.
11. Exhibit 19–43, Attachment I, "Economic and Technological Feasibility of a 5 Microgram per Cubic Meter Workplace Standard for Airborne Cadmium," Putnam, Hayes, & Bartlett, Inc., April 30, 1990.
12. Exhibit 118, Comments from Hoechst Celanese Corporation, October 5, 1990.
13. Exhibit 19–50, Comments of the United States Department of Commerce, May 22, 1990.
14. Exhibit 19–30, Big River Zinc Corporation, "Comments on OSHA Proposed Cadmium Regulation," May 10, 1990.

Electric Utilities

Industry overview. Electric utilities generate and distribute electricity throughout the United States. About 4,000 establishments produce over 2.5 trillion kilowatt-hours of electricity annually. Over half of the energy is produced from coal; most of the remainder is produced from nuclear power, hydropower, gas, and oil.

Production processes. Electric utilities convert energy sources into electricity by creating mechanical energy which then drives electric generators. Mechanical energy is produced by an engine, turbine, water wheel or similar machine, depending on the fuel or energy source used. Conventional steam systems produce over half of the nations electricity; nuclear steam, gas turbines, hydropower, and internal combustion engines are also used.

Employee exposures. Potential worker exposure to cadmium at an electric utility has two principal sources. First, repair and maintenance activities often involve welding, soldering, grinding, and cutting metals. Small quantities of cadmium may be released during these activities from cadmium-bearing base metals, cadmium-bearing surface deposits, welding rods, or solders. The second source is fly ash, a residue of burned coal, which may be present in and around negative pressure boilers. [1, p. 3].

Employee exposures do not normally occur during ordinary operating conditions in a utility plant. Exposures generally occur during intermittent inspection or maintenance activities associated with electrostatic precipitators, fly ash conveyance, and boiler outages. [1, p. 3].

According to the Edison Electric Institute (EEI), the "most comprehensive available exposure data pertaining to workers at electric utilities appear to be those compiled by the Tennessee Valley Authority representing cadmium fume exposures recorded between 1976 and 1985" [1, p. 4]. These data show that 45 percent of the workers sampled had exposures of 1 $\mu g/m^3$ or less as an eight-hour time-weighted average (TWA8) and that 92 percent had exposures of 5 $\mu g/m^3$ TWA8 or less. [1, p. 13]. There are approximately 25,000 to 50,000 workers potentially exposed to cadmium in this industry sector.

Occupational titles among employees with potential cadmium exposure include welder, boilermaker, steamfitter, and electrician [3, p. 2], but "it is correct to say that all jobs involved welding of some sort." [2, p. 4]. Comments from an electric utility confirmed that employees exposed to cadmium were "primarily welders and solderers" [3, p. 1].

A health hazard evaluation report conducted by NIOSH at a power plant in Columbus, Ohio also showed that exposures to cadmium are generally low and intermittent. Of the 37 samples analyzed, 32 did not have any detectable quantities of cadmium. Only one sample indicated an exposure above 7 $\mu g/m^3$, and it represented work on electrostatic precipitators. [4, table VI].

Existing and feasible additional controls. The final cadmium standard requires the use of feasible engineering and work practice controls as primary methods of compliance with the PEL. In addition, OSHA recognizes that respirators may be a necessary means of control in maintenance and repair activities and during brief or intermittent operations.

Activities with potential cadmium exposure in the electric utility industry may be amenable to engineering and work practice controls in some situations. For example, fly ash can be washed down prior to boiler maintenance activities, and fans or other ventilation systems can be used during maintenance operations. [1, p. 5].

Employees with potential exposure to cadmium would also have potential exposure to lead and arsenic [1, p. 9]. Existing occupational exposure standards for lead and arsenic already require feasible engineering controls to be used. Due to the nature of the activities with potential exposure and the unpredictability of exposure levels, the use of respiratory protection may be a necessary and appropriate means of controlling exposures in addition to feasible controls.

Employees performing welding, soldering, cutting, and maintenance and repair operations in this industry currently wear respirators to comply with the arsenic standards [5, p. 10–54]. In such circumstances, the use of respirators would also be an acceptable method of protection from cadmium exposure.

Technological feasibility of a 5 $\mu g/m^3$ PEL. The revised cadmium standard is technologically feasible in the electric utility industry. Exposure monitoring data demonstrate that current exposures are below the PEL for almost all employees. A representative of the industry trade association testified that the technological feasibility of the standard was not contested [5, p. 10–30].

Costs of compliance with a 5 $\mu g/m^3$ PEL. Compliance with the revised cadmium standard would not require additional costs for engineering controls or respiratory protection in this industry. Employees are protected from exposures to arsenic and lead in activities with potential cadmium exposure; no activities were identified for which protection from cadmium exposure would require protection in addition to that necessary for exposure to lead or arsenic. Because of the unpredictability of the work, "in most instances 100 percent of those workers * * * would be required to wear respiratory protection" at some point in time [5, p. 10–54].

Electric utilities currently conduct exposure monitoring for lead and arsenic as required by the existing standards. Employees with potential exposure to cadmium would be covered by this monitoring, but the samples may not be routinely analyzed for cadmium. Each plant may have five job categories or general types of work for which representative monitoring would be required on average. At a cost of $40 per sample, the required monitoring would cost $400 per plant and $1.6 million annually for the industry.

Medical surveillance is required by existing standards for employees with

exposure to lead and arsenic. Unlike the proposed cadmium rule, these standards require medical surveillance if an employee is exposed above the action level more than 30 days in a year. The revised cadmium rule includes a similar provision, requiring medical surveillance for employees exposed above the action level on 30 or more days per year. This change to the proposed cadmium rule should make the medical surveillance requirements more consistent with those in the lead and arsenic standards.

Employees receiving medical surveillance under the lead or arsenic standards are given annual physical exams [5, p. 10–55]. These exams could also satisfy the corresponding requirements of the revised cadmium standard. The cadmium standard also requires some additional tests that may not be currently provided. Biological monitoring for cadmium in blood, cadmium in urine, and β_2-microglobulin in urine would be required at least annually for employees qualifying for medical surveillance. The estimated cost for one set of these tests is $200.

Of the 500,000 employees comprising the entire work force in the electric utility industry, approximately 25,000 to 50,000 have potential cadmium exposure at some time during the year [5, p. 10–23]. Under an exclusion from medical surveillance of employees with less than 30 days of exposure above the action level, about 90 to 95 percent of those employees would be exempt from the biological monitoring requirements [5, p. 10–32].

OSHA estimates that the equivalent of about 3,000 employees would be given biological monitoring annually as required by the revised cadmium standard (this figure includes more frequent tests for some employees). The total annual cost to the industry would be $600,000. Provisions for medical removal are not expected to affect employees in this industry since exposures are relatively low and intermittent.

Existing requirements for arsenic and lead exposure include provisions for adequate hygiene facilities, regulated areas, protective clothing, information, and training. The requirements of the revised cadmium standard should not add any significant burden in these areas. Incremental costs and additional recordkeeping costs would be an estimated $5 per exposed employee annually. The estimated annual cost for the industry would be $188,000.

The estimated compliance costs for the electric utility industry are summarized in Table VIII–C39. Total annual costs of compliance are an estimated $2.388 million.

Economic feasibility of a 5 μg/m³ PEL. The revised cadmium standard with a PEL of 5 $\mu g/m^3$ is economically feasible for the electric utility industry. Testimony from the industry confirmed that the economic feasibility of the standard was not contested [5, p. 10–30].

TABLE VIII–C39.—ESTIMATED COSTS OF COMPLIANCE WITH THE REVISED CADMIUM STANDARD FOR THE ELECTRIC UTILITY INDUSTRY

Provision	Annualized cost ($thousands)
Exposure control	0.0
Exposure monitoring	1,600.0
Medical surveillance	600.0
Hygiene provisions	0.0
Recordkeeping and information	188.0
Total	2,388.0

Note: Costs do not include current expenditures.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

Operating revenues for electric utilities total over $140 billion; total operating income exceeds $20 billion. The estimated compliance cost represents less than one five-hundredth of one percent of the revenues and about one hundredth of one percent of operating income. Compliance with the cadmium standard is not expected to have any significant impact on the demand for electricity, on prices, on production, or on installed generating capacity.

The implementation of the cadmium standard would not involve new programs or large changes in procedures. The employees affected by the cadmium standard are already covered by the standards for lead and arsenic. An electric utility company commented that the standard "is quite similar to many recent standards (arsenic, asbestos, etc.) in the requirements imposed on the employer if certain exposure limits are exceeded." [3, p. 1]. Compliance with the revised cadmium standard would generally involve a minor expansion of established programs for exposure monitoring and medical surveillance.

Notes

1. Exhibit 9, Attachment A, "Testimony of James B. Lancour for the Edison Electric Institute," Jones, Day, Reavis & Pogue, July 10, 1990.
2. Exhibit 101, "Edison Electric Institute Post-Hearing Comments Occupational Exposure to Cadmium Proposed Rule," Edison Electric Institute, September 18, 1990.
3. Exhibit 19–5, "Tennessee Valley Authority Comments Applicable to Proposed Rule on Safety Standard 29 CFR 1910 Occupational Exposure to Cadmium," Tennessee Valley Authority, March 30, 1990.
4. Exhibit 19–26, Attachment 17, "Health Hazard Evaluation Report, City of Columbus Refuse Derived Fuel Power Plant, Columbus, Ohio," National Institute for Occupational Safety and Health, HETA 85–041–1709, July 1986.
5. Hearing Transcript, Thursday, July 19, 1990.

Iron and Steel

Industry overview. The U.S. iron and steel industry consists of about 80 companies operating over 120 facilities throughout the country [1, Attachment 2a, p. 1]. These plants produce about 100 million net tons of raw steel annually [1, Attachment 4, p. 1] and employ over 190,000 workers [1, Attachment 1, p. 1]. Steel is produced from molten iron, of which a small amount is also cast into solid forms to produce pig iron [1, Attachment 3, p. 13].

Over 90 percent of steel mill products are carbon steel; about 5 percent are alloys and the remainder are primarily stainless steel products. Over half of the products by weight are sheets and strip steel; bars, shapes, plates, piling, and tool steel make up about a third of steel shipments; and other products include pipe and tubing, tin mill products, and wire products. [1, Attachment 4, p. 1].

Production processes. The production of iron and steel begins with three basic raw materials: iron ore, limestone, and coal. Each of these materials is processed separately before being combined in a blast furnace.

Iron ore is crushed and further improved in one of several different process combinations that may involve mills, spiral concentrators, magnetic separators, sintering machines, or filters. Iron ore can also be prepared for steelmaking directly in some cases (bypassing the need for a blast furnace) through direct reduction.

Limestone is crushed and converted into lime by driving off carbon dioxide in either vertical or rotary lime kilns. Lime is primarily used as a flux in blast furnaces and steelmaking furnaces; it also has applications in drawing steel wire, in water treatment, and in acid neutralization.

Coal is crushed, sorted, and cleaned through the use of crushing machines, cyclones, washer jigs, and dryers. The cleaned coal is fed into coke ovens where high temperatures drive off gases, oils, and tar, which are made into various byproducts. The coke ovens convert coal into coke which is porous, burns uniformly, and retains its strength under other materials in a blast furnace.

Iron ore, lime, and coke are charged into the top of a blast furnace. Super-

heated air is blown upward from the bottom of the furnace, burning the coke. The interaction of the heat and gases removes oxygen from the iron ore; the lime acts as a cleansing agent. Molten iron collects in the bottom of the furnace and is drawn off as a white-hot stream of liquid iron. Most of the liquid iron is transferred to steelmaking furnaces, but it can also be cast into solid forms and sold.

Steel can be produced in different types of furnaces. In the United States approximately 60 percent of the steel is produced by basic oxygen furnaces; over 35 percent is produced in electric arc furnaces, and about 5 percent is produced in open hearth furnaces. In an oxygen furnace, high purity oxygen is blown into the top of the furnace at supersonic speed (in some modified oxygen furnaces, oxygen and other gases are blown in from the bottom). Electric arc furnaces use electrodes and open hearth furnaces use traditional open hearths to heat and burn the raw materials.

Steelmaking furnaces are charged with liquid iron from blast furnaces, iron ore from direct reduction, scrap material, lime and other fluxes. Impurities rise into a floating layer of slag which can be poured off. Alloys can be added to the furnace or combined with the steel as it is poured from the furnace into a ladle. The molten steel is then poured into molds to produce ingots or cast into slabs. Ingots and slabs are made into finished products through a variety of operations that shape the steel into strips, bars, plates, rods, beams, or rails. [1, Attachments 3 and 4].

Employee exposures. Cadmium is present only as a trace contaminant in the raw materials used for steelmaking and is not used in the manufacture of steel products. Cadmium has a boiling point one thousand degrees below the temperature needed to make iron and steel, and is volatized from the raw materials as they are melted. Potential exposures to cadmium may occur during furnace operations, welding operations, and other activities involving dust or fume such as maintenance work on pollution control equipment.

The American Iron and Steel Institute (AISI) submitted exposure monitoring data for steelmaking operations [1, p. 4–9]. These data include eight-hour time-weighted average (TWA8) personal samples and area samples and are summarized in Table VIII–C40. The ranges of exposures "are representative of the steel industry data and reflect current worker exposures." [1, p. 10].

TABLE VIII–C40.—CADMIUM EXPOSURE DATA FOR STEELMAKING OPERATIONS BASED ON AISI

Operation and occupation/area	Exposure range (μg/m³)
Blast furnaces:	
Keeper	0.01–0.04
Keeper helper	0.02–0.03
Trough repairman	0.03
General laborer	0.01
Mech. shop	0.00
Welder	0.30
Operator	0.50
Maintenance	3.00
Open hearth furnaces:	
Equipment operator	0.03
Third helper	0.01–0.44
Team leader	0.01
Third steel pourer	0.01
Basic oxygen furnaces:	
Craneman	0.23
First steel pourer	0.00–0.51
Material handler	0.05
Floor above vessel	0.90–1.00
Behind furnace	2.60
Lance change platform	1.30–2 90
Furnace charging aisle	1.30–6.90
Nozzle setter	0.20
Ladle liner and helper	0.20–0.30
Vesselman	0.20
Vessel operator	0.20
Binstocker	0.00–6.00
Millwright	0.09–1.73
Motor inspector	0.00–19.00
Desulfurizer	0.20
Laborer	0 20–5.70
Crane operator	0.00–0 20
Hot metal attendant	0.20
Melter	0.20
Lance changer	2.25
Elect. millwright	0.60
Equipment operator	0.14–0.40
Welder	0.04–0.40
Pipefitter	0.20–0.40
Metalographist	3.00
Pourman	0.00–0 01
Fabricator	0.12–0.50
Insulator	0.13–0.20
Scrap burner	0.00–0.07
Casting:	
Repairman	1.00
Runout operator	0.00–2.00
Helpers	2.00
Material handler	2.00
Caster operator	1.90
Tundish mason	0.08
Mech. and maintenance	0.76
Mold operator	2.00
Tundish repair	2.00
Ladleman and helper	0.90
Billet stocker	2.00
Runout helper	0.60–2.00
Millwright	2.00
Caster helper	2.00
Electric arc furnaces:	
Brickmason and attendants	0.02–2.00
Melt shop—mechanical	1.13–4.00
Motor inspector	1.06
Furnaceman and attendants	0.20–2.00
Helpers	0.40–1.04
Pourer	0.20–2.00
Melter	0.20–2.00
Laborer	0.20–22.00
Furnace pulpit operator	1.00–2.00
Caster operator and helper	1.00–2 00
Crane operator and chaser	0.20–42.00
Utility man	0.30–2 08
Electrician	0.20–0.90
Pitman and helper	0.20
Mobile equipment operator	0.20–1.10
Welder	0.90

TABLE VIII–C40.—CADMIUM EXPOSURE DATA FOR STEELMAKING OPERATIONS BASED ON AISI—Continued

Operation and occupation/area	Exposure range (μg/m³)
Ingot stripper and shopper	0.20
Boilermaker	2.40
Salvageman	0.60–0.90
Air pollution control operations:	
Electric furnace	86.00
BOF—Millwright	1.00
BOF—Laborer	370.00–510.00
Truck loader	9.24
Motor inspector	10.08
Millwright	12.25
Leaded steelmaking:	
Charging helper	11.34
3rd steel pourer	1.56
1st steel pourer	5.50
Welder	2.07
Scrap burner	8.70–11.60
Burner	2.60
Merchant mill operator	0.00
Looper	0.50
Galvanizing:	
Welder	1.19
Layout welder	1.19–1.50
Zinc pot tender	0.02
Miscellaneous	0.00–0.02
Utility man	0.20
Line inspector	0.20
Exit U-man	0.20
Line operator	0.05–0.20
Laborer	0.20
Assistant operator	0.20
Coil feeder	0.05
Elect. wireman	0.52
Millwright	0.02–0.03
Iron worker	0.21
Galvalume	0.50
Electroplating line	0.20
Potman	0.50
Craneman	0.50
Hot nail galvanizing operator	2.00
Sinter plants:	
Operator	0.50
Mechanic	1.30
Ore loader	0.30
Laborer	0.72–1.10
Baghouse attendant	0.60
Feederman	0.58
Mild steel cutting:	
Welder	1.60
Computer panel	1.60
Chalk tray	1.60
Terne operations:	
U-Man	0.00
Tract. operator	0.01
Line operator	0.08
Assistant operator	0.00
Line coiler	0.04
Equipment tender	0.00
Plate mill burner	1.94
Bar mill	0.00–0.15

Source: Exhibit 126, AISI, p. 4–9.

Exposure levels during open hearth furnace and blast furnace operations were less than 0.6 μg/m³ for all workers except for maintenance workers who had a level of 3.0 μg/m³. In basic oxygen furnace and casting operations, only four of the 43 job categories or areas listed had any TWA8 exposure levels above 3 μg/m³; two of these peaks involved area samples taken near the furnace. In electric arc furnace

operations the highest reported exposures for 17 of the 19 job categories are 4 $\mu g/m^3$ or less. During galvanizing operations, mild steel cutting, terne operations, and in sinter plants and mill operations, peak exposure levels did not exceed 2 $\mu g/m^3$ TWA8 in any of the 36 job categories and areas. Exposures above 5 $\mu g/m^3$ were reported for a few workers during leaded steelmaking and work on air pollution control systems.

Employee exposures in the steel industry were evaluated by JACA based on exposure monitoring data from NIOSH and OSHA. JACA characterized exposures for several occupations in the steel industry, including furnace operators; molding, casting, and forging operators; electroplaters; mechanics and maintenance employees; and millwrights. Employees in these occupations in the steel industry were considered to have exposures consistently below 5 $\mu g/m^3$. [2, p. 3–28 through 3–31, Table 3–10, and Appendix C].

AISI claimed that the NIOSH and JACA data were "not representative" of current exposures and expressed concern that OSHA's preliminary conclusions were not based on the best available information [1, p. 3]. The exposure data submitted by AISI appear to be consistent with the data used for the preliminary analysis and provide greater detail for specific types of operations in the steel industry. These data provide the basis for OSHA's revised analysis.

Existing and feasible additional controls. Steelmaking operations involve potential exposures to many hazardous substances and generate many emissions regulated by the Environmental Protection Agency (EPA). Steelmaking facilities have implemented and improved engineering controls constantly over the years to protect workers, comply with environmental regulations, and improve efficiency. The "best adequately demonstrated technological systems of continuous emission reduction controls are currently in place in steel making operations" [1, p. 2].

The OSHA lead standard requires all feasible engineering controls to be implemented to reduce lead exposures, and "[d]ue to the association of cadmium with lead" [1, p. 8] any engineering controls required by the revised cadmium standard should already be implemented. Requirements for engineering controls also apply to exposures to many other regulated substances found in the atmosphere of steelmaking plants. Since respirator use is common in the steelmaking industry, OSHA assumed that engineering controls have been implemented to the extent feasible.

AISI confirmed this conclusion and stated that "any further controls must be considered technically and/or economically infeasible." [1, p. 10]. Recent EPA regulations for both primary and secondary emissions for steelmaking operations "required the installation and use of the best demonstrated technological system of continuous emission reduction in new, modified, or reconstructed facilities. Virtually all steelmaking facilities are subject to these requirements." [1, p. 10]. AISI cited and included as part of its comments several studies of major steel operations conducted by EPA which describe feasible engineering controls extensively and document the above conclusion [1, p. 11 and Attachments 5 & 6].

Technological feasibility of a 5 $\mu g/m^3$ PEL. The revised cadmium standard with a PEL of 5 $\mu g/m^3$ is technologically feasible for the iron and steel industry. Current data submitted by industry demonstrate that employee exposures are consistently less than 5 $\mu g/m^3$ in almost all job categories.

Exposures may exceed the PEL in some operations, such as during leaded steelmaking or work on pollution control equipment. Five of 43 domestic member companies of AISI produce leaded steel [1, p. 12], and exposed employees wear respirators to comply with the current lead standard [1, p. 8]. To the extent that the requirements of the lead standard are being met, these employees are currently protected as required by the relevant provisions of the final cadmium standard. Respiratory protection may also be appropriate during other intermittent activities in which engineering controls are insufficient or infeasible, such as maintenance activities or work on dust collection systems.

Costs of compliance with a 5 $\mu g/m^3$ PEL. As discussed above, the implementation of additional engineering controls would generally be infeasible in steelmaking operations. Respiratory protection is used to reduce employee exposures to many other hazardous substances, including arsenic, lead, chromium, mercury, chlorine, and dozens of other elements or compounds [1, Attachment 5a, p. 3–40 and Attachment 6, p. 3–35]. Since cadmium is only present as a trace contaminant, exposures to cadmium would occur concomitantly with exposures to other regulated substances.

Based on the exposure monitoring data in the record, existing engineering controls should be able to keep cadmium exposures below 5 $\mu g/m^3$ for almost all employees. In addition, many or all of the remaining employees, such as those involved in leaded steel production and maintenance activities, are already provided with respiratory protection in accordance with the requirements of the revised cadmium standard [1, p. 3 and p. 8].

The record does not identify any situations for which it is demonstrated that protection from cadmium exposure would require measures beyond those already provided. Nevertheless, OSHA recognizes the possibility that the cadmium standard may require the use of respiratory protection for some employees for whom respirators would otherwise not be necessary.

The preliminary analysis accompanying the proposed cadmium standard, based on estimates provided by JACA, identified about 40,000 employees in the iron and steel industry potentially exposed to cadmium. This estimate included furnace operators, molders, casters, electroplaters, welders, maintenance and repair workers, and millwrights [2, p. 3–29 through 3–31 and Appendix C].

AISI emphasized that the data relied upon by OSHA were relevant to steel operations in the early 1980s and were "not representative of current operations" because since then "[t]he number of employees and job classifications have been reduced by more than 57 percent." [1, p. 3]. AISI also submitted data from the U.S. Department of Commerce indicating that the total number of production workers in 1990 was 194,000 [1, Attachment 1, p. 1] and testified that "[v]irtually all employees in the steelmaking operations are potentially exposed." [3, p. 9–284].

For purposes of estimating compliance costs, OSHA concluded that 190,000 employees may be potentially exposed to cadmium and that for all but 40,000 of these employees the exposure would be negligible. The exposure profile for the preliminary analysis indicated that about 10,000 employees in the iron and steel industry would potentially have exposures above 5 $\mu g/m^3$ [4, p. 4092–4093]. The exposure data from AISI indicate that less than 5 percent of the workforce would be potentially exposed above 5 $\mu g/m^3$. An estimated 90 percent of these workers would already be provided with respiratory protection due to the nature of the work and requirements of other standards [1, p. 3]. Thus, an additional 1,000 workers may need to wear respirators to comply with the cadmium rule. The estimated annual incremental cost to the industry would be $300,000.

Employees exposed to cadmium in the iron and steel industry are also exposed "to other substances that are currently regulated by OSHA substance-specific standards, such as arsenic and lead [and] a number of others." [3, p. 9–287]. As a result, "companies have in place medical surveillance programs for workers that are covered by these substances" [3, p. 9–287], and would also be conducting exposure monitoring for these substances. The incremental costs of compliance with the revised cadmium standard would involve costs for analyses of cadmium-specific biological and exposure monitoring samples.

The monitoring data submitted by AISI suggests that employees exposed below the PEL would generally have exposures below the action level as well. In addition, many employees would only be intermittently exposed above the action level and may fall outside of the coverage of the medical surveillance provisions [3, p. 9–288]. The number of employees for whom annual monitoring may be required is estimated to be less than 5,000; however, more frequent monitoring may be required for a few of these employees. An estimated 5,000 sets of biological monitoring tests would be necessary each year for full compliance.

The analysis of one set of samples for cadmium in urine, cadmium in blood, and β_2-microglobulin in urine would cost an estimated $200. The total annual cost for the industry would be $1 million. Employees in this industry are not expected to be affected by the requirements for medical removal since occupational exposures are relatively low and intermittent.

Analyses for cadmium of exposure monitoring samples may be necessary on a regular basis for an average of ten job categories per facility. Samples would be analyzed for each of three shifts every six months at about 120 facilities, and each analysis would cost about $40. The total annual cost for the industry would be $288,000. This estimate may include some current expenditures for cadmium monitoring; the potential overestimate may be offset by potential costs for collecting additional samples.

Hygiene facilities and related practices required by the cadmium standard (including work clothing) and provisions concerning information and training in the cadmium standard are similar to corresponding requirements in existing standards for lead and arsenic. Employees exposed to cadmium are also potentially exposed to lead or arsenic [3, p. 9–288]. According to AISI, appropriate hygiene facilities "are provided in all leaded steel production areas." [1, p. 12]. Exposures above the PELs for lead or arsenic may also occur during some activities in any steel plant (e.g., maintenance, cleaning, or repair of baghouses, electrostatic precipitators, waste gas systems, etc.); hygiene facilities and practices are already required for these employees.

Estimated additional costs for recordkeeping are $5 per employee annually. The total estimated industry cost for the 10,000 affected employees would be $50,000 annually.

Estimated compliance costs for the iron and steel industry are summarized in Table VIII–C41. The total estimated cost is $1.64 million annually.

Economic feasibility of a 5 $\mu g/m^3$ PEL. The revised cadmium standard with a PEL of 5 $\mu g/m^3$ is economically feasible for the iron and steel industry.

TABLE VIII–C41.—ESTIMATED COSTS OF COMPLIANCE WITH THE REVISED CADMIUM STANDARD FOR THE IRON AND STEEL INDUSTRY

Provision	Annualized cost ($thousands)
Exposure control	0.0
Respirator use	300.0
Exposure monitoring	288.0
Medical surveillance	1,000.0
Hygiene provisions	0.0
Recordkeeping and information	50.0
Total	1,638.0

Note: Costs do not include current expenditures. Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

Compliance with the rule does not threaten the dislocation of firms or the competitive structure of the industry.

The U.S. Department of Commerce reported that in 1989 the value of blast furnace and basic steel industry shipments exceeded $64 billion [5, p. 1–20]. The ratio of the estimated compliance cost to the value of shipments is less than 0.00003. Compliance with the revised cadmium standard should not have any significant effect on total revenues, shipments, or employment.

New capital expenditures for the blast furnace and basic steel industry were over $3 billion in 1989, an increase of about 33 percent over 1988 [5, p. 1–51]. Strong prospects for continuing future profitability are expected for this industry. Expectations of profits would hardly be affected by the cadmium standard: labor costs are about $12.4 billion annually [5, p. 1–33], and the estimated compliance cost represents an increase in labor costs of less than 0.014 percent.

The iron and steel industry is subject to environmental and other regulations that impose costs far greater than the cadmium standard. EPA estimated that annualized costs of compliance for the steel industry for a new emissions standard were over $34 million (1981 dollars) [1, p. 11 and 1, Attachment 5a, p. 8–17]. Additional expenses are incurred for compliance with other regulations, including occupational exposure to lead and arsenic. The cadmium standard represents a minimal increase in total regulatory burden and involves provisions consistent with requirements imposed by existing regulations.

The costs of compliance have not and will not threaten the existence of the industry, reduce its competitiveness, or cause its contraction. From 1984 through 1989 (the latest year for which data are available), the percentage of imports of steel mill products purchased in the United States decreased steadily from 26.4 percent to 17.9 percent. In the same period, exports of steel mill products from the United States increased by 470 percent from less than one million tons to 4.6 million tons. Revenues from exports were over $2.7 billion in 1989. [1, Attachment 4, p. 1]. The cadmium standard is not expected to affect the competitive position of the industry.

Notes

1. Exhibit 126, "RE: Cadmium in Steelmaking—OSHA Docket No. H–057a," American Iron and Steel Institute, Washington, D.C., October 17, 1990.
2. Exhibit 13, "Economic Impact Analysis of the Proposed Revision to the Cadmium Standard," Final Report, JACA Corporation, March 15, 1988.
3. Hearing Transcript, Wednesday, July 18, 1990.
4. Occupational Exposure to Cadmium, Proposed Rule, Occupational Safety and Health Administration, Federal Register Volume 55, Number 25, February 6, 1990.
5. U.S. Department of Commerce, Bureau of the Census, 1989 Annual Survey of Manufacturers, Economics and Statistics Administration, June, 1991.

General Industry, Except Establishments Included Above

Industry overview. Potential exposures to cadmium may occur in many different industries which use cadmium or products containing cadmium as part of their operations. Activities which produce concentrations of dust or fume may cause employee exposures if cadmium is a component of the materials involved.

JACA Corporation reviewed occupations in each industry and compiled a list of industries and occupations which involve relevant activities and potential exposure to

cadmium [1; p. C–4 through C–10]. JACA identified occupations in industries with specific uses for cadmium or cadmium compounds in production processes, and occupations in industries that are not directly associated with cadmium but may involve incidental exposure in the use of products containing cadmium.

The chemical properties of cadmium lead to its usefulness in several diverse areas. JACA described a variety of industrial applications for cadmium, including the use of cadmium in alloys [1, p. 2–57]. The principal alloys which use cadmium are zinc, lead, and copper alloys; cadmium may also be used for silver and tin alloys.

Copper-cadmium alloys typically contain 0.8 to 1.2 percent cadmium. This small amount of cadmium doubles the strength of the alloy and reduces its electrical conductivity by only 10 percent, making the alloy ideal for overhead conductors for trains and for use in multi-strand conductors. The mechanical properties of rolled, drawn, and extruded zinc can be improved with 0.05 to 0.10 percent cadmium in the alloy. Lead alloys and solders may contain cadmium for its strengthening properties and low melting temperature. Cadmium may also be added to silver and gold alloys for the production of jewelry.

New materials used in the production of photovoltaic cells include copper indium diselenide, gallium arsenide, and cadmium telluride. Electrical contacts made with cadmium compounds have high tensile strength and are corrosion resistant; they are used in heavy duty applications such as relays, switches, and thermostats. Cadmium also has applications in the production phosphors in television picture tubes, photographic equipment, and lighting, and in catalysts for the production of esters. Cadmium-based control elements are used in some nuclear reactors. Cadmium compounds may be used in the production of phosphatic fertilizers, fungicides, and other chemicals. JACA identified many other industries, ranging from semiconductors to refuse systems, where materials containing cadmium may be present. [1, p. 2–11, 2–58, 3–28, and C–4 through C–10].

The U.S. Department of Commerce provided a consumption analysis of cadmium that showed how much cadmium was used for the output of each industry [2, Attachment A]. An accompanying input-output matrix showed how much cadmium each industry supplied to other industries as inputs for the production of final goods [2, Attachment B]. The industries identified in these tables generally parallel the JACA exposure profile, except that JACA identified a wider range of potentially affected industries. The Department of Commerce consumption analysis may not accurately portray employee exposures because products can be assembled with cadmium-containing parts without resulting in cadmium exposure. Alternatively, as recognized by JACA and discussed above, cadmium exposures are possible in industries not listed on the input-output tables. In order to ensure a complete and full analysis of the impact of the revised cadmium standard, OSHA considered all industries identified by JACA and the Department of Commerce as potentially affected by the new requirements and included each in the revised analysis.

NIOSH provided data to the record from the National Occupational Exposure Survey (NOES) [3, Attachment 1]. The NOES data was collected during the period 1981 to 1983 from a sample of 4,490 businesses and was designed to characterize employee exposures to chemicals by occupation and industry. The list of industries with potential cadmium exposures identified by NIOSH is generally consistent with that compiled by JACA and also includes some additional sectors. OSHA added the industries identified by NIOSH to those identified by JACA and the Department of Commerce to create a combined and complete list of potentially affected industries.

Several commenters criticized JACA and the preliminary analysis for not including all affected industries. However, OSHA found that often the industries listed to support such claims had been previously identified by JACA and were covered by the preliminary analysis. For example, one commenter stated that the "analysis of the proposed regulation is incomplete. Not included in your analysis are industries such as specialty alloy foundries, cadmium use in brazing, babbitt metal production, cadmium vapor lighting, photoelectric cell production, and the production of cadmium-based chemicals." [4, p. 1]. Many employees in these industries were included in the exposure profile developed by JACA and used for the preliminary analysis [1, p. 2–57 through 2–59, p. 3–28 through 3–32, and p. C–4 through C–10]. The revised analysis includes all industries identified in the record as potentially affected.

Table VIII–C42 presents a complete list of the industries potentially affected by the revised standard. The table also shows which industries were identified by JACA, the Department of Commerce, and NIOSH.

Production processes. JACA evaluated the specific activities involving cadmium in each industry and determined which processes and occupations would be potentially affected. JACA also assessed the nature of exposures in each case and categorized occupations by the type of work performed and by the degree of exposure. [1].

Comments and evidence submitted to the record in response to the proposed rule confirmed the potential for cadmium exposures in many processes identified preliminarily. As discussed above, information was also provided by some commenters which enabled a more detailed and comprehensive analysis to be developed for the final rule.

TABLE VIII–C42.—INDUSTRIES POTENTIALLY AFFECTED BY THE REVISED CADMIUM STANDARD

SIC Code	Industry title	Identified by		
		JACA (1)	DOC (2)	NIOSH (3)
16	Heavy construction	x		x
17	Construction trades	x		x
22	Textile mill products	x		x
23	Apparel			x
25	Furniture	x		x
26	Paper & allied products	x		x
27	Printing & publishing			x
28	Chemicals	x	x	x
29	Petroleum refining			x
30	Rubber & plastics	x		x
31	Leather products			x

TABLE VIII–C42.—INDUSTRIES POTENTIALLY AFFECTED BY THE REVISED CADMIUM STANDARD—Continued

SIC Code	Industry title	Identified by		
		JACA (1)	DOC (2)	NIOSH (3)
32	Stone, clay, glass			
33	Primary metal			
34	Fabricated metal prod.		x	x
35	Machinery & equipment	x	x	x
36	Electrical equipment	x	x	x
37	Transportation equip.	x	x	x
38	Measuring instruments	x	x	x
39	Miscellaneous manufac.	x	x	x
40	Railroad transportation	x		x
42	Motor Trans. & warehsing.	x		
45	Air transportation			x
48	Communications	x		x
49	Utilities			x
50	Wholesale durables	x		x
51	Wholesale nondurables	x		
55	Automotive dealers			x
73	Business services			x
75	Automotive services			x
76	Misc. repair services	x		
80	Health services	x		x

[1] Exhibit 13, JACA Corporation, p. C–4 through C–10.
[2] Exhibit 19–50, U.S. Department of Commerce, Attachment B.
[3] Exhibit 106, NIOSH, Attachment 1.

Employees in each industry were classified into different occupational categories depending on their job and on their exposure profile. A sufficient number of occupational categories was defined to ensure that occupations in each industry were provided with a representative exposure profile. The classification of occupations was consistent with the standard concepts and descriptions presented in the Dictionary of Occupational Titles (DOT) [5].

In addition to the occupations included in the industry sectors analyzed in the preceding sections, employees in general industry were classified into the ten occupational categories described below.

Chemical mixers may be exposed to dust generated when adding compounds to a chemical or mechanical mixing operation, tending mixing equipment, or operating machines to crush, grind, polish, and blend a variety of materials. Employees may be exposed to cadmium-based plastic stabilizers, cadmium-based pigments, compounds used for metallic coatings, compounds used in the production of fungicides, and other cadmium compounds. [1, p. 3–28]. Applicable titles listed in the DOT include chemical mixer, chemical operator, chemical compounder, chemical milling processor, and chemical preparer.

Electroplaters are employed in several industries that perform electroplating as part of their manufacturing operations. These employees include plating and coating machine setters, operators, and tenders who provide protective or decorative surfaces for metals and other materials. Because electroplating is a wet process, employees are generally only exposed for short periods while measuring and adding dry cadmium-bearing powder to the plating tank. [1, p. 3–28].

Furnace operators and molders may be exposed to cadmium fumes released by molten metal during smelting, refining, molding, casting, and forging operations. Employees engaged in these activities include forging machine operators; metal molding, coremaking, and casting machine operators; operators of melting and refining furnaces; and metal pourers and casters. [1, p. 3–29]. Specific job titles listed in the DOT include furnace operator, charger, helper, loader, tender, and worker; molder, molder machine tender, molder operator; and mold checker, clamper, closer, dresser, maker, setter, stamper, worker, filler, and finisher.

Kiln or kettle operators may be exposed to cadmium compounds in chemical conversions, or while heating materials with glazes, paints, or other coatings which may contain cadmium. Employees in this category operate kilns, kettles, ovens, or furnaces for annealing, roasting, or converting processes. Employees may have occupational titles such as kiln operator, burner, feeder, firer, loader, helper, or worker; oven tender; and kettle operator, tender, or worker.

Heat treaters may be exposed to cadmium fumes when heating metals coated with or containing cadmium. These employees set up, operate, and tend flame-hardening machines, electronic induction machines, furnaces, and baths to harden, anneal, and heat treat metal products or metal parts.

Equipment cleaners may be exposed to cadmium when cleaning equipment contaminated with dusts containing cadmium or cadmium compounds. Industrial cleaners and cleaner operators would also be included in this category. Exposures may occur while cleaning baghouses, electrostatic precipitators, process equipment, and process areas.

Metal machine operators may be exposed to cadmium generated while grinding or forming metals bearing cadmium as a component or as part of a coating. Employees engaged in these activities include machinists; grinders; filers; sharpeners; lapping and buffing machine tool operators; operators of machines that roll steel or plastic material to form bends, beads, knurls, or plate, or to flatten, temper, or reduce the gauge of material; workers who set up and operate magnetic or other controlled machine tools that automatically mill, drill, broach, or ream metal parts; and general metal machining or metal working occupations.

Painters may be exposed to cadmium contained in paints or metal sprays during spray painting or nonelectrolytic metal coating. Activities included in this category are coating machine operation; painting and spraying machine operation; operation of nonelectrolytic plating and coating machines such as hot dip lines and metal spraying machines to coat metal, plastic, and other materials with metal; and painting, coating, and decorating a wide variety

of manufactured items using hand tools or hand held power tools.

Repair and utility workers may be exposed to cadmium during repair or maintenance activities and work on industrial equipment. These employees would include millwrights who dismantle, move, and install machinery and heavy equipment; general utility repairers performing a variety of maintenance tasks; automotive and motorcycle mechanics; automotive body repairers; aircraft mechanics and engine specialists; farm equipment mechanics; mechanics who repair mobile heavy equipment such as cranes, bulldozers, graders, and conveyors; rail car repairers; electricians; plumbers; pipefitters; steamfitters; and boilermakers who construct, assemble, maintain, and repair steam boilers and boilerhouse auxiliaries.

Welders, brazers, and solderers may be exposed to cadmium fumes released from cadmium-bearing base metals, brazing rods, or solders. This category includes employees operating welding, brazing, or soldering machines and employees performing such work with hand tools. Workers engaged in this type of work include structural steel workers who raise, place, and unite girders, columns, and other components; metal pattern makers who lay out, machine, assemble, and fit pattern parts; metal fabricators who make and assemble sheet metal products and equipment or other metal products such as frameworks or shells for machinery, ovens, tanks, stacks, buildings, and bridges; precision assemblers of products such as machinery, aircraft, electrical, or electronic equipment; other machine, electrical, or electronic assemblers; employees who use welding and flamecutting equipment such as arc welders, gas welders, and gas torches to join, cut, trim, and scarf metal components; and solderers and brazers who join metal parts or fill holes, indentations, and seams of fabricated metal products.

Table VIII-C43 shows the estimated number of employees in each occupational category for each industry. This table summarizes the best available information regarding production processes, occupations, and numbers of employees potentially affected, as provided by the record.

The compilation of the data in Table VIII-C43 from evidence in the record did not involve significant conflicts of information. Industries, occupations, or processes identified by any source were included. Those included in the preliminary analysis and receiving no comments were also included in the final analysis. None of the comments in response to the proposed rule or other comments argued that a previously identified industry, process, or occupation should be excluded.

Employee exposures. Estimated employee exposures in the occupational categories described above were presented in the preliminary analysis [6, p. II-37; and 7, p. 4092]. These data, compiled by JACA Corporation [1], were based on NIOSH and OSHA exposure monitoring results from over 2,400 samples analyzed for cadmium. Table VIII-C44 summarizes these data, showing the geometric mean, the median, and the range of exposures for each occupational category.

TABLE VIII–C43.— EMPLOYEES POTENTIALLY EXPOSED TO CADMIUM IN GENERAL INDUSTRY BY OCCUPATION

[Excluding Sectors Covered Elsewhere]

	Industry	Chemical Mixers	Electro-platers	Furnace operators	Kiln/kettle operators	Heat treaters	Equipment cleaners	Metal machining	Painters	Repair/utility	Welders, brazers, solderers	Industry total
2200	Textile mill products	47								364		411
2300	Apparel	201										201
2500	Furniture								772		460	1232
2600	Paper products	195										195
2700	Printing and publishing	1400					100			100		1600
2810	Inorganic chemicals								52		143	195
2820	Plastics and synthetics	870										870
2830	Drugs	50										50
2851	Paints & allied products	4724										4724
2860	Organic chemicals	1861			85						587	2533
2870	Agricultural chemicals	1533								974		2507
2890	Miscellaneous chemicals	1024										1024
2900	Petroleum refining									807		807
3000	Rubber & plastic prod.	8715							785		1633	11133
3100	Leather products	902										902
3211	Flat glass	321			345							666
3220	Glassware	298							278	2353		2929
3250	Structural clay products	400			1500					523		2423
3260	Pottery products							79	95			174
3270	Concrete products										624	624
3280	Stone products										200	200
3290	Mineral products				594						305	899
3313	Alloy products			244						244		488
3315	Steel wiredrawing			250							250	500
3316	Cold-rolled steel		37									37
3317	Steel pipe and tubes									100	300	400
3320	Iron and steel foundries			5157						5469	182	10808
3330	Primary nonferrous metals			1400						400		1800
3340	Secondary nonferrous mtls			600						150		750
3350	Nonferrous rolling, etc.	150		733				2239			13	3135
3360	Nonferrous foundries	139		8754		51		1078				10022
3390	Misc. primary metal	103				175					7	285
3410	Metal shipping containers							70			70	140
3420	Hand tools & hardware							2676			105	2781
3430	Heating & plumbing equip.							241	127	703	115	1186
3440	Fabricated struct. metal							6955	902		9208	17065
3450	Screws, etc.		868									868
3460	Forgings & stampings							612				612
3470	Coating and engraving							200				200
3480	Ordnance										265	265
3490	Misc. fabr. metal prod.		1454					3258			4359	9071
3510	Engines and turbines							1533			1503	3036
3520	Farm and garden machinery								199			199
3530	Construction machinery								287		10166	10453
3540	Metalworking machinery							15318			809	16127
3550	Special machinery							1200	79	340	4914	6533
3560	General machinery			64				1800		204	9565	11633
3570	Computer & office equip		400								1200	1600
3580	Refrig. & service mach.							2480	338	2221	9141	14180
3590	Miscellaneous machinery							14325			5290	19615
3610	Elec. transmission equip.		267								6121	6388
3620	Electrical apparatus		800						65		11595	12460
3630	Household appliances		500								7086	7586
3640	Lighting and wiring		200								13066	13266
3650	Audio & video equip.										3021	3021
3660	Communications equip.		1188						2282		14416	17886
3670	Electronic components	373	63				133	2700	1199		10945	15412

3690	Misc. elect. equip.		50								300	350
3710	Motor vehicles									11460	6572	18032
3720	Aircraft		791								1985	2776
3730	Ship building					293		4587		1227	1800	7907
3743	Railroad equipment							1047			411	1458
3760	Missiles & space vehicles		30								329	359
3790	Misc. trans. equip.										119	119
3812	Detection equipment, etc.										67	67
3820	Meas. & contr. instr.										216	216
3840	Medical instruments										337	337
3860	Photographic equipment								669			669
3870	Watches & clockwork										173	173
3910	Jewelry & plated ware										79	79
3930	Musical instruments										16	16
3940	Toys and sporting goods										1004	1004
3950	Artists' materials	60										50
3960	Costume jewelry & notions										29	29
3990	Misc. manufacturing								2749			2749
4011	Railroads									21	2	23
4200	Motor freight & warehsing										586	586
4500	Air transportation								89	52058		52147
4810	Telephone communications									2474		2474
4830	Radio & TV broadcasting										149	149
4920	Gas prod. & dist.										1213	1213
4950	Sanitary services									5204		5204
5000	Wholesale trade, durables							77			613	690
5100	Wholesale nondurables	3080										3080
5500	Service stations										538	538
7530	Automotive repair shops								357		2837	3194
7600	Misc. repair services							1592		1702	200	3494
8060	Hospitals							277				277
	Totals	26436	6648	17202	2524	519	233	64344	11323	89098	147239	365566

Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

TABLE VIII–C44.—CADMIUM EXPOSURE DATA FOR GENERAL INDUSTRY OCCUPATIONS BASED ON JACA

Job category	Concentration in μg/m³		
	Geometric mean	Median	Range
Chemical mixer	2.7	5.0	0.1–710.0
Electroplater	0.6	1.0	0.1–29.0
Furnace operator	0.1	0.1	0.1–530.0
Kiln/Kettle operator	0.5	0.3	0.1–10.0
Heat treater	2.6	6.5	0.1–100.0
Equipment cleaner	2.0	3.0	0.1–34.5
Metal machining	1.3	2.0	0.1–470.0
Painter	0.4	0.1	0.1–1,700.0
Repair/Utility	2.0	3.0	0.1–271.0
Welder, brazer, solderer	0.3	0.1	0.1–3,400.0

Source: Exhibit 13, JACA, Table 3–10.

TABLE VIII–C45.—FREQUENCY DISTRIBUTION OF OCCUPATIONAL EXPOSURE OBSERVATIONS

[In percent]

Occupation	Range of exposure observations [μg/m³]						
	0–5	6–9	10–19	20–29	30–49	50–99	100+
Chemical mixers	51	11	8	6	7	7	9
Electroplaters	88	0	4	11	0	0	0
Furnace operators	91	2	1	1	1	2	1
Kiln/kettle operators	87	7	7	0	0	0	0
Heat treaters	50	0	17	0	17	0	17
Equipment cleaners	83	0	13	0	4	0	0
Metal machine operators	63	4	9	7	7	5	6
Painters	77	2	3	1	3	4	10
Repair/utility workers	57	10	6	10	6	3	9
Welders, brazers, solderers	88	3	2	1	1	3	2

Source: Office of Regulatory Analysis, OSHA; based on JACA [1].

Table VIII–C45 presents the estimated frequency distribution of exposures for each of the occupational categories.

Comments and evidence submitted to the record in response to the proposed rule were generally consistent with the characterization of exposures presented for the occupational categories. Some industry representatives argued that due to unique circumstances specific to their industry it was inappropriate to include employees from their industry in the occupational categories. In response to these concerns, employee exposures in the dry color formulator industry, the electric utility industry, the iron and steel industry, and the construction industry are excluded from the occupational categories in the revised analysis and are analyzed separately.

Evidence specific to the remaining industries was generally consistent with and confirmed the representativeness of the preliminary exposure profiles for the relevant occupational categories. Employee exposures are generally similar within occupations across all industry groups.

Several commenters emphasized that employees in certain occupational categories have potential exposures to cadmium in specific circumstances that should not be overlooked. For example, the brass mill industry, the copper refining industry, copper and brass fabricators, silver alloying facilities, and aluminum casting operations may involve metal machining and furnace activities with cadmium exposures [8, 9, 10, 11, 12].

Exposure levels can be expected to vary among establishments as well as across shifts for individual operations. Variation in exposures and the possibility of higher exposures in certain activities were included in the frequency distribution of cadmium exposure observations for the occupational categories. The preliminary analysis showed that of the 83,000 metal machine operators and furnace operators potentially exposed to cadmium, over 16,000 may be exposed to levels above 20 μg/m³ [7, Table VIII–B].

OSHA believes that the exposure profiles in the revised analysis adequately reflect the extent of cadmium exposures in the occupations and include circumstances identified by commenters across industry.

Existing and feasible additional controls. Occupational exposures to cadmium can be controlled with a number of conventional technologies that are commonly known, readily available, and currently used in many industries. OSHA does not specify which controls must be implemented. Rather, OSHA allows the employer to choose a combination of control methods that is best suited to the particular characteristics of the work place. Industry may also devise additional ways to successfully control exposure levels.

JACA described several controls applicable for reducing cadmium exposures [1, p. 4–3 et seq.]. Local exhaust ventilation systems can be applied at a wide variety of emissions sources by designing hoods for the close capture of dusts or fumes. Such systems can be highly effective in reducing employee exposures because potential contaminants may be captured at the point of generation.

Another basic type of engineering control is process enclosure. Enclosure may consist of sealed paneling or covers for equipment, or may involve more sophisticated strategies. For example, an enclosed screw conveyor may be an effective alternative to manually transferring material in some operations. In addition to enclosure, or in operations for which enclosure is not an amenable strategy, separation and isolation of the process may provide an effective solution for reducing cadmium exposures among employees.

Improvements in work practices may aid in significantly reducing the generation of airborne cadmium and in ensuring that employees are not

unnecessarily exposed to elevated concentrations. Cadmium exposures for maintenance workers may be reduced through additional cleanup of equipment and surrounding areas prior to maintenance and repair operations.

Principles of controlling occupational exposure to cadmium were described by NIOSH [13, p. 11 et seq.]. The system of control measures outlined by NIOSH provides a flexible and reliable approach applicable to establishments in all industries. NIOSH recommends the selection of a control strategy as a critically important first step. A careful application of a system of controls is usually required to adequately control cadmium exposures. This would include measures applied to the hazard source, to the general work environment, at or near the employees potentially exposed, and other measures for hazard control.

Specific measures listed by NIOSH that should be considered include substitution of materials, process modification or substitution, equipment selection and modification for containment, wet processing, isolation of the source and automation of operations, local exhaust ventilation, work practices to maintain containment and control effectiveness, dilution ventilation, room air cleaning devices, housekeeping and other work practices, personal hygiene, isolation of workers in booths or cabs, personal protective equipment, management commitment to controlling exposures, work place and process monitoring systems with feedback, training for workers and supervisors, and preventive maintenance of equipment and controls.

Descriptions of controls were also provided for the record by other commenters [8, 10, 12, 16, and others]. Different controls are available for many diverse operations and generally provide examples of achieving exposure reductions according to the basic principles outlined by NIOSH. Controls with applications in a wide variety of industries include clean air islands, glove boxes, and equipment for handling, dumping, and packaging materials.

Technological feasibility of a 5 μg/m³ PEL. Compliance with the final cadmium standard is considered technologically feasible in each of the affected industries. This determination is based on and is consistent with the evidence in the record, the criteria established by the courts in applicable case law, and the understanding of technological feasibility developed through OSHA policy (see, for example, OSHA's statement of reasons made in response to the U.S. Court of Appeals regarding the final rule on occupational exposure to lead [14]).

OSHA recognizes that in some operations employee exposures may not be consistently controllable to below 5 μg/m³ with engineering and work practice controls alone. Respirators are permitted to supplement feasible engineering and work practice controls and are capable of providing sufficient protection for all employees as required by the revised standard.

The typical firm in each of the industries considered in this section should be able to achieve levels below 5 μg/m³ for most employees most of the time. As shown in Table VIII–C44, geometric mean exposures in all of the occupations are less than 3 μg/m³. Furthermore, as shown in Table VIII–C46, the total number of potentially affected employees in each industry is less than 13% of the work force in each industry. In all but four industries the proportion of affected workers was less than 8%. The record did not contain evidence demonstrating that any establishment would not be able to achieve the PEL for most of its employees.

Compliance with the revised cadmium standard is technologically feasible. The standard requires engineering and work practice controls to be implemented to the extent feasible. Respirators can be used to provide necessary protection as required by the standard.

TABLE VIII–C46.—RATIO OF POTENTIALLY AFFECTED EMPLOYEES TO TOTAL EMPLOYMENT BY INDUSTRY

	Industry	Potentially exposed employees (A)	Total industry employees (B)	Ratio of A/B
2200	Textile mill products	411	675,000	0.001
2300	Apparel	201	1,038,800	0.000
2500	Furniture	1,232	483,600	0.003
2600	Paper products	195	693,000	0.000
2700	Printing and publishing	1,600	1,523,600	0.001
2810	Inorganic chemicals	195	137,800	0.001
2820	Plastics and synthetics	870	178,100	0.005
2830	Drugs	50	247,900	0.000
2851	Paints and allied products	4,724	59,100	0.080
2860	Organic chemicals	2,533	153,500	0.017
2870	Agricultural chemicals	2,507	55,800	0.045
2890	Miscellaneous chemicals	1,024	98,600	0.010
2900	Petroleum refining	807	161,200	0.005
3000	Rubber and plastic products	11,133	866,000	0.013
3100	Leather products	892	122,500	0.007
3211	Flat glass	666	15,700	0.042
3220	Glassware	2,929	81,800	0.036
3250	Structural clay products	2,423	32,500	0.075
3260	Pottery products	174	36,530	0.005
3270	Concrete products	624	196,200	0.003
3280	Stone products	200	34,000	0.006
3290	Mineral products	899	76,300	0.012
3313	Alloy products	488	14,100	0.035
3315	Steel wiredrawing	500	11,300	0.044
3316	Cold-rolled steel	37	14,900	0.002
3317	Steel pipe and tubes	400	24,200	0.017
3320	Iron and steel foundries	10,898	125,200	0.088
3330	Primary nonferrous metals	1,800	44,800	0.040
3340	Secondary nonferrous metals	750	17,000	0.044
3350	Nonferrous rolling, etc	3,135	167,600	0.019
3360	Nonferrous foundries	10,022	81,000	0.124
3390	Miscellaneous primary metals	285	25,000	0.011
3410	Metal shipping containers	140	48,700	0.003

TABLE VIII-C46.—RATIO OF POTENTIALLY AFFECTED EMPLOYEES TO TOTAL EMPLOYMENT BY INDUSTRY—Continued

	Industry	Potentially exposed employees (A)	Total industry employees (B)	Ratio of A/B
3420	Hand tools and hardware	2,781	122,600	0.023
3430	Heating and plumbing equipment	1,186	58,300	0.020
3440	Fabricated structures—metal	17,065	412,000	0.041
3450	Screws, etc	868	90,500	0.010
3460	Forgings and stampings	612	218,600	0.003
3470	Coating and engraving	200	116,600	0.002
3480	Ordnance	265	69,700	0.004
3490	Miscellaneous fabricated metal products	9,071	229,200	0.040
3510	Engines and turbines	3,036	88,900	0.034
3520	Farm and garden machinery	199	97,600	0.002
3530	Construction machinery	10,453	212,400	0.049
3540	Metalworking machinery	16,127	308,600	0.052
3550	Special machinery	6,533	146,800	0.045
3560	General machinery	11,633	238,700	0.049
3570	Computer and office equipment	1,600	414,500	0.004
3580	Refrigeration and service machinery	14,180	166,700	0.085
3590	Miscellaneous machinery	19,615	297,900	0.066
3610	Electrical transmission equipment	6,388	91,300	0.070
3620	Electrical apparatus	12,460	159,500	0.078
3630	Household appliances	7,586	121,800	0.062
3640	Lighting and wiring	13,266	177,100	0.075
3650	Audio and video equipment	3,021	80,100	0.038
3660	Communications equipment	17,886	246,200	0.073
3670	Electronic components	15,412	542,900	0.028
3690	Miscellaneous electrical eqiupment	350	164,400	0.002
3710	Motor vehicles	18,032	807,400	0.022
3720	Aircraft	2,776	641,500	0.004
3730	Ship building	7,907	174,600	0.045
3743	Railroad equipment	1,458	30,600	0.048
3760	Missiles and space vehicles	359	165,200	0.002
3790	Miscellaneous transmission equipment	119	40,900	0.003
3812	Detection equipment, etc	67	257,100	0.000
3820	Measurement and construction instrument	216	305,500	0.001
3840	Medical instruments	337	254,200	0.001
3860	Photographic equipment	669	100,000	0.007
3870	Watches and clockwork	173	9,900	0.017
3910	Jewelry and plated ware	79	52,900	0.001
3930	Musical instruments	16	12,100	0.001
3940	Toys and sporting goods	1,004	105,500	0.010
3950	Artists' materials	50	32,100	0.002
3960	Costume jewelry and notions	29	31,600	0.001
3990	Miscellaneous manufacturing	2,749	136,800	0.020
4011	Railroads	23	230,500	0.000
4200	Motor freight and warehousing	586	1,667,000	0.000
4500	Air transportation	52,147	750,900	0.069
4810	Telephone communications	2,474	887,800	0.003
4830	Radio and TV broadcasting	149	231,200	0.001
4920	Gas production and distribution	1,213	165,300	0.007
4950	Sanitary services	5,204	130,300	0.040
5000	Wholesale trade, durables	690	3,493,000	0.000
5100	Wholesale nondurables	3,080	2,572,000	0.001
5500	Service stations	538	2,054,000	0.000
7530	Automotive repair shops	3,194	526,400	0.006
7600	Miscellaneous repair services	3,494	382,800	0.009
8060	Hospitals	277	3,676,100	0.000
	Totals	365,566	32,342,400	0.011

Source: Table VIII-C43 and "Employment and Earnings," Bureau of Labor Statistics, November 1991.

Several comments submitted to the record expressed concern about the technological feasibility of the standard. Often the concern was based on the misconception that OSHA had assumed the PEL could be achieved with engineering controls for all employees in all circumstances. The revised standard requires controls to be implemented to the extent feasible but is not based on the assumption that the PEL will be achieved through engineering controls in all operations.

Based on evidence and comments in the record, OSHA concluded that respirator use would probably be necessary in some situations. These may occur in the production of cadmium alloys, in processes using powdered cadmium-bearing materials, and in activities producing fumes from substances containing cadmium.

Costs of compliance with a 5 μg/m³ PEL. Costs of compliance for establishments affected by the revised cadmium standard include costs for engineering controls, respiratory protection, protective clothing, exposure monitoring, medical surveillance, hygiene facilities, information and training, and recordkeeping. Costs for each of these elements are estimated by industry.

In evaluating compliance costs for each industry, OSHA considered the number of employees potentially exposed in each industry, the respective occupations represented, and the nature of exposures in the industry. The extent and degree of exposure among the affected employees was determined

unnecessarily exposed to elevated concentrations. Cadmium exposures for maintenance workers may be reduced through additional cleanup of equipment and surrounding areas prior to maintenance and repair operations.

Principles of controlling occupational exposure to cadmium were described by NIOSH [13, p. 11 et seq.]. The system of control measures outlined by NIOSH provides a flexible and reliable approach applicable to establishments in all industries. NIOSH recommends the selection of a control strategy as a critically important first step. A careful application of a system of controls is usually required to adequately control cadmium exposures. This would include measures applied to the hazard source, to the general work environment, at or near the employees potentially exposed, and other measures for hazard control.

Specific measures listed by NIOSH that should be considered include substitution of materials, process modification or substitution, equipment selection and modification for containment, wet processing, isolation of the source and automation of operations, local exhaust ventilation, work practices to maintain containment and control effectiveness, dilution ventilation, room air cleaning devices, housekeeping and other work practices, personal hygiene, isolation of workers in booths or cabs, personal protective equipment, management commitment to controlling exposures, work place and process monitoring systems with feedback, training for workers and supervisors, and preventive maintenance of equipment and controls.

Descriptions of controls were also provided for the record by other commenters [9, 10, 12, 16, and others]. Different controls are available for many diverse operations and generally provide examples of achieving exposure reductions according to the basic principles outlined by NIOSH. Controls with applications in a wide variety of industries include clean air islands, glove boxes, and equipment for handling, dumping, and packaging materials.

Technological feasibility of a 5 μg/m³ PEL. Compliance with the final cadmium standard is considered technologically feasible in each of the affected industries. This determination is based on and is consistent with the evidence in the record, the criteria established by the courts in applicable case law, and the understanding of technological feasibility developed through OSHA policy (see, for example, OSHA's statement of reasons made in response to the U.S. Court of Appeals regarding the final rule on occupational exposure to lead [14]).

OSHA recognizes that in some operations employee exposures may not be consistently controllable to below 5 μg/m³ with engineering and work practice controls alone. Respirators are permitted to supplement feasible engineering and work practice controls and are capable of providing sufficient protection for all employees as required by the revised standard.

The typical firm in each of the industries considered in this section should be able to achieve levels below 5 μg/m³ for most employees most of the time. As shown in Table VIII–C44, geometric mean exposures in all of the occupations are less than 3 μg/m³. Furthermore, as shown in Table VIII–C46, the total number of potentially affected employees in each industry is less than 13% of the work force in each industry. In all but four industries the proportion of affected workers was less than 8%. The record did not contain evidence demonstrating that any establishment would not be able to achieve the PEL for most of its employees.

Compliance with the revised cadmium standard is technologically feasible. The standard requires engineering and work practice controls to be implemented to the extent feasible. Respirators can be used to provide necessary protection as required by the standard.

TABLE VIII–C46.—RATIO OF POTENTIALLY AFFECTED EMPLOYEES TO TOTAL EMPLOYMENT BY INDUSTRY

	Industry	Potentially exposed employees (A)	Total industry employees (B)	Ratio of A/B
2200	Textile mill products	411	675,000	0.001
2300	Apparel	201	1,039,800	0.000
2500	Furniture	1,232	463,600	0.003
2600	Paper products	195	693,000	0.000
2700	Printing and publishing	1,600	1,523,600	0.001
2810	Inorganic chemicals	195	137,800	0.001
2820	Plastics and synthetics	870	178,100	0.005
2830	Drugs	50	247,900	0.000
2851	Paints and allied products	4,724	59,100	0.080
2860	Organic chemicals	2,533	153,500	0.017
2870	Agricultural chemicals	2,507	55,800	0.045
2890	Miscellaneous chemicals	1,024	98,600	0.010
2900	Petroleum refining	807	161,200	0.005
3000	Rubber and plastic products	11,133	866,000	0.013
3100	Leather products	902	122,500	0.007
3211	Flat glass	666	15,700	0.042
3220	Glassware	2,929	81,300	0.036
3250	Structural clay products	2,423	32,500	0.075
3260	Pottery products	174	36,500	0.005
3270	Concrete products	624	198,200	0.003
3280	Stone products	200	34,000	0.006
3290	Mineral products	899	76,300	0.012
3313	Alloy products	486	14,100	0.035
3315	Steel wiredrawing	500	11,300	0.044
3316	Cold-rolled steel	37	14,900	0.002
3317	Steel pipe and tubes	400	24,200	0.017
3320	Iron and steel foundries	10,808	125,200	0.086
3330	Primary nonferrous metals	1,800	44,800	0.040
3340	Secondary nonferrous metals	750	17,000	0.044
3350	Nonferrous rolling, etc	3,135	167,600	0.019
3360	Nonferrous foundries	10,022	81,000	0.124
3390	Miscellaneous primary metals	285	25,000	0.011
3410	Metal shipping containers	140	48,700	0.003

based on information in the record for specific industries.

In response to concerns of several commenters, the revised analysis presents estimated compliance costs for each industry affected. Variations in compliance costs between industries were primarily due to the numbers of affected employees and the mix of occupations represented.

Engineering controls are available for reducing most of the exposures in the affected occupations. In some applications, employers may be able to eliminate cadmium exposure through substitution of products. Such alternatives may be feasible for some uses of cadmium pigments, cadmium stabilizers, cadmium plating, and cadmium alloys [1, 17, 18]. Improved work practices can significantly reduce exposures by preventing the unnecessary generation or inhalation of airborne cadmium and by increasing employees' awareness of potential hazards. General dilution ventilation and local exhaust ventilation are effective means of reducing exposures and are adaptable to a wide variety of circumstances.

The installation of a new ventilation system would have an estimated capital cost of $80,000 and an annual operating cost of $8,000. Controls such as enclosures and glove boxes may have estimated capital costs of about $9,000. Some establishments may also install other feasible controls instead of those specified depending on the circumstances involved. The estimated costs of compliance would be expected to be similar. [1, 16].

Exposures for most chemical mixers may be controlled with local exhaust ventilation systems. Such systems would be applicable in about 75 percent of the situations in which exposures need to be reduced [19]. New controls would be necessary for reducing exposures for an estimated 40 percent of the total number of chemical mixers, and on average one control would be sufficient for every 10 employees [6, p. V-13]. Additional engineering controls would not be required for employees with exposures below the action level, in operations for which engineering controls are infeasible, or in operations for which feasible controls have already been implemented. After the implementation of feasible additional controls, exposures for an estimated 30 percent of the chemical mixers may exceed the action level, and 20 percent would exceed the PEL. For these latter employees respirators would be required.

The number of engineering controls required for chemical mixers in each industry was thus calculated as N*0.40/10, where N is the number of chemical mixers potentially exposed in the industry. The annualized cost of engineering controls for the chemical mixers in each industry would be (N*0.40/10)*$21,020.

Electroplater exposures may be reduced with ventilation systems and use of a glove box. Electroplating facilities are generally provided with adequate ventilation systems, but some may require new or improved glove boxes to better control exposures. A new glove box would have an estimated capital cost of $9,000, an annualized cost of about $1,465, and would be sufficient for about 10 affected employees on average. The exposure data indicate that the additional protection would be necessary for about 20 percent of the electroplaters. The annualized cost of engineering controls for electroplaters in each industry would thus be (N*0.20/10)*$1,465, where N represents the number of electroplaters in each industry. After the implementation of feasible controls, an estimated 10 percent of the electroplaters may have exposures above the action level. Five percent may have exposures above the PEL and would be required to wear respirators.

Feasible engineering controls for furnace operators include local exhaust ventilation systems and furnace enclosures. It is expected that furnace operations already utilize feasible ventilation systems. Use of additional enclosures or furnace covers may be feasible to reduce exposures for about 30 percent of the furnace operators. (The percent of employees and establishments requiring additional controls is greater than that indicated by the full-time equivalent percentage of employees exposed above the PEL because controls may be required regardless of intermittency of exposure.) Each control would reduce exposures for about ten employees on average. The annualized cost of engineering controls for furnace operators in each industry would be (N*0.30/10)*$1,465.

Exposures for furnace operators should generally be below the action level after the implementation of feasible controls. However, some furnace operations may involve melts that contain a significant percentage of cadmium. As a result, employees may be exposed to concentrations in excess of the PEL [10]. OSHA estimates that after the implementation of additional controls up to 15 percent of the affected furnace operators would have exposures above the action level. About 10 percent of the employees may also have exposures above the PEL and would be required to wear respirators.

Kiln and kettle operators affected by the revised standard would need to be protected with feasible controls that may include local exhaust ventilation systems and enclosures. This set of additional controls would need to be provided for about 30 percent of these employees, with one set of controls sufficient for 10 employees on average. (The percent of employees and establishments requiring additional controls is greater than that indicated by the full-time equivalent percentage of employees exposed above the PEL because controls may be required regardless of intermittency of exposure.) The capital cost for the combination of controls would be $89,000, and the annual costs would be $8,000. The annualized cost for each industry would be (N*0.30/10)*$22,485. Resulting exposures should be below the action level for almost all employees. About 5 percent of the kiln and kettle operators may face unique circumstances or work with relatively high concentrations of cadmium; exposures for these employees may exceed both the action level and the PEL.

Exposures for heat treaters may not be reducible with additional feasible controls. OSHA estimates that about 70 percent of the affected employees would be exposed above the action level, and that about 50 percent of the affected employees would be required to wear respirators.

Equipment cleaners may have exposures for which engineering controls are often not feasible. It is estimated that about 50 percent of the affected employees would be exposed above the action level; approximately 20 percent of the employees may also be required to use respiratory protection.

Feasible additional engineering controls consisting of new or improved local exhaust ventilation systems may reduce exposures associated with metal machining. Such controls would be applicable in about 60 percent of the situations in which exposures need to be reduced [19]. Additional controls would be necessary for about 30 percent of the total number of metal machinists potentially exposed. The controls should be sufficient for an average of ten employees each. The annualized cost would be (N*0.30/10)*21,020. Resulting exposures should be below the action level for 85 percent of the affected employees. Approximately 15 percent of the employees may be engaged in metal machining activities that involve elevated concentrations of cadmium and

produce exposures which require the use of respiratory protection.

Painters affected by the revised standard are expected to be protected by feasible engineering controls already due to the presence of other potentially hazardous substances. Most painters with significant exposure would also already be provided with respiratory protection. OSHA estimates that about 30 percent of the affected painters would be exposed above the action level. Compliance with the cadmium standard may require additional respirator use for about 10 percent of the affected employees.

Exposures for repair and utility workers may not be amenable to additional feasible controls in most situations. However, some activities conducted routinely and continually in one location may be controlled with local exhaust ventilation systems. New or improved ventilation systems may be necessary for an estimated 5 percent of the affected employees, and on average each system would be sufficient for ten employees. Additional controls would not be required for employees with exposures below the action level, in operations for which engineering controls are infeasible, or in operations for which feasible controls have already been implemented. The engineering controls would have an estimated capital cost of $80,000 and an annual cost of $8,000. The annualized cost of engineering controls for these employees would be (N*0.05/10]*$21,020.

Employees engaged in repair and utility operations would be exposed to cadmium for an average of one fifth of the work days [7, p. 4096, Table VIII–D], and exposures for most of these employees would be below the action level. In addition, the intermittency and relatively low levels of exposure may exempt many employees from medical surveillance and other provisions. After the implementation of feasible controls, and with the necessary adjustment to reflect the nature of the exposures, an estimated 20 percent of the affected employees would be considered exposed above the action level, and additional respirator use may be required for about 7 percent of the affected employees.

For welders, brazers, and solderers exposures are generally below the action level, but exposures above the PEL may occur if the materials involved contain significant concentrations of cadmium. Some employers may choose to substitute materials that do not contain cadmium, and some employees may already be adequately protected. The implementation of additional engineering controls, beyond those already used, is not expected to be feasible. An estimated 10 percent of the affected employees may have exposures above the action level. These employees may also be required to wear respiratory protection to avoid potential exposures above the PEL.

The estimated cost of additional respiratory protection in each industry was based on the estimated number and percent of employees in each occupation for which respirators would be required. Providing respiratory protection was estimated to cost about $300 per employee per year [20, Attachment III].

The revised standard would also require protective clothing to be provided for employees exposed above the PEL. The cost of such clothing would be an estimated $104 per employee annually [20, Attachment III]. The estimated total annual cost for each industry was calculated by multiplying the annual unit cost by the total number of employees exposed above the PEL in each industry.

Exposure monitoring would be required at least twice each year for each shift of each job category. On average, each exposure monitoring sample would be representative of an estimated ten employees [1, p. 6–23]. It is assumed that representative monitoring would be conducted semi-annually for all employees exposed above the action level.

The costs of exposure monitoring involve the collection and the analysis of the samples. The estimated cost of analyzing the samples is $40 per sample, and the cost of collection would be approximately $200 per sample [1, p. 6–23].

Compliance with the medical surveillance provisions of the revised standard would require medical exams to be provided every two years and biological monitoring to be provided annually for qualifying employees. More frequent exams and testing may be required for some employees.

JACA found that employees in the occupations were generally already provided with annual medical exams [1, p. 6–26], and the evidence in the record does not contradict this conclusion. Additional medical exams may be necessary for employees in some nonmanufacturing industries.

For establishments in industries with an SIC code of 50 or higher, the estimated compliance costs include the cost of biennial medical exams for employees exposed above the action level. The estimated cost of the exams is $250 each, and the estimated number of biennial exams required is increased by 5 percent. This overall increase reflects a combination of factors such as more frequent exams for some employees as necessary, medical surveillance for some previously exposed employees, and exclusions from medical surveillance for intermittently exposed employees. The total annual cost of medical exams for these industries is thus calculated as M*$250*0.5*1.05, where M is the number of employees exposed above the action level.

Biological monitoring is generally not provided for the affected employees. The costs of the required tests for cadmium in urine and cadmium in blood would be about $60 each [1, p. 6–27], and the cost of a test for β_2–microglobulin in urine would be about $80 [21, p. 4]. In addition, the estimated average cost of collection would be about $5 for each sample. Thus, one set of biological monitoring tests would cost an estimated $215.

The total number of each of these tests that would be required annually in each industry is estimated at 1.05 times the number of employees exposed above the action level. This figure would include more frequent testing for some employees as required by the revised standard, tests for previously exposed employees as necessary, and exclusions from medical surveillance for intermittently exposed employees.

Provisions for medical removal are not expected to affect many employees. However, it may be possible for some employees to meet the criteria for mandatory removal or to be removed on the basis of a physician's determination. On average, an estimated 0.1 percent of the employees exposed above the action level may be removed each year. The number of employees removed should be small enough to enable establishments to provide removed employees with alternative positions. Costs to the employer would include paying wage subsidies for removed employees and hiring and training new employees. The average cost per removed employee would be an estimated $5,000.

The revised standard requires employers to provide change rooms and showers for employees exposed above the PEL. Based on an estimate from industry the capital cost of installing the required facilities would be an estimated $35,000 per affected establishment [16, Table A6–4]. This amount would be annualized at $5,700 per year, and the facilities should be sufficient for 20 employees. Estimated annual costs associated with providing showers would be approximately $900 per employee [20, Attachment III]. Thus, the annualized cost of providing hygiene

facilities for twenty employees would be an estimated $23,700.

Requirements regarding information, training, and recordkeeping would involve additional compliance costs for affected employers. These may include costs for establishing regulated areas, notifying employees of monitoring results, and preparing and updating written compliance programs. The incremental costs imposed by the revised standard should be relatively small as compliance may be achieved by expanding existing programs and efforts in some or all of these areas. An estimated average of $100 annually per employee exposed above the action level should provide sufficient resources to achieve compliance with the relevant elements of the standard.

Table VIII–C47 summarizes the breakdown of employee exposures in each industry after the implementation of feasible engineering controls. Of the 365,566 employees potentially exposed in these industries, an estimated 57,374 employees would be exposed above the action level, and an estimated 39,517 employees would be exposed above the PEL and require respiratory protection.

Table VIII–C48 presents the estimated costs of compliance for each industry and each provision. The total estimated annualized cost of compliance for the industries is about $160 million. Almost half of the compliance costs are attributable to engineering controls ($75 million); most of the remaining costs are associated with hygiene facilities/protective clothing ($51 million), medical surveillance ($14 million), and respiratory protection ($12 million). The compliance costs are spread over a large number of industries. Four industries would have annualized costs over $10 million, rubber and plastic products, metalworking machinery, miscellaneous machinery manufacturing, and air transportation.

Economic feasibility of a 5 μg/m³ PEL. Based on the evidence in the record, OSHA has determined that compliance with the final cadmium standard is economically feasible in each of the affected industries. For the industries considered in this section, the standard generally affects a small part of the workforce and a limited number of activities. As shown in Table VIII–C49, the costs of compliance represent less than 1 percent of the revenues of the affected establishments for each of the affected industries, and less than 0.06 percent of revenues of affected establishments across all affected industries.

TABLE VIII–C47.—EMPLOYEE EXPOSURES AFTER THE IMPLEMENTATION OF FEASIBLE ENGINEERING CONTROLS

	Industry	Potentially exposed employees	Employees exposed above action level	Employees requiring respirators
2200	Textile mill products	411	87	35
2300	Apparel	201	60	40
2500	Furniture	1,232	278	123
2600	Paper products	195	59	39
2700	Printing and publishing	1,600	490	307
2810	Inorganic chemicals	195	30	20
2820	Plastics and synthetics	870	261	174
2830	Drugs	50	15	10
2851	Paints and allied products	4,724	1,417	945
2860	Organic chemicals	2,533	621	435
2870	Agricultural chemicals	2,507	655	375
2890	Miscellaneous chemicals	1,024	307	205
2900	Petroleum refining	807	161	56
3000	Rubber and plastic products	11,133	3,013	1,985
3100	Leather products	902	271	180
3211	Flat glass	666	114	81
3220	Glassware	2,929	643	252
3250	Structural clay products	2,423	300	192
3260	Pottery products	174	40	21
3270	Concrete products	624	62	62
3280	Stone products	200	20	20
3290	Mineral products	899	60	60
3313	Alloy products	488	85	41
3315	Steel wiredrawing	500	63	50
3316	Cold-rolled steel	37	4	2
3317	Steel pipe and tubes	400	50	37
3320	Iron and steel foundries	10,808	1,886	917
3330	Primary nonferrous metals	1,800	290	168
3340	Secondary nonferrous metals	750	120	71
3350	Nonferrous rolling, etc	3,135	492	440
3360	Nonferrous foundries	10,022	1,552	1,090
3390	Miscellaneous primary metal	285	154	109
3410	Metal shipping containers	140	18	18
3420	Hand tools and hardware	2,781	412	412
3430	Heating and plumbing equipment	1,166	226	110
3440	Fabricated structural metal	17,065	2,235	2,054
3450	Screws, etc	868	87	43
3460	Forgings and stampings	612	92	92
3470	Coating and engraving	200	30	30
3480	Ordnance	265	27	27
3490	Miscellaneous fabricated metal products	9,071	1,070	997
3510	Engines and turbines	3,036	380	380
3520	Farm and garden machinery	199	60	20
3530	Construction machinery	10,453	1,103	1,045
3540	Metalworking machinery	16,127	2,379	2,379
3550	Special machinery	6,533	763	703
3560	General machinery	11,633	1,277	1,247
3570	Computer and office equipment	1,600	160	140

TABLE VIII-C47.—EMPLOYEE EXPOSURES AFTER THE IMPLEMENTATION OF FEASIBLE ENGINEERING CONTROLS—Continued

Industry	Potentially exposed employees	Employees exposed above action level	Employees requiring respirators
3580 Refrigeration and service machinery	14,180	1,832	1,475
3590 Miscellaneous machinery	19,615	2,678	2,678
3610 Electrical transmission equipment	6,388	639	625
3620 Electrical apparatus	12,460	1,259	1,206
3630 Household appliances	7,586	759	734
3640 Lighting and wiring	13,266	1,327	1,317
3650 Audio and video equipment	3,021	302	302
3660 Communications equipment	17,886	2,245	1,729
3670 Electronic components	15,412	2,044	1,724
3690 Miscellaneous electrical equipment	350	35	33
3710 Motor vehicles	18,032	2,949	1,459
3720 Aircraft	2,776	278	238
3730 Ship building	7,907	1,319	1,100
3743 Railroad equipment	1,458	198	198
3760 Missiles and space vehicles	359	36	34
3790 Miscellaneous transportation equipment	119	12	12
3812 Detection equipment, etc	67	7	7
3820 Measurement and contractor instruments	216	22	22
3840 Medical instruments	337	34	34
3860 Photographic equipment	669	201	67
3870 Watches and clockwork	173	17	17
3910 Jewelry and plated ware	79	8	8
3930 Musical instruments	16	2	2
3940 Toys and sporting goods	1,004	100	100
3950 Artists' materials	50	15	10
3960 Costume jewelry and notions	29	3	3
3990 Miscellaneous manufacturing	2,749	825	275
4011 Railroads	23	4	2
4200 Motor freight and warehousing	586	59	59
4500 Air transportation	52,147	10,438	3,653
4810 Telephone communications	2,474	495	173
4830 Radio and TV broadcasting	149	15	15
4920 Gas production and distribution	1,213	121	121
4950 Sanitary services	5,204	1,041	364
5000 Wholesale trade, durables	690	73	73
5100 Wholesale nondurables	3,080	924	616
5500 Service stations	538	54	54
7530 Automotive repair shops	3,194	391	319
7600 Miscellaneous repair services	3,494	599	378
8060 Hospitals	277	42	42
Totals	365,566	57,374	39,517

Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

TABLE VIII-C48.—ESTIMATED ANNUAL COSTS OF COMPLIANCE BY INDUSTRY AND BY PROVISION

[In thousands of dollars]

Industry	Engineering controls	Respiratory protection	Protective clothing	Exposure monitoring	Medical surveillance	Hygiene facilities	Information, training, and recordkeeping	Total
2200 Textile mill products	78	10	4	4	20	41	9	166
2300 Apparel	169	12	4	3	14	48	6	256
2500 Furniture	0	37	13	13	64	146	28	301
2600 Paper products	164	12	4	3	13	46	6	248
2700 Printing and publishing	1,188	92	32	24	113	364	49	1,861
2810 Inorganic chemicals	0	6	2	1	7	23	3	42
2820 Plastics and synthetics	731	52	18	13	60	206	26	1,107
2830 Drugs	42	3	1	1	3	12	2	64
2851 Paints and allied products	3,972	283	98	68	327	1,120	142	6,010
2860 Organic chemicals	1,622	131	45	30	143	516	62	2,549
2870 Agricultural chemicals	1,391	112	39	31	151	444	65	2,235
2890 Miscellaneous chemicals	861	61	21	15	71	243	31	1,303
2900 Petroleum refining	85	17	6	8	37	67	16	236
3000 Rubber and plastic products	7,328	595	206	145	695	2,352	301	11,623
3100 Leather products	758	54	19	13	62	214	27	1,148
3211 Flat glass	503	24	8	5	26	97	11	675

TABLE VIII-C48.—ESTIMATED ANNUAL COSTS OF COMPLIANCE BY INDUSTRY AND BY PROVISION—Continued

[In thousands of dollars]

Industry	Engineering controls	Respiratory protection	Protective clothing	Exposure monitoring	Medical surveillance	Hygiene facilities	Information, training, and recordkeeping	Total
3220 Glassware	498	76	26	31	148	299	64	1,142
3250 Structural clay products	1,403	57	20	14	69	227	30	1,821
3260 Pottery products	50	6	2	2	9	25	4	99
3270 Concrete products	0	19	6	3	14	74	6	123
3280 Stone products	0	6	2	1	5	24	2	39
3290 Mineral products	401	18	6	3	14	71	6	519
3313 Alloy products	36	12	4	4	20	49	9	135
3315 Steel wiredrawing	11	15	5	3	14	59	6	114
3316 Coldrolled steel	1	1	0	0	1	2	0	5
3317 Steel pipe and tubes	11	11	4	2	12	44	5	88
3320 Iron and steel foundries	801	275	95	91	435	1,086	189	2,972
3330 Primary nonferrous metals	104	50	17	14	67	199	29	480
3340 Secondary nonferrous metals	42	21	7	6	28	84	12	200
3350 Nonferrous rolling, etc	1,570	132	46	24	114	522	49	2,457
3360 Nonferrous foundries	1,181	327	113	75	358	1,292	155	3,502
3390 Miscellaneous primary metal	87	33	11	7	36	129	15	318
3410 Metal shipping containers	44	5	2	1	4	21	2	79
3420 Hand tools and hardware	1,687	124	43	20	95	488	41	2,498
3430 Heating and plumbing equipment	226	33	11	11	52	130	23	486
3440 Fabricated structure metal	4,386	616	214	107	516	2,434	223	8,496
3450 Screws, etc	25	13	5	4	20	51	9	127
3460 Forgings and stampings	386	28	10	4	21	109	9	567
3470 Coating and engraving	126	9	3	1	7	36	3	185
3480 Ordnance	0	8	3	1	6	31	3	52
3490 Miscellaneous fabricated metal products	2,097	299	104	51	247	1,182	107	4,087
3510 Engines and turbines	967	114	40	18	88	451	38	1,715
3520 Farm and garden machinery	0	6	2	3	14	24	6	54
3530 Construction machinery	0	314	109	53	254	1,239	110	2,079
3540 Metalworking machinery	9,660	714	247	114	549	2,819	238	14,340
3550 Special machinery	792	211	73	37	176	833	76	2,199
3560 General machinery	1,159	374	130	61	295	1,478	128	3,625
3570 Computer and office equipment	12	42	15	8	37	166	16	295
3580 Refrigeration and service machinery	1,797	443	153	88	423	1,748	183	4,835
3590 Miscellaneous machinery	9,033	803	278	129	618	3,173	268	14,302
3610 Electrical transmission equipment	8	188	65	31	147	741	64	1,244
3620 Electrical apparatus	23	362	125	60	291	1,429	126	2,417
3630 Household appliances	15	220	76	36	175	869	76	1,468
3640 Lighting and wiring	6	395	137	64	308	1,560	133	2,600
3650 Audio and video equipment	0	91	31	15	70	358	30	594
3660 Communications equipment	35	519	180	108	518	2,049	225	3,633
3670 Electronic components	2,018	517	179	98	472	2,043	204	5,531
3690 Miscellaneous electrical equipment	1	10	3	2	8	39	4	68
3710 Motor vehicles	1,204	438	152	142	681	1,729	295	4,640
3720 Aircraft	23	71	25	13	64	282	28	507
3730 Shipbuilding	3,022	330	114	63	304	1,304	132	5,270

TABLE VIII–C48.—ESTIMATED ANNUAL COSTS OF COMPLIANCE BY INDUSTRY AND BY PROVISION—Continued

[In thousands of dollars]

Industry	Engineering controls	Respiratory protection	Protective clothing	Exposure monitoring	Medical surveillance	Hygiene facilities	Information, training, and recordkeeping	Total
3743 Railroad equipment	660	59	21	10	46	235	20	1,050
3760 Missiles and space vehicles	1	10	4	2	8	41	4	69
3790 Miscellaneous transmission equipment	0	4	1	1	3	14	1	23
3812 Detection equipment, etc	0	2	1	0	2	8	1	13
3820 Measurement and construction instruments	0	6	2	1	5	26	2	43
3840 Medical instruments	0	10	4	2	8	40	3	66
3860 Photographic equipment	0	20	7	10	46	79	20	182
3870 Watches and clockwork	0	5	2	1	4	21	2	34
3910 Jewelry and plated ware	0	2	1	0	2	9	1	16
3930 Musical instruments	0	0	0	0	0	2	0	3
3940 Toys and sporting goods	0	30	10	5	23	119	10	198
3950 Artists' materials	42	3	1	1	3	12	2	64
3960 Costume jewelry and notions	0	1	0	0	1	3	0	6
3990 Miscellaneous manufacturing	0	82	29	40	190	326	82	749
4011 Railroads	2	1	0	0	1	2	0	7
4200 Motor freight and warehousing	0	18	6	3	14	69	6	115
4500 Air transportation	5,471	1,026	360	501	2,409	4,329	1,044	15,229
4810 Telephone communications	260	52	18	24	114	205	49	723
4830 Radio and TV broadcasting	0	4	2	1	3	18	1	29
4920 Gas product and distribution	0	36	13	6	28	144	12	239
4950 Sanitary services	547	109	38	50	240	432	104	1,520
5000 Wholesale trade, durables	49	22	8	3	26	86	7	201
5100 Wholesale nondurables	2,590	185	64	44	334	730	92	4,040
5500 Service stations	0	18	6	3	18	64	5	113
7530 Automotive repair shops	0	96	33	19	141	378	39	707
7600 Miscellaneous repair services	1,183	113	39	29	217	448	60	2,089
8060 Hospitals	175	12	4	2	15	49	4	262
Totals	74,820	11,855	4,110	2,764	13,512	46,827	5,737	159,616

Note: This table does not include costs for industry sectors covered separately elsewhere in this analysis.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

TABLE VIII–C49.—COMPLIANCE COSTS PER EMPLOYEE AND AS A PERCENTAGE OF REVENUES AND PROFITS BY INDUSTRY

Industry	Annual compliance cost ($thousands)	Number of effected employees	Average annual cost of compliance per employee ($)	Annual revenues ($millions)	Compliance cost as a percent of revenues	Annual pre-tax profits ($millions)	Compliance cost as a percent of profits
2200 Textile mill products	166	411	404	246	0.0675	12	1.3507
2300 Apparel	256	201	1,272	74	0.3477	4	6.4700
2500 Furniture	301	1,232	244	629	0.0478	31	0.9567
2600 Paper products	248	195	1,272	222	0.1118	11	2.1825
2700 Printing and publishing	1,861	1,630	1,163	945	0.1970	58	3.2167
2810 Inorganic chemicals	42	195	217	205	0.0206	15	0.2750
2820 Plastics and synthetics	1,107	870	1,272	1,481	0.0747	70	1.5733
2830 Drugs	64	50	1,272	59	0.1070	2	2.8540
2851 Paints & allied products	6,010	4,724	1,272	6,549	0.0917	287	2.0974
2860 Organic chemicals	2,549	2,533	1,006	8,534	0.0390	384	0.6639
2870 Agricultural chemicals	2,235	2,507	891	4,840	0.0481	197	1.1332
2890 Miscellaneous chemicals	1,303	1,024	1,272	1,156	0.1126	64	2.0489
2900 Petroleum refining	236	607	292	4,316	0.0054	183	0.1284

TABLE VIII–C49.—COMPLIANCE COSTS PER EMPLOYEE AND AS A PERCENTAGE OF REVENUES AND PROFITS BY INDUSTRY—Continued

	Industry	Annual compliance cost ($thousands)	Number of affected employees	Average annual cost of compliance per employee ($)	Annual revenues ($millions)	Compliance cost as a percent of revenues	Annual pre-tax profits ($millions)	Compliance cost as a percent of profits
3000	Rubber & plastic prod.	11,623	11,133	1,044	7,591	0.1531	427	2.7218
3100	Leather products	1,148	902	1,272	435	0.2636	24	4.6870
3211	Flat glass	675	666	1,014	630	0.1070	39	1.7131
3220	Glassware	1,142	2,929	390	1,897	0.0602	114	1.0035
3250	Structural clay products	1,821	2,423	752	1,362	0.1337	75	2.4317
3260	Pottery products	99	174	569	75	0.1328	5	1.8973
3270	Concrete products	123	624	197	471	0.0260	21	0.5797
3280	Stone products	39	200	197	33	0.1192	2	2.0301
3290	Mineral products	519	899	577	751	0.0691	53	0.9873
3313	Alloy products	135	488	276	264	0.0510	10	1.3179
3315	Steel wiredrawing	114	500	228	1,095	0.0104	42	0.2690
3316	Cold-rolled steel	5	37	147	94	0.0057	4	0.1398
3317	Steel pipe and tubes	88	400	221	473	0.0186	11	0.8298
3320	Iron and steel foundries	2,972	10,808	275	6,360	0.0467	286	1.0384
3330	Primary nonferrous metals	480	1,800	267	3,963	0.0121	218	0.2203
3340	Secondary nonferrous mtls.	200	750	266	1,759	0.0113	77	0.2593
3350	Nonferrous rolling, etc.	2,457	3,135	784	4,720	0.0520	207	1.1895
3360	Nonferrous foundries	3,502	10,022	349	5,655	0.0619	240	1.4570
3390	Misc. primary metal	318	285	1,115	246	0.1289	12	2.5799
3410	Metal shipping containers	79	140	561	218	0.0360	14	0.5445
3420	Hand tools & hardware	2,498	2,781	898	2,024	0.1233	154	1.6183
3430	Heating & plumbing equip.	486	1,186	410	722	0.0672	32	1.5382
3440	Fabricated struct. metal	8,496	17,065	498	11,061	0.0768	567	1.4988
3450	Screws, etc.	127	868	147	502	0.0253	24	0.5333
3460	Forgings & stampings	567	612	926	518	0.1094	28	2.0354
3470	Coating and engraving	185	200	926	95	0.1953	7	2.7419
3480	Ordnance	52	265	197	167	0.0311	18	0.2830
3490	Misc. fabr. metal prod.	4,087	9,071	451	6,685	0.0611	368	1.1116
3510	Engines and turbines	1,715	3,036	565	3,469	0.0494	117	1.4646
3520	Farm and garden machinery	54	199	273	183	0.0295	9	0.5912
3530	Construction machinery	2,079	10,453	199	8,725	0.0238	425	0.4886
3540	Metalworking machinery	14,340	16,127	889	8,367	0.1713	554	2.5870
3550	Special machinery	2,199	6,533	337	5,595	0.0392	343	0.6415
3560	General machinery	3,625	11,633	312	8,427	0.0430	474	0.7646
3570	Computer & office equip.	295	1,600	184	1,515	0.0194	66	0.4446
3580	Refrig. & service mach.	4,835	14,180	341	13,809	0.0350	656	0.7372
3590	Miscellaneous machinery	14,302	19,615	729	9,177	0.1558	574	2.4936
3610	Elec. transmission equip.	1,244	6,388	195	3,946	0.0315	202	0.6148
3620	Electrical apparatus	2,417	12,460	194	8,416	0.0287	442	0.5469
3630	Household appliances	1,468	7,586	193	6,852	0.0214	240	0.6120
3640	Lighting and wiring	2,600	13,266	196	8,763	0.0296	570	0.4585
3650	Audio & video equip.	594	3,021	197	2,132	0.0278	173	0.3431
3660	Communications equip.	3,633	17,886	203	15,307	0.0237	497	0.7302
3670	Electronic components	5,531	15,412	359	10,205	0.0541	485	1.1410
3690	Misc. elect. equip.	66	350	190	294	0.0226	15	0.4306
3710	Motor vehicles	4,640	18,032	257	30,234	0.0153	1,323	0.3508
3720	Aircraft	507	2,776	182	2,180	0.0232	139	0.3644
3730	Ship building	5,270	7,907	666	4,179	0.1260	136	3.8799
3743	Railroad equipment	1,050	1,458	720	1,266	0.0829	70	1.5081
3760	Missiles & space vehicles	69	359	193	385	0.0179	19	0.3595
3790	Misc. trans. equip.	23	119	197	100	0.0235	4	0.5704
3812	Detection equipment, etc.	13	67	197	55	0.0238	3	0.4154
3820	Meas. & contr. instr.	43	216	197	126	0.0338	7	0.6291
3840	Medical instruments	66	337	197	216	0.0306	15	0.4543
3860	Photographic equipment	182	669	273	913	0.0199	59	0.3073
3870	Watches & clockwork	34	173	197	152	0.0224	9	0.3986
3910	Jewelry & plated ware	16	79	197	53	0.0293	3	0.4891
3930	Musical instruments	3	16	197	6	0.0487	1	0.5904
3940	Toys and sporting goods	198	1,004	197	607	0.0325	36	0.5537
3950	Artists' materials	64	50	1,272	30	0.2135	1	4.4963
3960	Costume jewelry & notions	6	29	197	11	0.0517	1	0.5835
3990	Misc. manufacturing	749	2,749	273	1,603	0.0467	74	1.0107
4011	Railroads	7	23	284	17	0.0389	2	0.2888
4200	Motor freight & warehsing.	115	586	197	217	0.0530	10	1.1169
4500	Air transportation	15,229	52,147	292	22,530	0.0675	1,070	1.4230
4810	Telephone communications	723	2,474	292	1,961	0.0368	135	0.5359
4830	Radio & TV broadcasting	29	149	197	136	0.0215	1	4.3064
4920	Gas prod. & dist.	239	1,213	197	3,098	0.0077	228	0.1044
4950	Sanitary services	1,520	5,204	292	5,674	0.0267	596	0.2551
5000	Wholesale trade, durables	201	690	292	1,516	0.0132	70	0.2873
5100	Wholesale nondurables	4,040	3,080	1,312	8,953	0.0451	302	1.3369
5500	Service stations	113	538	210	165	0.0685	4	2.6127
7530	Automotive repair shops	707	3,194	221	1,044	0.0677	70	1.0034
7600	Misc repair services	2,089	3,494	598	1,141	0.1830	94	2.2187

TABLE VIII-C49.—COMPLIANCE COSTS PER EMPLOYEE AND AS A PERCENTAGE OF REVENUES AND PROFITS BY INDUSTRY—Continued

Industry	Annual compliance cost ($thousands)	Number of affected employees	Average annual cost of compliance per employee ($)	Annual revenues ($millions)	Compliance cost as a percent of revenues	Annual pre-tax profits ($millions)	Compliance cost as a percent of profits
8060 Hospitals	262	277	945	149	0.1762	7	4.0284
Totals	159,616	365,566	437	290,820	0.0548	14,731	1.0835

Sources: *1989 Annual Survey of Manufacturers*, U.S. Department of Commerce, June 1991; *1987 Census of Industries*, U.S. Department of Commerce, 1990; *Statistical Abstract of the United States, 1991*, U.S. Department of Commerce; *Duns Insight*, Dun & Bradstreet, 1989.

Establishments in each of the affected industries would either need to raise prices or reduce profits (or a combination of these) to compensate for compliance costs. A significant increase in prices can usually be expected to result in a loss of sales; the relationship between these variables is determined by the price elasticity of demand (the ratio of the percent change in quantity demanded associated with a percent change in price). A reduction in profits may enable an individual firm to maintain sales volume, but would be likely to result in lower production or slower growth if applied to an industry as a whole; lower profits reduce the value of the industry's capital and firms operating on the margin may exit the market.

The impact of the revised cadmium standard would probably be a combination of increased prices and reduced profits in the affected industries. To the extent that profits are reduced to mitigate the effects of price increases, smaller potential changes in output and employment can be expected. However, reductions in profits may also affect employment and output indirectly. Lower profits tend to depress the value of capital which reduces the incentive for additional investment in the affected industries.

Although a significant reduction in profits for an industry may cause some contraction as marginal firms exit the market, compliance with the cadmium standard is not expected to be a determining factor for such occurrences. Even under the extreme assumption that compliance costs would be wholly absorbed from profits (preventing any effects from price increases), the maximum effect in any industry would be an average reduction in profits among the affected establishments of less than 7 percent, and the overall reduction among affected establishments would be about 1 percent. Changes of this magnitude would not substantially affect the viability of continuing operations.

Ultimately, compliance with the cadmium standard causes production resources to be shifted from the affected industries and from other sectors of the economy to compliance-related activities. The proportion of resources diverted from the affected industries is determined by the extent to which reductions in profits are taken and the extent to which reductions in output are caused by price increases. The proportion of resources diverted from other sectors of the economy is represented by increases in prices paid for the output of the affected industries. The small relative size of compliance costs in relation to revenues, profits, and other influences in the business environment makes the overall potential impact of the cadmium standard virtually undetectable.

Notes

1. Exhibit 13, "Economic Impact Analysis of the Proposed Revision to the Cadmium Standard," Final Report, JACA Corporation, March 15, 1988.
2. Exhibit 19-50, "Comments of the United States Department of Commerce," U.S. Department of Commerce, May 21, 1990.
3. Exhibit 106, "Post-Hearing Comments of the National Institute for Occupational Safety and Health on the Occupational Safety and Health Administration's Proposed Rule on Occupational Exposure to Cadmium," U.S. Department of Health and Human Services, NIOSH, September 18, 1990.
4. Exhibit 19-9, "Duriron Comments on Proposed Cadmium Exposure Rule," Duriron Company, Inc., April 19, 1990.
5. U.S. Department of Labor, Employment and Training Administration, *Dictionary of Occupational Titles*, Fourth Edition, Revised 1991.
6. Exhibit 15A, "Preliminary Regulatory Impact and Regulatory Flexibility Analysis for the Proposed 5 $\mu g/m^3$ Cadmium Standard," U.S. Department of Labor, Occupational Safety and Health Administration, Office of Regulatory Analysis, January 22, 1990.
7. Federal Register, Volume 55, Number 25, "Occupational Exposure to Cadmium; Proposed Rule," U.S. Department of Labor, Occupational Safety and Health Administration, February 6, 1990.
8. Exhibit 19-34, Comments of the Copper & Brass Fabricators Council, Inc., May 11, 1990.
9. Exhibit 19-32, "Comments of ASARCO Incorporated," ASARCO, May 9, 1990.
10. Exhibit 19-44, Comments of Texas Instruments Incorporated, May 11, 1990.
11. Exhibit 105, "Economic Impacts of the Proposed Permissible Exposure Limits for Cadmium," U.S. Department of the Interior, Bureau of Mines, September 18, 1990.
12. Exhibit 42, Testimony of Michael A. Coffman, June 11, 1990.
13. Exhibit 57, "Testimony of the National Institute for Occupational Safety and Health on the Occupational Safety and Health Administration's Proposed Rule on Occupational Exposure to Cadmium, Draft 2," U.S. Department of Health and Human Services, NIOSH, July 6, 1990.
14. "Occupational Exposure to Lead; Final Rule; Statement of Reasons," Federal Register, Volume 54, Number 131, pp. 29142 et seq., July 11, 1989.
15. *United Steel Workers of America* v. *Marshall*, 647 F.2d. (D.C. Cir. 1980).
16. Exhibit 19-43, Attachment L, "Feasibility and Cost Study of Engineering Controls for Cadmium Exposure Standard," PACE Incorporated, April 30, 1990.
17. Exhibit 19-43, Attachment I, "Economic and Technological Feasibility of a 5 Microgram per Cubic Meter Workplace Standard for Airborne Cadmium," Putnam, Hayes & Bartlett, Inc., April 30, 1990.
18. Exhibit 144-2, Comments from AIM Products, Incorporated, October 7, 1991.
19. Exhibit 15B, "Preliminary Regulatory Impact and Regulatory Flexibility Analysis for the Proposed 1 $\mu g/m^3$ Cadmium Standard," U.S. Department of Labor, Occupational Safety and Health Administration, Office of Regulatory Analysis, January 22, 1990.
20. Exhibit 19-30, "Comments on OSHA Proposed Cadmium Regulation," Big River Zinc Corporation, May 10, 1990.
21. Exhibit 123, "Comments of Public Citizen Health Research Group and the International Chemical Workers Union on OSHA's Proposed Standard Governing Occupational Exposure to Cadmium," Public Citizen, October 17, 1990.

Construction

Industry overview. The construction industry includes establishments engaged in building construction (residential, commercial, industrial, etc.) and heavy construction (streets, bridges, pipelines, power plants, etc.). The term construction may include new work,

additions, alterations, reconstruction, installations, and repairs. General contractors usually assume responsibility for an entire construction project and often subcontract substantial amounts of work to special trade contractors. Over half of the five million employees in the construction industry work for special trade contractors specializing in plumbing, painting, electrical, carpentry, roofing, or other construction activities.

Production processes. Construction employees are potentially exposed to cadmium when welding, soldering, brazing, cutting, or burning steel and other metals in which cadmium may be present. Most metals, such as steel, only contain trace amounts of cadmium; some specialty alloys may include greater concentrations of cadmium; some objects may be coated with cadmium; and cadmium may be present in furnace dust accumulated on the surface of some equipment.

Activities potentially generating airborne concentrations of cadmium fume or dust occur during several types of construction work. These may include boiler installation and repair, steam fitting, furnace repair, installation of machinery and other equipment, electrical work, structural steel and iron work, dismantling of machinery, and general welding operations. Establishments involved in these activities include plumbing, heating and air conditioning contractors; electrical work contractors; sheet metal contractors; structural steel erection contractors; wrecking and demolition contractors; miscellaneous contractors engaged in the installation or erection of building equipment; and welding contractors.

Employee exposures. Cadmium exposures experienced by construction workers were researched by JACA Corporation. Estimated exposure levels were determined separately for different types of work. Exposures for electricians, plumbers, pipefitters, steamfitters, boilermakers, workers who install or dismantle machinery and heavy equipment, and other repair or maintenance workers employed in the construction industry were represented by the exposure profile for the occupational group of repair and utility workers. [1, p. 3–30 and Table 3–10]. Exposures for construction workers welding, brazing, or soldering during structural steel erection, heavy construction, demolition, and other jobs done by special trade contractors were represented by the exposure profile for the occupational group of welders, brazers, and solderers. [1, p. 3–31 and Table 3–10]. The exposure profiles developed by JACA are presented in Table VIII–C50. These data were derived from OSHA inspection data and from relevant NIOSH Health Hazard Evaluations [1, p. 3–32]. Estimated mean and median exposures for each type of construction work are 3 $\mu g/m^3$ or less.

TABLE VIII–C50.—CADMIUM EXPOSURE DATA FOR CONSTRUCTION WORKERS BASED ON JACA

Job category	Concentration in $\mu g/m^3$		
	Geometric mean	Median	Range
Repair and utility workers [1]	2.0	3.0	0.1–271.0
Welders, brazers, and solderers [2]	0.2	0.1	0.1–163.0

[1] Includes pipefitters, steamfitters, boilermakers, electricians, plumbers, and maintenance and repair employees in the construction industry.
[2] Includes all construction workers welding, cutting, soldering, or brazing, except those included above.
Note: Exposure data reflect 8-hour time-weighted average exposures.
Source: Exhibit 13, JACA, Table 3–10.

The data also indicate that significantly higher exposures may be possible under relatively infrequent circumstances.

An estimated 70,000 employees in the construction industry are potentially exposed to cadmium throughout the year. For most of these workers, exposure to cadmium would occur on one out of ten working days on average.

The proposed rule and preliminary analysis did not elicit many comments from construction employers or employees or their representatives. OSHA believes that the proposed rule was regarded as having little impact in the construction industry. The Advisory Committee on Construction Safety and Health (ACCSH) reviewed the proposed regulation with the accompanying analysis and did not question the characterization of exposures for the construction industry.

Existing and feasible additional controls. Construction workers with potential exposure to cadmium would also have potential exposure to other hazardous substances. Depending on the material worked with, activities with potential cadmium exposure may involve exposure to aluminum, antimony, arsenic, copper, iron oxide, lead, magnesium oxide, manganese, molybdenum, silver, tin oxide, and zinc oxide. Many construction employees may be generally protected from exposure to these substances, and this protection would also be effective for reducing cadmium exposures.

OSHA requested information regarding the need for additional controls for cadmium exposure. Construction employers did not identify any conditions in which controls beyond those currently provided for concomitant exposures would be necessary for cadmium exposure.

In some applications, cadmium exposure may be eliminated through substitution of products without cadmium. At least one firm offers a range of cadmium-free products designed to replace alloys made with cadmium in several applications. [3].

Feasible engineering controls and work practices for reducing cadmium exposure should be implemented when possible. In construction these may include portable hoods, exhaust ventilation, fans, enclosures, and tools and work practices designed for minimizing employee exposures.

Although some construction activities affected by the revised regulation would be amenable to engineering controls, respirators would be an acceptable method of protection in situations where engineering controls are infeasible. Construction activities are often intermittent and of short duration with unpredictable exposures. The activities may not involve a fixed work place and frequently occur in circumstances where engineering controls are not feasible. Respirators capable of providing the necessary protection are currently available and widely used in the construction industry.

Technological feasibility of a 5 $\mu g/m^3$ PEL. The revised cadmium standard with a PEL of 5 $\mu g/m^3$ is technologically feasible for the construction industry. The potential impact would affect a small fraction of the work force; the

cadmium exposures experienced by these workers are intermittent and generally below the PEL. Feasible engineering controls and/or appropriate use of respirators are capable of providing the required protection and currently do so for many of the affected workers in this industry.

The ACCSH reviewed the proposed cadmium regulation and suggested several relatively minor changes to provisions involving exposure monitoring, medical surveillance, and recordkeeping, but did not oppose the proposed PEL or question its feasibility. No comments from the industry in response to the proposed rule raised any concerns about the feasibility of achieving the PEL.

Costs of compliance with a 5 μg/m³ PEL. Potential employee exposures to cadmium in the construction industry generally occur with exposures to other hazardous substances, and employers should already be using feasible engineering controls for these exposures. Employees are often provided with respirators in such situations as an appropriate form of protection when engineering controls need to be supplemented or are infeasible. The revised cadmium standard would not require the implementation of additional engineering controls for these employees. In addition, engineering controls would not be required by the cadmium standard for employees exposed less than thirty days per year.

Respiratory protection should already be provided to many employees with potential cadmium exposure under requirements of existing standards. However, achieving full compliance with the revised cadmium standard with a PEL of 5 μg/m³ may require some additional respirator use.

OSHA estimates that 70,000 employees in the construction industry are potentially exposed to cadmium for an average of one out of ten working days. Most of these employees would be exposed below the PEL or would be adequately protected from cadmium exposure. Additional respirator use may be necessary on an intermittent basis for about 5 percent of the employees with potential exposure. An estimated 3,500 workers would need to be provided with respirators to achieve compliance with the revised standard. At a cost of $100 per employee per year for the intermittent use of respirators, the total annual cost for the construction industry would be $0.35 million.

In addition to adequately controlling cadmium exposures, compliance with the revised cadmium standard would require construction establishments with employees potentially exposed to cadmium to establish exposure monitoring and medical surveillance programs and to provide appropriate hygiene facilities.

Exposure monitoring would probably not be necessary for most construction employees for whom exposures are consistently below the action level. Exposure monitoring would be necessary when higher cadmium exposures can be anticipated, and an estimated 10 percent of the employees potentially exposed (7,000 employees) may work in such circumstances at least once per year. On average, representative exposure monitoring may be conducted semi-annually with each sample representing three employees. At an estimated average cost of $240 per sample for collection and analysis, the total annual cost would be about $1.12 million.

In addition, employers would be required to conduct and maintain a written record of a determination of potential cadmium exposures for each employee. The cost of such a determination may average $25 annually for each employee potentially exposed. The total annual cost would be an estimated $1.75 million.

Requirements to provide medical surveillance depend on the nature of exposures experienced by employees. Exposures in construction are generally intermittent, and medical surveillance may need to be provided for some employees. As provided in the final standard, medical surveillance includes initial, periodic, and termination exams; employees with intermittent exposures may be excluded from medical surveillance, and some previously exposed employees may be included. Medical exams and biological monitoring would be necessary for all employees required to wear respirators. An estimated 7,000 employees (including employees performing tasks, operations, or jobs as specified by the standard) encountering exposures above the action level at some time each year may require medical surveillance. The estimated annual cost per employee would be $340 ($215 per year for annual biological monitoring and $125 per year for biennial medical exams), and the total annual cost for the construction industry would be $2.38 million. Provisions for medical removal are not expected to involve additional compliance costs since exposures for construction employees are relatively low and intermittent.

Additional hygiene facilities may be necessary at some operations with cadmium exposures above the PEL. A mobile trailer with the necessary facilities including a water supply, showers and lockers could be rented for about $100 per day. On average, an estimated 700 employees may need to be provided with such facilities daily. Assuming one trailer would be rented for every five employees exposed above the PEL, then on average 140 such trailers would each be rented for 250 days each year. The total annual cost for the trailers would be $3.5 million. The estimated cost of showering on work time is $900 per full-time equivalent employee annually (based on fifteen minutes per day for 240 days per year at $15 an hour). This cost would apply to an estimated 700 employees daily, and the total annual cost would be $630,000. The total annual cost associated with requirements for hygiene facilities would be $4.13 million.

In addition, employees exposed above the PEL would be required to be provided with protective clothing. The estimated cost per employee would be $104 per year, and the total cost for the industry would be about $73,000 annually. The total annual cost for hygiene facilities and protective clothing for the construction industry would be an estimated $4.203 million.

Provisions in the final cadmium standard for information (including warning signs, labels, and other information-related provisions), training, and recordkeeping may impose additional costs of compliance on construction employers with employees exposed to cadmium. For operations where exposures may exceed the PEL, regulated areas would need to be established. Employers would be required to train employees and to develop written compliance programs. These requirements would apply infrequently and only for work that involves potential cadmium exposure.

These requirements should not involve substantial burdens for construction employers. Regulated areas can be established at construction sites with inexpensive barricade tape; training is required by existing standards, and incremental training required by this standard can be incorporated into current training programs; a written compliance program would describe the use of respirators or other measures used to limit employee exposures. The compliance costs for these provisions may average about $100 for each employee exposed above the PEL at some time during the year; the total annual cost for the industry would be an estimated $700,000.

The annual costs of compliance for the construction industry are

summarized Table VIII-C51. The total estimated annual cost is $10.503 million.

Economic feasibility of a 5 μg/m³ PEL. The final cadmium standard for the construction industry is economically feasible. The total annual costs of compliance would be about $10.5 million and would not threaten the competitive stability or the existence of the construction industry. The value of construction work done by these employees is estimated to be $490 million, or an average of about $70,000 for the 7,000 full-time equivalent employees potentially exposed annually.

TABLE VIII-C51.—ESTIMATED COSTS OF COMPLIANCE WITH THE REVISED CADMIUM STANDARD FOR THE CONSTRUCTION INDUSTRY

Provision	Annualized cost ($thousands)
Exposure Control	0.0
Respirator Use	350.0
Exposure Monitoring	2,870.0
Medical Surveillance	2,380.0
Hygiene Provisions	4,203.0
Recordkeeping and Information	700.0
Total	10,503.0

Note: Costs do not include current expenditures.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

The compliance costs represent less than 2.2 percent of the revenues associated with the activities affected by the requirements of the cadmium standard.

Costs incurred by construction employers would probably be passed through to customers, and prices would generally increase for work involving employee exposures to cadmium. Employers should be able to anticipate cost increases and include compliance costs in their price estimates. Compliance with the cadmium standard would not require large capital expenditures. The costs would primarily be incurred on a per-project basis and would vary according to the size of the project.

In response to OSHA's requests for information and comments from the public, no construction employers questioned the economic feasibility of the proposed cadmium standard or OSHA's estimated costs of compliance for the construction industry. The ACCSH recommended modifications to the proposed rule that generally would increase its stringency and cost [4 and 5]. A representative of the Committee testified that the cost of these requirements would be bearable and that the resulting standard would be "one that [construction employers] can implement and comply with" [6, p. VII-15].

Notes

1. Exhibit 13, "Economic Impact Analysis of the Proposed Revision to the Cadmium Standard," Final Report, JACA Corporation, March 15, 1988.
2. Occupational Exposure to Cadmium, Proposed Rule, OSHA, F.R. Vol. 55, No. 25, Tuesday, February 6, 1990.
3. Exhibit 144-2, "Comments of Aim Products, Inc.," Aim Products, Inc., October 7, 1991.
4. Exhibit 14-5, "Modifications to Regulatory Text of Cadmium Proposal Submitted by the Construction Advisory Committee for Development of Separate Cadmium Standard for the Construction Industry," Advisory Committee on Construction Safety and Health, November 20, 1989.
5. Exhibit 14-5, "Testimony in Support of a Construction Specific Standard," Ronald R. Amerson, Advisory Committee on Construction Safety and Health, June 13, 1990.
6. Hearing Transcript, June 13, 1990.

D. Economic Feasibility and Regulatory Flexibility Analysis

Economic Impacts

Based on the evidence in the record, OSHA has determined that compliance with the final cadmium standard is economically feasible in each of the affected industries.

Table VIII-D1 summarizes the economic impacts for the industries affected by this rulemaking. For most industries, the standard affects a limited number of activities and the costs of compliance represent less than 0.1 percent of revenues. The compliance costs are generally expected to result in slight increases in prices for goods and services associated with occupational cadmium exposures.

In some industries price increases needed to recoup compliance costs may decrease sales volume. For these establishments the standard may result in some reduction in profits. OSHA does not expect the standard to significantly affect the viability of continuing operations in any industry or to result in any plant closures. However, to the extent that compliance costs contribute marginally to increased production costs, prospects for economic expansion and employment growth in industries with cadmium exposure may be diminished. Additional details of the economic analysis for each industry can be found in the preceding sections in which the specific industries are analyzed.

Basically, the regulation tends to trade some of the societal benefits of producing and using products containing cadmium for greater protection among exposed employees.

TABLE VIII-D1.—SUMMARY OF ECONOMIC IMPACTS BY INDUSTRY

[Thousands of dollars]

Industry	Number of affected establishments	Total annual costs of compliance	Average annual cost per affected establishment	Total annual revenues	Ratio of compliance costs to revenues	Total annual profits	Ratio of compliance costs to profits
Batteries	6	1,947	324.5	185,000	0.011	7,400	0.263
Zinc/cadmium	5	1,723	344.6	230,000	0.007	NA	NA
Pigments	4	473	118.4	30,000	0.016	1,500	0.316
Formulators	700	7,370	10.5	900,000	0.008	45,000	0.164
Stabilizers	5	935	187.1	92,000	0.010	8,300	0.113
Lead	4	283	70.7	176,000	0.002	NA	NA
Plating	400	787	2.0	200,000	0.004	8,800	0.089
Utilities	4,000	2,388	0.6	140,000,000	0.000	7,000,000	0.000
Iron/steel	120	1,638	13.7	64,000,000	0.000	NA	NA
Subtotal	5,244	17,545	3.3	205,813,000	0.000	7,071,000	0.002
Other general industry	50,000	159,615	3.2	290,820,000	0.001	14,731,000	0.011
Construction	10,000	10,503	1.1	490,000	0.021	NA	NA
Total	65,244	187,663	2.9	497,123,000	0.000	21,802,000	0.009

Note: (1) Costs do not include current expenditures. (2) Where sales or profit data provided to the record for specific companies or industries were used, the information was verified through publicly available sources such as Dun & Bradstreet, DIALOGUE, Dow Jones News Retrieval, and Nexis.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

Compliance with the standard ultimately causes production resources to be shifted from the regulated industries and from other sectors of the economy to compliance-related activities. Although the overall effect on the economy will probably be undetectable, a very slight increase in prices may result from the improvement in the protection of the health of employees exposed to cadmium.

Regulatory Flexibility Analysis

In accordance with the Regulatory Flexibility Act of 1980 (Pub. L. 96-353, 94 Stat. 1164 [5 U.S.C. 601]), OSHA has evaluated the potential impact of the revised standard on small establishments. As a result of this review, OSHA has determined that the revised standard would not have a significant adverse impact on a substantial number of small establishments.

Establishments with employees exposed to cadmium may incur compliance costs to protect the health of their employees. The cost of providing adequate protection would depend on the existing exposure levels, the extent of current protective measures, and on the nature of the operation. As demonstrated, above, the estimated compliance costs would be feasible for establishments in each affected industry.

The affected establishments in each industry may include some small establishments. Smaller establishments would have fewer employees and correspondingly lower compliance costs. Since the impacts would generally be proportionally lower for smaller establishments, the revised standard would not create any significant competitive disadvantage based on firm size. Table VIII-D2 shows the estimated average annual costs of compliance for small and large establishments.

The Small Business Administration (SBA) objected to the proposed standard because the proposed PEL "is not warranted by health risks nor is it technically feasible" [1]. The health risks are discussed extensively in other sections of the preamble, and OSHA believes that the potential benefits of the final standard are real and substantial, as supported by the record. The regulatory impact analysis has also shown that the final standard is both technologically and economically feasible.

OSHA has included provisions in the final standard to minimize the burden for small establishments. In response to one of the primary concerns of the SBA, OSHA relaxed requirements for firms with employees with intermittent exposures by changing the trigger mechanism for medical surveillance. OSHA also reviewed other non-engineering requirements to ensure that only those necessary to protect the health of employees would be included in the final standard.

The final standard may impose compliance costs on some small establishments, but the ability of small establishments to compete effectively, remain in business, and retain market share would not be inhibited. Small establishments may find themselves at an advantage in some cases with the flexibility to adapt or specialize in markets involving cadmium products. Whether an industry is dominated by small businesses or by large companies, the final cadmium standard would not impose a greater relative burden on small establishments.

TABLE VIII-D2.—COMPARISON OF IMPACTS ON SMALL AND LARGE ESTABLISHMENTS

	Small	Large	Total
Number of affected establishments	45,580	19,664	65,244
Number of affected employees	73,000	452,000	525,000
Annual compliance cost (in thousands)	$27,410	$160,323	$187,733
Average annual cost per affected establishment	$601	$8,153	$2,877
Average annual cost per affected employee	$375	$355	$358

Note: Small establishments are defined as having fewer than 20 employees.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

OSHA recognizes that some establishments may need assistance in complying with safety or health regulations. The OSHA Office of Compliance Assistance and representatives of regional and area OSHA offices are available for answering questions and offering advice to small businesses. In addition, small businesses may take advantage of OSHA's consultation program which conducts a comprehensive assessment of facilities, provides guidance, and makes recommendations. The final cadmium rule also incorporates extended compliance dates for small businesses.

OSHA recognizes the importance of avoiding unnecessary burdens on small (and also larger) establishments and has taken steps to ensure that the revised cadmium standard would not involve such consequences. Small establishments should be able to continue to profitably provide goods and services demanded in the economy without endangering the health of their employees.

Notes

1. United States Small Business Administration, "Comments of the Chief Counsel for Advocacy of the United States Small Business Administration," Mark S. Hayward, Acting Chief Counsel, October 18, 1990.

E. Environmental Impact Assessment

This final rule has been reviewed in accordance with the requirements of the National Environmental Policy Act (NEPA) of 1969 (42 U.S.C. 4321 et seq.), the Guidelines of the Council on Environmental Quality (40 CFR parts 1500-1517), and OSHA's DOL NEPA procedures (29 CFR part 11). As a result of this review, OSHA has determined that the promulgation of this rule would have no significant environmental impact. Any changes that would result from compliance with this rule would tend to reduce emissions of cadmium from the work place.

F. Benefits

Introduction

The health risks associated with exposure to cadmium are discussed at length in other sections of the preamble. Potential health effects include increased risks of lung cancer and of

kidney dysfunction. The excess risks attributable to cumulative exposures were estimated and quantified. The estimated incremental increase in risk corresponding to various levels of exposure was expressed as a dose-response relationship.

In this section the dose-response formula is applied to the existing exposure levels of the exposed employees to determine the excess risk faced by the employees and the total number of fatalities and illnesses that may result from the exposures. In addition, the dose-response formula is applied to the projected exposure levels that would result from full compliance with the final cadmium standard, and the expected reduction in the incidence rates and in the total number of fatalities and illnesses is calculated.

The resulting numbers representing expected benefits from this regulation should be viewed in context. First, the numbers are derived through the complex process of quantitative risk assessment which involves a series of assumptions in evaluating epidemiological evidence and animal studies. Second, additional benefits may not be included in these numbers, such as reduced exposure resulting from restricted access to exposure areas, increased awareness of hazards, improved hygiene practices, and early detection of potential problems. Third, the estimates of lifetime excess risk are based on full-time exposure over 45 years; to the extent that employees are not so exposed, the total excess risk may be spread over a larger population and the actual risk may vary.

Cancer Risk

Table VIII–F1 shows the estimated number of exposed employees in the affected industries and the current average exposure level among the exposed employees. For purposes of estimating benefits, the current average exposure level reflects the estimated mean concentration of cadmium in the air inhaled by the employees. For employees currently wearing respirators exposure levels were adjusted down to one tenth of the ambient concentration.

Quantitative risk assessments (QRAs) for lung cancer were applied to the number of employees and the exposure level in each job category to determine the number of excess cases attributable to current exposures. The calculation was repeated using the projected exposure levels estimated to be achieved under compliance with the final standard; the difference determined the number of cases potentially preventable by the standard.

Based on four risk models developed by OSHA Health Standards, compliance with the reduced exposure limit is expected to prevent from 9 to 27 cancer fatalities each year out of 13 to 40 excess cancer fatalities currently taking place. Within this range, OSHA's Multistage Model predicts 17 to 18 cancers avoided annually out of 25 excess cancer fatalities (see Table VIII–F1).

TABLE VIII–F1.—EXPECTED REDUCTION IN EXCESS CANCER CASES USING THE MULTISTAGE MODEL

Industry	Number of exposed employees	Current average exposure [1] µg/m³	Total excess cases after 45 years	Average annual excess number of cancer cases	Projected average exposure [1] µg/m³	Average annual excess cancer cases prevented
Nickel-cadmium batteries	1,500	20	33	0.74	3.0	0.66
Zinc/cadmium production	1,350	14	21	0.46	3.0	0.38
Cadmium pigments	100	28	3	0.07	3.0	0.06
Dry color formulators	7,000	5	38	0.85	2.0	0.54
Cadmium stabilizers	200	24	5	0.12	3.0	0.11
Lead smelting/refining	400	5	2	0.05	2.0	0.03
Cadmium plating	1,200	2	3	0.06	1.0	0.03
Electric utilities	37,500	1	41	0.91	1.0	0.00
Iron and steel	40,000	2	88	1.95	1.0	1.02
General industry, nec:						
Chemical mixers	26,436	8.0	174	3.87	1.0	3.37
Electroplaters	6,648	3.0	22	0.49	1.0	0.34
Furnace oper.	17,202	1.0	19	0.42	0.8	0.09
Kiln/kettle oper.	2,524	1.0	3	0.06	0.6	0.03
Heat treaters	519	6.0	3	0.08	1.0	0.07
Equip. cleaners	233	2.0	1	0.01	1.0	0.01
Metal machining	64,344	5.0	353	7.85	1.5	5.74
Painters	11,323	0.4	5	0.11	0.3	0.03
Repair/utility	89,098	1.0	98	2.17	0.3	1.58
Welder/solderer	147,239	1.0	161	3.58	0.2	2.99
Construction	70,000	0.5	38	0.85	0.3	0.36
Total	524,816		1,112	24.70		17.40

[1] Estimates of exposures include reductions for respirator use as applicable.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

The reductions would apply to risks associated with cumulative exposures over working lifetime, and thus the annual benefits would be phased in over 45 years. Employee turnover in occupations with exposure would result in a greater number of individuals at risk with a lower excess risk for each individual. The total excess risk is assumed to remain unchanged.

Based on the Multistage Model quantitative risk assessment, about 1,112 cases of lung cancer would be attributable to cadmium exposure among the equivalent of 525,000 employees with a working lifetime of exposure at current levels. Compliance with the revised cadmium standard should prevent 783 of these cases.

The estimated annual number of excess and prevented cancer cases associated with each of the QRAs for lung cancer are shown in Table VIII–F2.

Kidney Dysfunction Risk

As discussed in the health effects section of the preamble, exposure to cadmium may result in damage to the kidneys. Levels of urinary proteins can be used as indicators of kidney damage. These levels may vary depending on a variety of temporary and permanent conditions, and will usually increase with age as the capacity of the kidneys naturally deteriorates. In addition to

other causes of kidney damage, most people absorb small amounts of cadmium as part of their diet. Cadmium is collected in the kidneys, and its low excretion rate causes the effects to be largely cumulative.

For purposes of estimating the benefits associated with compliance with this standard, an elevated level of urinary proteins was considered an illness (kidney dysfunction).

TABLE VIII–F2.— ESTIMATED BENEFITS BASED ON VARIOUS RISK MODELS

Model	Annual cancer cases with a PEL of 5 μg/m³ (prevented/total excess)	Annual kidney cases with a PEL of 5 μg/m³ (prevented/total excess)
Poisson	27.3/40.4	
Cox	13.1/17.5	
Multistage	17.4/24.7	
Relative Risk	9.0/13.4	
Ellinder		1.1/1.6
Ellis		273.0/391.6
Jarup 1		77.8/111.2
Jarup 2		46.1/65.9
Mason 1		69.1/98.9
Mason 2		112.0/160.8

Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

Persons with kidney dysfunction would be at an increased risk of developing more serious kidney-related problems. The quantitative risk assessment developed by OSHA (explained in detail in the preamble) indicates the average excess risk of kidney dysfunction faced by individuals with a given cumulative level of occupational exposure.

The total excess risk addressed by this standard was calculated by assuming that cumulative exposure levels of employees would be represented by 45 years of exposure at current levels. To the extent that the total amount of exposure may involve a larger number of employees with lower cumulative exposures, individual risks may vary but the aggregate risk should not change significantly.

Table VIII–F3 shows the estimated number of exposed employees in the affected industries and the current average exposure level among the exposed employees. For purposes of estimating benefits, the current average exposure level reflects the estimated mean concentration of cadmium in the air inhaled by the employees. For employees currently wearing respirators exposure levels were adjusted down to one tenth of the ambient concentration.

Quantitative risk assessments (QRAs) for kidney dysfunction were applied to the number of employees and the exposure level in each job category to determine the number of excess cases attributable to current exposures. The calculation was repeated using the projected exposure levels estimated to be achieved under compliance with the final standard; the difference determined the number of cases potentially preventable by the standard.

TABLE VIII–F3.— EXPECTED REDUCTION IN EXCESS KIDNEY DYSFUNCTION CASES USING THE JARUP–1 MODEL

Industry	Number of exposed employees	Current average exposure [1] (μg/m³)	Total excess cases after 45 years	Average annual excess number of cases	Projected average exposure [1] (μg/m³)	Average annual excess cases prevented
Nickel-cadmium batteries	1,500	20	192	4.27	3.0	3.79
Zinc/cadmium production	1,350	14	116	2.57	3.0	2.13
Cadmium pigments	100	28	18	0.40	3.0	0.36
Dry color formulators	7,000	5	189	4.20	2.0	2.75
Cadmium stabilizers	200	24	31	0.69	3.0	0.62
Lead smelting/refining	400	5	11	0.24	2.0	0.16
Cadmium plating	1,200	2	11	0.25	1.0	0.14
Electric utilities	37,500	1	153	3.39	1.0	0.00
Iron and steel	40,000	2	374	8.32	1.0	4.72
General Industry, NEC:						
Chemical mixers	26,436	6.0	875	19.45	1.0	16.26
Electroplaters	6,648	3.0	100	2.22	1.0	1.49
Furnace oper.	17,202	1.0	70	1.56	0.8	0.31
Kiln/kettle oper.	2,524	1.0	10	0.23	0.6	0.09
Heat treaters	519	6.0	17	0.38	1.0	0.32
Equip. cleaners	233	2.0	2	0.05	1.0	0.03
Metal machining	64,344	5.0	1,736	38.59	1.5	27.11
Painters	11,323	0.4	15	0.33	0.3	0.08
Repair/utility	89,098	1.0	363	8.06	0.3	5.66
Welder/solderer	147,239	1.0	599	13.31	0.2	10.69
Construction	70,000	0.5	122	2.71	0.3	1.09
Total	524,816		5,005	111.22		77.79

[1] Estimates of exposures include reductions for respirator use as applicable.
Source: Office of Regulatory Analysis, OSHA, U.S. Department of Labor.

Based on OSHA's best estimate of kidney dysfunction risks (as described in the quantitative risk assessment section), from 68 to 112 cases are expected to be prevented out of a total of 97 to 160 cases. Within this range, OSHA's Jarup-1 Model predicts 78 kidney dysfunctions avoided annually out of 111 kidney dysfunction cases (see Table VIII–F3). The reductions would apply to risks associated with cumulative exposures over working lifetime, and thus the annual benefits would be phased in over 45 years. Employee turnover in occupations with exposure would result in a greater number of individuals at risk with a lower excess risk for each individual. The estimated total excess risk is assumed to remain unchanged.

Based on the Jarup-1 Model quantitative risk assessment, about 5,005 cases of kidney dysfunction would be attributable to cadmium exposure among the equivalent of 525,000 employees with a working lifetime of exposure at current levels. Compliance with the revised cadmium standard should prevent 3,510 of these cases.

The estimated annual number of excess and prevented kidney dysfunction cases associated with each of the QRAs for kidney dysfunction are shown in Table VIII–F2.

IX. Summary and Explanation of the Final Standard (General Industries, Agriculture, and Maritime)

OSHA believes that, based on currently available information in the cadmium rulemaking record, the requirements set forth in this final rule are necessary and appropriate to provide adequate protection to employees exposed to cadmium.

The language of the standard and the order of the various provisions are consistent with other recent OSHA health standards, such as the formaldehyde and benzene standards. OSHA believes that a similar style should be followed from standard to standard to facilitate uniformity of interpretation of similar provisions. Some modifications have been made to this standard in response to the particular nature of cadmium as an occupational health hazard and to experience previously gained with other health standards. Section 6(b)(5) of the Act states that health standards shall also be based on "experience gained under this and other health and safety laws."

Scope and Application: Paragraph (a)

This final cadmium standard applies to all occupational exposure to cadmium and all cadmium compounds, in all forms, including fume and dust. The addition to the final standard of the words "all cadmium compounds" and "all forms" only clarifies and makes explicit the broad scope that was intended and implicit in the proposal. The standard applies to all industries covered by the OSH Act, including shipyards, marine terminals, longshoring, and agriculture, except the construction industry. OSHA is amending Parts 1915, 1917, 1918 and 1928 to apply this standard to these industries. Exposure to cadmium in the construction industry is covered by a separate cadmium standard for that industry, 29 CFR 1926.63. All occupational exposures to cadmium are covered, because the risk from exposure to cadmium is dependent on the extent of exposure and not on the segment of industry where the employee may be employed.

The categorization of workers who are covered by this standard is slightly different from the categorization used in the proposal (55 FR 4052). The explanation of the need for this change is discussed under the section on the Regulatory Impact Analysis.

OSHA estimates that about 524,816 workers are potentially exposed to cadmium. Of these, approximately 70,000 workers are potentially exposed in the construction industry. Of the remaining 455,000 workers, approximately 89,250 are exposed in nine industries where cadmium exposure is more prevalent. These nine are: nickel-cadmium (Ni-Cd) battery manufacturing, zinc/cadmium production, cadmium pigments production, lead smelting/refining, cadmium plating, plastic stabilizer production, dry color formulation, electric utilities, and iron and steel. (Table VIII–A1, Office of Regulatory Analysis, Regulatory Impact Assessment Section).

The remaining 366,000 employees covered by the standard, who constitute about 70% of all employees potentially exposed to cadmium, are in 10 separate occupations common to approximately 98 industries. These occupations involve exposure to cadmium during the handling, heating, or other processing of cadmium or its compounds. The occupations are: Chemical mixers, electroplaters, furnace operators, kiln/kettle operators, heat treaters, equipment cleaners, metal machinists, painters, repair/utility workers, and welders/solderers. The industries in which one or more of these occupations are found include foundries, machinery production, electronic components production, automotive repair, photographic equipment production, aircraft and ship building, paper production, glass and pottery production, and air transportation, among others. (Table VIII–A1, Office of Regulatory Analysis, Regulatory Impact Assessment Section).

The only important issue raised in the rulemaking concerning the scope of the proposed cadmium standard was whether a separate standard should apply to the construction industry. Several commenters favored covering the construction industry in the general industry standard (Exs. 19–8; 19–21; 57). However, a representative of OSHA's Advisory Committee on Construction Safety and Health testified in opposition to extending the general industry standard to construction and in favor of a construction-specific standard that would address the unique conditions in that industry (Tr. 6/13/90, pp. 4–16).

OSHA agrees with the Advisory Committee that such a standard is needed. OSHA is therefore promulgating a separate standard for the construction industry that is adapted to the particular conditions of that industry and assures protection to construction workers that, to the extent feasible, is comparable to the protection afforded workers in general industry by this standard. OSHA does not understand the comments favoring inclusion of the construction industry within the scope of the general industry standard as opposed to this result. The primary concern reflected in those comments is that construction workers be assured prompt and adequate protection from excess exposure to cadmium. OSHA believes that this can be accomplished more effectively by promulgation of a comparably protective, construction-specific standard in conjunction with the promulgation of a general industry standard that excludes the construction industry. Based upon the record evidence in this rulemaking, including pre-hearing comments submitted by the Advisory Committee concerning special working conditions in the construction industry, testimony at the public hearing by a representative of the Committee, and the draft of recommended modifications to the proposed rule submitted by the Committee (Exs. 8–665; 14–5; 53), OSHA has developed a separate and somewhat modified cadmium standard for the construction industry, 29 CFR 1926.63. A full disucssion of the development of that standard can be found in the preamble to the construction standard.

Other issues were raised in the rulemaking that have some relevance to the scope of the standard, but these issues are best addressed elsewhere in this preamble. For example, a dispute about the regulation of cadmium fume and dust is not a dispute about whether both should be regulated in this standard. Rather, the dispute only concerns whether dust and fume should be regulated differently as they were in the pre-existing OSHA PELs. (For a complete discussion of this issue, see Section IX—Summary and Explanation under (g), below, and Section V—Health Effects.) Similarly, a discussion of the carcinogenicity and toxicity of cadmium pigments is provided under Section V—Health Effects and Section VI—Quantitative Risk Assessment.

Definitions: Paragraph (b)

Action level. The final standard retains the same definition of "action level" (AL) incorporated in the proposal for the permissible exposure limit (PEL) of 5 $\mu g/m^3$. The action level is defined as an airborne concentration of cadmium of 2.5 $\mu g/m^3$, calculated as an 8-hour, time-weighted average (TWA).

The action level provides the airborne exposure of cadmium at or above which medical surveillance, air monitoring, and the provision of a respirator to any employee who requests one are required. Other requirements of the standard are not triggered until exposures exceed the PEL. Where exposures are determined to be below the action level, no compliance activities are required of the employer, except those required by paragraphs (d)(4), (m)(3), and (m)(4) of this standard.

In this and other standards the action level has been set at one-half of the PEL (e.g., Arsenic Final Standard, 29 CFR 1910.1018; Benzene Final Standard, 29 CFR 1910.1028). The action level provides a mechanism to tailor certain requirements of the standard to a minimum level of employee exposure to cadmium by triggering preventive action by the employer for employees who face exposure at or above that level. The use of the action level to trigger various provisions of the cadmium standard is consistent with other final OSHA health standards (e.g., Asbestos, 51 FR 22612, June 20, 1986; Benzene, 52 FR 34460, September 11, 1987; Formaldehyde, 52 FR 4668, December 4, 1987; Ethylene Oxide decision (796 F.2d 1479 (D.C. Cir., 1986) and, *Public Citizen Health Research Group* v. *Tyson*, 796 F.2d 1479 (D.C. Cir., 1986), and Acrylonitrile, 43 FR 45809, October 3, 1978).

This substantive consistency provides administrative consistency and continuity to employers in developing and implementing compliance strategies for this and other applicable OSHA health standards at individual worksites. In addition, use of an action level has been found to encourage employers, where feasible, to lower exposure levels to below the action level to avoid the added costs of required compliance with provisions triggered by the action level.

As exposures are lowered, the risk of illness among workers also decreases. Cadmium accumulates in the body over time. Obviously, cadmium accumulates more slowly at lower exposure levels. (See section VI, Quantitative Risk Assessment.) When exposure measurements are below the action level, the employer can be reasonably confident that an employee will not be overexposed. Because of the somewhat variable nature of employee exposures to airborne concentrations of cadmium, maintaining exposures below the action level provides considerable assurance to the employer that employees will not be overly exposed to cadmium; i.e. over the permissible exposure limit (PEL). (For a more detailed discussion of the concept of an action level, see, for example, the Acrylonitrile preamble (43 FR 45809, October 3, 1978), and the Ethylene Oxide preamble (48 FR 17284, April 21, 1983 (Ex. No. 159–49A)).)

The action level serves other functions, for example, it defines the coverage of medical surveillance. For employees exposed to cadmium at or above the action level on 30 or more days per year (twelve consecutive months), employers are required to provide a medical surveillance program. In addition, the employer is also required to provide medical surveillance to all employees who prior to the effective date of this section might previously have been exposed to cadmium at or above the action level by the same employer for an aggregated total of more than 60 months.

As discussed under (l) in this Summary and Explanation, the medical surveillance program triggered by the action level is targeted to the organ system most sensitive to non-carcinogenic cadmium toxicity, the kidney. The medical surveillance program will facilitate the identification and reduction of kidney dysfunction and is expected to result in an overall reduction of cadmium exposure and of all cadmium-related illnesses.

According to OSHA's risk assessment, which does not take into account further reductions in risk attributable to the ancilliary provisions of this standard, there appears to be continuing significant cancer risk at the PEL. Under the recent asbestos decision (*Building and Construction Trades Department, AFL–CIO* vs. *Brock*, 838 F.2d 1258, D.C. Cir. 1988), where such continuing significant risk appears to exists, OSHA should use its legal authority to impose additional requirements on employers to further reduce risk when those requirements will result in a greater-than-*de-minimis* incremental benefit to workers' health. OSHA concludes that the action level will result in a very real and necessary further reduction in risk over that provided by the PEL alone. The action level provides added employee protection while increasing the cost-effectiveness and performance-orientation of the standard.

The main issue raised in the rulemaking regarding the action level was whether OSHA should set it at the conventional level of one-half the PEL. OSHA had considered setting the action level still lower in the proposal (55 FR 4104–05) to expand coverage of workers for whom medical surveillance would be required. The Agency decided to set the PEL at 5 $\mu g/m^3$, the higher of the two proposed alternatives and to set the action level at half the PEL, being 2.5 $\mu g/m^3$.

One commenter, representing Duke Power Company, opposed setting the action level at less than half the PEL because it would require medical surveillance for a significant number of workers who do not need it (Ex. 19–18). OSHA agrees that setting the action level at less than half the PEL primarily to identify more workers who had been excessively exposed in the past would be an overly broad mechanism for accomplishing a relatively narrow, if important, purpose. Instead, as discussed below, OSHA relies in this final standard on a specific provision requiring the employer to also provide medical surveillance to certain employees who prior to this standard were exposed to cadmium. This provision triggers medical surveillance independently of the current action level. Thus, in addition to having to provide medical surveillance to certain employees who are currently exposed, employers also are required to provide medical surveillance to employees who were or might have been previously exposed at or above the action level by the current employer for a specified period of time, regardless of whether they are currently exposed at or above the action level.

OSHA received numerous comments on the need to protect veteran employees. While some commenters were of the opinion that veteran employees would not need coverage because good medical evaluations will identify older workers at risk (e.g., Ex. 19–31), others were of the opinion that specific coverage was necessary (Exs. 19–23; 123). OSHA decided to set the action level at half the PEL, as proposed, and to establish a separate provision to address the issue of veteran employees.

Employee exposure is defined as the exposure to airborne cadmium that would occur if the employee were not using respiratory protective equipment. This definition is intended to apply to all variations of the term "employee exposure" that have essentially the same meaning, such as "exposed employee" and "exposure." The definition is consistent with OSHA's previous use of the term in other standards (Asbestos, 29 CFR 1910.1001; Benzene, 29 CFR 1910.1028, Ethylene Oxide, 29 CFR 1910.1047). Employee exposure or "exposed" means the level of cadmium that an employee is subjected to in the course of employment.

Final medical determination is the physician's written medical opinion of the employee's health status. Under

paragraphs (1)(3)–(1)(12), the written medical opinion of the examining physician is the "final medical determination." Where either multiple physician review or the alternative physician determination mechanism has been invoked under paragraphs (1)(13) or (1)(14), respectively, the final medical determination is the final, written medical finding, determination or recommendation that emerges from that process.

The terms *"Assistant Secretary", "authorized person", "Director", "high-efficiency particulate absolute [HEPA] air filter",* and *"regulated area"* are defined in this final standard essentially as proposed. These definitions are based on OSHA's previous experience and are consistent with OSHA's use of these terms in other health standards. These definitions generally have not been commented upon.

Permissible Exposure Limit (PEL): Paragraph (c)

Employers are required to assure that no employee is exposed to an airborne concentration of cadmium in excess of the permissible exposure limit (PEL) of 5 micrograms of cadmium per cubic meter of air ($\mu g/m^3$).

In its proposed rule, OSHA proposed two kinds of PELs, an 8-hour, time-weighted-average permissible exposure limit (TWA PEL) and an excursion limit (EL), a limitation on short-term exposures averaged over a 15-minute period (55 FR 4105–05). For the TWA PEL, OSHA proposed two limits: 1 and 5 $\mu g/m^3$. On the one hand, OSHA proposed a PEL of 1 $\mu g/m^3$ to substantially lower risk of death from cancer (55 FR 4076, Table VI–C and 4080, Table VI–G). On the other hand, OSHA proposed a PEL of 5 $\mu g/m^3$ due to serious concerns about the technological feasibility of the lower PEL (55 FR 4053). OSHA proposed an EL on the basis of good industrial hygiene practices (55 FR 4105) (Ex. 8–664).

OSHA's risk assessment indicates that significant risks of cancer and kidney damage exist at the prior PELs [100 $\mu g/m^3$ for fume and 200 $\mu g/m^3$ for dust] for cadmium. There is a consensus among participants in the rulemaking that these PELs are much too high to protect the health of exposed employees. The Cadmium Council, a trade association whose members are producers and commercial consumers of cadmium or of other metals from ores containing cadmium, indicated that there is some broad agreement among its constituents that, leaving feasibility considerations aside, the PEL should be set no higher than 20 $\mu g/m^3$ (Ex. 19–43). The disagreement arises over whether the health science data requires that the PEL be set below 20 $\mu g/m^3$ and, if so, how far below. Most of the public health officials, unions, scientists and physicians who participated in the rulemaking conclude that the PEL should be set between 1 $\mu g/m^3$ and 5 $\mu g/m^3$ (Ex. 19–8, 123; Tr. 6/7/90, pp. 72–200; Ex. 57; Trs. 7/17/90, pp. 51–217; 6/6/90, pp. 69–119; 7/17/90, pp. 258–277; Ex. L–140–50). Some industry representatives and experts who testified and commented for industry generally believe the health evidence requires that the PEL be set at 20 $\mu g/m^3$ (Exs. 19–43, 77, 119), though other industry sources support a PEL of 10 $\mu g/m^3$ or lower (Exs. 19–13, 19–24, 19–36, 19–31). Thus, disagreement in the rulemaking about the level at which the PEL should be set to adequately protect workers is focused primarily on the range between 1 $\mu g/m^3$ and 20 $\mu g/m^3$, although some commenters recommended establishing a higher PEL (Ex. 105), especially for pigment workers (Ex. 19–17, 19–40). Setting aside the issue of pigment workers who are covered by this standard, (See Health Effects Section), OSHA, therefore, focused primarily on levels between 1 $\mu g/m^3$ and 20 $\mu g/m^3$ in establishing the PEL (Ex. 19–43).

Establishing a PEL anywhere within that range would greatly reduce the excess risks of cancer and kidney damage from the current PELs. The lower the level selected, the greater the reduction in risk. However, even at the low end of this range of PELs, some risks above one in one thousand would remain if OSHA did nothing other than impose a new PEL. As a result, under the asbestos decision (*Building and Construction Trades Department, AFL–CIO* v. *Brock*, 838 F.2d 1258 (D.C.Cir, 1988)) and the Ethylene Oxide decision (*Public Citizen Health Research Group* v. *Tyson*, 796 F.2d 1479 (D.C.Cir, 1986), OSHA is under a legal obligation to take additional actions to the extent feasible to require employers to further reduce risk. Consequently, OSHA does not rely exclusively on the PEL to eliminate significant risk. The Agency relies, as well, upon other provisions of the final standard, such as the action level (AL), the very strict, multi-layered medical surveillance program, and the medical removal protection provisions, among others, to eliminate significant risk. In fulfilling this obligation, the Agency has discretion to determine which particular, additional actions should be required of employers.

The Agency, however, decided not to include an excursion limit (EL) in the cadmium standard for two reasons. First, unlike OSHA's benzene rulemaking (52 FR 34460, 34532, Sept. 11. 1987), no evidence was submitted to the record to persuade the Agency that an EL was needed to protect employees from short term excursions as low as the proposed EL. Moreover, although in theory imposing an EL might further lower the daily dose of cadmium to which the employee is exposed, there is little or no record evidence supporting this supposition. Under the standard, employers already are likely to seek to control exposures to levels below the PEL which also will minimize the occurrence of high exposure excursions.

Second, in some plants, employees appear to be exposed to cadmium only intermittently and for short periods but not infrequently at levels exceeding the proposed EL. For these users, compliance with an EL might be infeasible (Ex. 19–24) or might require the expenditure of considerable resources without providing much additional protection to workers (Tr. 6/12/90, pp. 21–22; Ex. 19–5). These resources could more effectively be allocated to other forms of worker protection.

Without better justification for an EL in general, OSHA does not feel free to impose an EL. OSHA understands that, notwithstanding the absence of evidence that cadmium-induced diseases are dose-rate dependent and notwithstanding the likelihood that, even without an EL, employers will seek to control excursions, the opinion of the Court of Appeals for the D.C. Circuit in Ethylene Oxide (EtO) might still be read as requiring OSHA to impose an EL, when feasible, to reduce remaining significant risk (EtO decision (*Public Citizen Health Research Group* v. *Tyson*, 796 F.2d 1479 (D.C.Cir, 1986). However, OSHA does not believe the court in the EtO case intended to legally compel the Agency to select a particular method among the number of ancillary provisions available to reduce remaining significant risk. On the contrary, OSHA understands that decision as leaving the Agency the choice of which methods to adopt to achieve its legal obligation to reduce remaining significant risk. Thus, while the court did say that "[i]f in fact a STEL [or an EL] would further reduce a significant health risk and is feasible to implement, then the OSH Act *compels* the agency to adopt it * * *." (emphasis in the original), it then parenthetically added, "barring alternative avenues to the same result." 796 F.2d at 1505. In the cadmium standard, OSHA has chosen to follow "alternative avenues to the same result."

Regarding the disagreement in the rulemaking about the level at which the PEL should be set to adequately protect

workers, OSHA has decided to set the PEL at 5 $\mu g/m^3$. Excluding partial bans on cadmium in Sweden and Germany, this is the lowest PEL in the industrialized world. There are two main reasons for this decision. First, the health science data in the record considered as a whole indicate that to eliminate significant risk the PEL should be set no higher than 5 $\mu g/m^3$ (Ex. L–140–50) (See sections on Health Effects and the QRA). At a PEL of 5 $\mu g/m^3$, OSHA is assured that the Agency is not regulating an insignificant excess risk of cancer or kidney damage. Estimates of risks for both kidney damage and lung cancer at a PEL of 5 $\mu g/m^3$ generally are similar and complementary. On the other hand, along with the ancillary provisions of the standard, a PEL of 5 $\mu g/m^3$ appears to reasonably protect cadmium exposed workers from a significant risk of material impairment of health.

Second, a PEL of 5 $\mu g/m^3$ appears to be at or very near the limits of technological feasibility for many workers in industries where there is no separate engineering control air limit (SECAL). Setting the PEL lower would require many more of these workers to wear respirators full time. For example, based on estimates in the proposal, if the PEL were set at the lower of the two proposed alternatives, 1 $\mu g/m^3$, approximately 37% of these exposed employees would be expected to have to wear respirators (55 FR 4097–98, Tables VIII–C and VIII–D). As OSHA indicated in the proposal, such heavy reliance upon respirators would raise extremely serious questions about the technological feasibility of achieving the PEL by engineering and work practice controls. By contrast, at a PEL of 5 $\mu g/m^3$, only approximately 1% of these employees would have to wear respirators (55 FR 4097–98, Tables VIII–E and VIII–F). Although estimates of respirator usage required at a PEL of 5 $\mu g/m^3$ are higher in the final standard (RIA, Table VIII–C46) than in the proposal, OSHA continues to expect that the number of employees required to wear respirators at a PEL of 1 $\mu g/m^3$ would be much higher than at 5 $\mu g/m^3$.

Regarding the feasibility issue, OSHA considered the main arguments made by rulemaking participants in opposition to the proposed PEL of 5. The Cadmium Council and some of its members opposed a PEL of 5 $\mu g/m^3$ (and 1 $\mu g/m^3$) primarily on grounds of infeasibility (Big River Zinc, Ex. 19–30; Cadmium Council, Ex. 19–43; Synpro, Ex. 19–46/Appendix I). The Council argued that a PEL of 5 $\mu g/m^3$ could not be achieved by engineering and work practice controls in each of the primary cadmium producing industry segments represented by the Council.

Consequently, several commenters argued that OSHA should adopt a two-tiered approach to controlling worker exposure to airborne cadmium (Ex. L–140–28). The first tier would be a PEL, set at the level required by the health science data to protect workers' health. The PEL, in the case of industries where compliance by means of engineering and work practice controls was infeasible, could be achieved by any allowable (e.g., not worker rotation) combination of work practice and engineering controls and respirators. The second tier would be set above the PEL at the lowest feasible level that could be achieved by engineering and work practice controls.

OSHA, with some qualifications, agrees with industry's arguments in this regard and has responded by establishing separate engineering control air limits (SECALs) at the lowest feasible levels above the PEL for specified processes in particular industries. Employers in a particular industry covered by the SECAL will be obligated to achieve the SECAL by engineering and work practice controls to the extent feasible and to protect employees from exposures above the PEL by any mix of compliance methods, including engineering and work practice controls and respirators.

The establishment of a SECAL in this cadmium standard is similar to provisions in the asbestos standard [29 CFR 1910.1001 (f)(1)(ii); 1926.58 (g)(1)(ii)], requiring the employer to use engineering and work practice controls to attain the lowest achievable levels in specified processes and to supplement those controls with respirator use. In the asbestos standard, OSHA identified certain processes as ones in which it is not presumptively possible to attain the PEL through engineering and work practice controls (*Building and Construction Trades Department, AFL–CIO* v. *Brock;* 647 F.2d 1272 (D.C. Cir, 04/24/87). For these processes, OSHA set a higher PEL until such time as the lower PEL could be attained [29 CFR 1910.1001 (f)(1)(iii)] (See discussion under Section VIII—Regulatory Impact Analysis.)

The Cadmium Council and its experts and witnesses also opposed a PEL of 5 $\mu g/m3$ (and 1 $\mu g/m3$) on health grounds. They claimed that a PEL so low was not necessary to adequately protect workers. As discussed above in this preamble, OSHA rejects this argument.

A small number of health experts and others opposed a PEL of 5 as being too high to adequately protect workers from excess cadmium exposure (Public Citizen, Ex. 19–33; Massachusetts Organization of State Engineers and Scientists, Ex. 19–21). However, the Agency after careful analysis of the evidence in the record concluded that a PEL of 5 $\mu g/m^3$ is at or very near the limits of feasibility. Furthermore, the Agency concluded that a PEL of 5 $\mu g/m^3$, in conjunction with all the ancillary provisions of the standard, is sufficiently protective and that setting the PEL any lower would create additional health and safety problems. A more complete analysis of the feasibility issue can be found in the final Regulatory Impact Analysis section in this preamble.

Finally, in comments to the record (Duke Power, Ex. 19–18), OSHA was asked to clarify the allowable exposure where an employee is exposed to cadmium for more than 8 hours in any work day. The 8-hour time weighted average (TWA) for that day has to be reduced accordingly so that the employee is not exposed to greater amounts of cadmium by working more hours than he/she would have been by working eight hours. The reduction is made according to the following formula:

$$\text{Maximum permissible limit (in } \mu g/m^3) = 40 \div \text{hours worked in the day.}$$

Consequently, if the employee were to work 10 hours, the adjusted allowable exposure for this employee under the formula, 40 ÷ 10, would be reduced to 4 $\mu g/m^3$. Though the employee may be exposed during part of the day to exposures above 5 $\mu g/m^3$, the PEL cannot be raised. No other formula is required for that adjustment. OSHA provides this explanation partly in response to a request from Duke Power Company (Ex. 19–18).

Exposure Monitoring: Paragraph (d)

This final standard imposes monitoring requirements pursuant to section 6(b)(7) of the OSH Act [29 U.S.C. 655], which mandates that any standard promulgated under section 6(b) shall, where appropriate, "provide for monitoring or measuring of employee exposure at such locations and intervals, and in such manner as may be necessary for the protection of employees." To this end, as discussed below, OSHA has made several significant changes to the monitoring requirements included in the proposed cadmium rule.

The purposes served by requiring air sampling for employee exposures to cadmium include: Determination of the extent of exposure at the worksite;

prevention of employee overexposure; identification of the sources of exposure to cadmium; collection of exposure data so that the employer can select the proper control methods to be used; and evaluation of the effectiveness of selected controls. Monitoring further enables employers to notify employees of their exposure levels, as required by section 8(c)(3) of the Act.

Periodic monitoring provides the employer with assurance that employees are not experiencing higher exposures that may require the use of additional controls. In addition, periodic monitoring reminds employees and employers of the continued need to protect against the hazards associated with exposure to cadmium.

The collection of exposure monitoring data also enables an examining physician to be informed of the existence and extent of potential sources of occupational diseases.

The results of initial and periodic monitoring determine whether subsequent monitoring is necessary. Exposure monitoring is important not only to determine the level of cadmium to which employees are exposed and the frequency at which employees should be monitored, but also to determine whether other protective provisions of the standard need to be implemented. The employer's obligation to provide medical surveillance, for example, is triggered by monitoring results showing that an employee is exposed at or above the action level on 30 or more days per year (or 12 consecutive months). Other provisions of the standard typically are triggered by employee exposure levels above the PEL.

The exposure monitoring provisions in paragraph (d)(1) of this standard require the employer to determine the exposure of each employee exposed to cadmium. Samples must be taken within the employee's breathing zone (i.e., personal samples) and must reflect the employee's exposure, without regard to the use of respirators, to airborne concentrations of cadmium over an eight-hour period. A full description of "Breathing zone" is provided in the OSHA Instruction CPL 2-2.20B, CH-1, Nov. 13, 1990, Directory of Technical Support. Basically, it encompasses a sampling area as close as practical to the nose and mouth of the employee.

In certain circumstances, sampling each employee's exposure to cadmium may be required for initial monitoring. However, in many cases, the employer under paragraph (d)(1)(iii) may monitor selected employees to determine "representative employee exposures." Representative exposure sampling is permitted when there are a number of employees performing essentially the same job, with cadmium exposure of similar duration and level, under essentially the same conditions. In authorizing representative personal sampling for employees engaged in similar work, the standard requires that the member(s) of the exposed group reasonably expected to have the highest exposure shall be the one(s) monitored. This result is then attributed to the remaining employees of the group. At the very least in representative sampling, full-shift sampling must be conducted for each job function in each job classification, in each work area, and for each shift. At least one sample of the entire shift or consecutive representative samples over the length of the shift must be taken.

Although one commenter expressed opposition to the proposed requirement that sampling be conducted on each work shift (Tr. 7/18/90; 9-279), other commenters stated that the variation in exposure levels for the same job across shifts can be great (e.g., Tr. 7/17/90, pp. 41-217). Based upon its experience, OSHA agrees that such variation requires that sampling be conducted on each shift.

Initial monitoring of workplace exposures is required under paragraph (d)(2) of this standard for all employers who have a place of employment covered by this standard. The initial monitoring must be conducted as soon as possible and in any event no later than 60 days after the effective date of this standard. However, to eliminate unneeded monitoring, under conditions specified in paragraph (d)(2)(ii) of this standard, historic monitoring may be relied upon by the employer to satisfy the obligation to conduct initial monitoring. Thus, if an employer previously monitored an employee under exposure conditions closely resembling those currently prevailing and that monitoring satisfies all other requirements of this standard and was conducted within 12 months prior to the publication date of this standard, then the results of that monitoring can be used to satisfy the requirements for initial monitoring.

This constitutes a change from the cadmium proposal, where historic monitoring had to be conducted within 180 days of the publication date of this final standard to be useable in place of initial monitoring (55 FR 4121). Several industry commenters criticized the proposed limit of 180 days on the usability of historic monitoring data (Exs. 19-9 and 19-18). OSHA, in seeking to eliminate all unnecessary requirements and attendant costs from the final standard, felt that, so long as the strict conditions of paragraph (d)(2)(ii) were met, employee monitoring results obtained as long as 12 months prior to publication of this standard would be sufficiently reliable to make the requirement for initial monitoring of those employees unnecessary. However, OSHA does not feel comfortable accepting historic monitoring data from any era for these purposes, as some industry representatives have sought (Exs. 19-9 and 19-18). Indeed, the Agency believes that accepting historical data from periods greater than six months prior to the publication date of the standard is already somewhat incongruous since the minimum acceptable frequency for periodic monitoring required by the final standard is semi-annual. Furthermore, NIOSH and others have argued that even semi-annual monitoring is insufficient and have maintained that monitoring cadmium on a quarterly basis is good industrial hygiene practice (Tr. 7/17/90, p. 78; Exs. 8-62, 9-8, 57, 106).

OSHA recognizes these countervailing interests and concerns and seeks through a combination of requirements to achieve a balance that is both protective and efficient. In determining how to most efficiently protect employees, OSHA chooses to accept historic data from up to 12 months before promulgation of the standard, while requiring a minimum of semi-annual monitoring, supplemented by the two additional requirements for more frequent monitoring in paragraphs (d)(3)(i) and (d)(4).

The provision for use of "objective data" in paragraph (d)(2)(iii) of this standard is, except for the deletion of the reference to an EL (excursion limit), the same as in the proposal. The provision is discussed below in this summary and explanation in connection with paragraph (n)(2), where "objective data" is defined and the obligation to keep a record of it specified.

As suggested above, the requirements for monitoring frequency in paragraph (d)(3) of this standard also have been somewhat changed from those proposed. What remains the same are the following two basic rules. First, if the initial or periodic monitoring results (confirmed by another monitoring taken at least seven days later) show that employee exposures are below the action level, then under paragraph (d)(3)(ii) no further monitoring is required. OSHA estimates that most of the workers potentially exposed to cadmium are currently exposed to a geometric mean level below the AL of 2.5 $\mu g/m^3$ (see final RIA, e.g., Tables

VIII–C43 and VIII–C44) and that these workers generally will be exposed below the AL. For these workers, OSHA expects that the employer will be required to comply only with the training provisions under paragraph (m) of the standard. Second, if initial or periodic monitoring results show employee exposures at or above the action level, then under paragraph (d)(3)(i) the employer must repeat monitoring for these individuals at least every six months.

What is different is that, unlike paragraph (d)(3)(i) of the proposal (55 FR 4121), there is no requirement in the final standard that the employer must monitor every three months (quarterly) employees whose monitoring results are above the PEL. The deletion of this specific requirement is partly in response to comments that the proposed monitoring requirements were too inflexible (American Iron and Steel Institute Tr. 7/18/90, p. 279). While opinions vary on the proper periodicity for monitoring, OSHA acknowledges the merit of more flexible monitoring for cadmium-related exposures (Ex. 106). Instead of the requirement for quarterly monitoring, OSHA in paragraph (d)(3)(i) of this final standard imposes a performance requirement on employers, requiring them to monitor with the frequency and pattern needed to assure that the following purposes of exposure monitoring be achieved: the monitoring results should reflect with reasonable accuracy the levels of exposure of employees and should assure the adequacy of respiratory selection and the effectiveness of engineering and work practice controls.

Depending upon exposure conditions, this performance criterion might require monitoring that is more or less frequent than the proposed quarterly monitoring. If, for example, exposure levels and patterns are well known and stable over time, monitoring as often as each quarter could well be redundant, in which case semi-annual monitoring probably would suffice. On the other hand, where exposure conditions change dramatically and more frequently than quarterly, more frequent monitoring probably would be required under paragraphs (d)(3)(i) as well as (d)(4).

Thus, the Agency has increased the flexibility of its monitoring requirements to give employers greater latitude to monitor according to the concrete conditions and industrial hygiene needs of their particular facilities. However, this flexibility is not without bounds. OSHA has supplemented it with the minimum requirement of semi-annual monitoring. Employers must monitor employees whose exposures are, or may be, at or above the action level at least semi-annually (55 FR 4121), assuring that these employees will be monitored at a reasonable interval (AISI, Tr. 7/18/90, p. 252). Requiring periodic monitoring at a stated frequency also facilitates enforcement by providing a clear compliance minimum.

The requirement for semi-annual monitoring at or above the action level was incorporated in the proposed cadmium standard (55 FR 4121) and has been incorporated into some OSHA health standards (Arsenic, 29 CFR 1910.1018; Lead, 26 CFR 1910.1025). The requirement for semi-annual monitoring above the PEL has been incorporated into other health standards (Benzene, 29 CFR 1910.1028). The requirement to monitor semi-annually employees exposed at or above the action level and/or the PEL is similar to the requirement in OSHA's standard for Formaldehyde (29 CFR 1910.1048). OSHA believes the monitoring schedule set forth in this final standard is necessary and sufficient.

In addition, whenever changes occur that may expose additional employees to cadmium at or above the action level or may expose employees already exposed at or above the action level to levels of cadmium above the PEL, additional monitoring is required under paragraph (d)(4). Such changes may occur in the production process, raw materials, equipment, personnel, work practices, or finished products. Whenever the employer has any reason to suspect that any other change might lead to such further exposure, then under paragraph (d)(4) the employer must resume monitoring. There is considerable support in the record for this requirement for additional monitoring (AISI Tr. 7/18/90, p. 280; Exs. 19–8; 19–21). OSHA considers this requirement necessary to protect employees from excessive exposures from changed circumstances.

OSHA recognizes that monitoring can be a time-consuming, expensive endeavor and therefore in paragraph (d)(3)(ii) of this standard allows employers to discontinue monitoring for employees whose sampling results indicate exposures are below the action level. It is hoped that this will provide incentive to employers to control their employees' exposures to cadmium to below the action level, thus maximizing the protection of employees' health.

Since OSHA has eliminated the proposed requirement that employers comply with an EL from this final standard, all of the proposed requirements for monitoring and notification of employees relating to an EL have likewise been eliminated.

The standard in paragraph (d)(5) further requires that employers notify each of their employees individually of the results of monitoring that reflects their exposure. Notification is to be given in writing. In addition, employers must post monitoring results in an appropriate location accessible to all affected employees.

Several employers opposed parts or all of these notification requirements in the cadmium proposal. Duke Power, for example, opposes posting results as a violation of employee privacy and as potentially alarming and instead favors providing notice at crew meetings when questions can be answered (Ex. 19–18). OSHA does not believe an employee has a privacy interest in the air cadmium levels to which he/she is exposed. In addition, OSHA sees no reason or evidence in the record that posting sampling results is likely to alarm employees any more than individual written notification or notice given at crew meetings.

By contrast, McDonnell Douglas generally supports the proposed written notification provision but favors posting over individual written notification because it is more efficient (Ex. 19–22). AISI feels the requirements for individual notification and posting are "duplicative and unnecessarily burdensome" (Tr. 7/18/90, p. 280). The requirement for individual written notification, AISI says, will "dramatically increase cost without a commensurate advantage to the employee" (Tr. 7/18/90, p. 281). AISI suggests that OSHA allow the employer to choose between these two methods of notification (Tr. 7/18/90, p. 280).

In other health standards, OSHA typically has required written notification of employees either individually or by posting (Ethylene Oxide 29 CFR 1910.107; Formaldehyde 29 CFR 1910.1048; or Lead, 29 CFR 1910.1025). The additional requirement to do both was incorporated into the proposal (55 FR 4122). No evidence was submitted to the record that posting of results is costly or inefficient. The issue is whether the notification is redundant (Tr. 7/18/90; p. 252). OSHA added this requirement in the proposal because the Agency believes that the two forms of notification enhance and complement each other to the benefit of the employee. Posting enhances the collective knowledge in the workplace of employee exposures, which in turn enhances each employee's understanding of his/her own exposure. Thus, each notification requirement

performs a different function. Individual, written notice assures that each employee is notified. Posting the results facilitates other employees, their designated representatives, supervisors, and employers as well in becoming aware of exposure levels within the workplace.

The employer is obligated to provide written notice and post results within 15 working days after receipt of the results. Whenever the PEL is exceeded, the written notification must contain a statement that the PEL has been exceeded and a description of the corrective action(s) being taken by the employer to reduce the employee's exposure to or below the PEL. This requirement to inform employees is in accordance with section 8(c)(3) of the Act and is necessary to assure that employees are informed whenever the PEL is being exceeded and to assure employees that the employer is making efforts to furnish them with a safe and healthful work environment.

In order to obtain accurate exposure monitoring results, the employer under paragraph (d)(6) is required to use monitoring and analytical methods that have an accuracy, at a confidence level of 95%, of not less than plus or minus 25% for airborne concentrations of cadmium at all the relevant levels (i.e., levels between the action level (AL), the PEL, and, where relevant, the SECAL). The main reason OSHA is requiring this degree of accuracy for air monitoring results is to ensure that air monitoring results are sufficiently accurate across the relevant range of exposure levels. Accuracy of measurements is critical since monitoring results serve a number of important functions in the cadmium standard. For example, certain central requirements of the standard, like medical surveillance, engineering controls, and respirator use, are triggered by employee exposures exceeding particular levels like the AL or the PEL. In addition, the medical removal provision requires that a removed employee not be placed in a job where exposure levels are at or above the AL.

Although not a requirement of the standard under paragraph (d), OSHA expects that all laboratory analyses of air sampling data will be performed in laboratories with demonstrated proficiency for measuring cadmium in air at these levels.

The accuracy requirements in paragraph (d)(6) are basically the same as the proposal (55 FR 4121) and are similar to the precision and accuracy requirements in other OSHA health standards (e.g., Lead, 29 CFR 1910.1025; Benzene, 29 CFR 1910.1028). By defining the precision and accuracy requirements for samples used to determine the TWA airborne concentration of cadmium in the workplace, OSHA ensures that the method of monitoring and analysis is adequate whether single or multiple samples are taken. While some may argue that such a stringent requirement for accuracy is unwarranted or unobtainable, (Exs. 19–14; 19–18) OSHA is of the opinion that, given the current state-of-knowledge among laboratories in which analyses for heavy metals are routinely performed, it is not unreasonable to require such accuracy. Recent NIOSH Proficiency Analytical Testing (PAT) rounds have included samples containing cadmium as low as 6 μg with a performance limit of ± 0.8 μg. The analytical range for cadmium in the PAT samples is 2 to 20 μg. Inclusion of this requirement will provide incentive for other laboratories to improve their accuracy over time. In addition, with the TWA PEL set at 5 $\mu g/m^3$, the higher of the two PELs included in the proposal (55 FR 4052), and with the deletion of the excursion limit, the comments suggesting that current methods and laboratories are unable to achieve such accuracy are no longer relevant. The OSHA method ID–189, listed in Appendix E, provides analytical precision and accuracy capability for a standard that is five times lower than the final standard. By using this method, and currently available instrumentation, analytical laboratories can perform a sample analysis that meets the required level of both precision and accuracy of paragraph (d)(6).

The employer is also required under paragraph (o) of this standard to allow employees or their designated representatives an opportunity to observe employee exposure monitoring. This provision is required by Section 8(c)(3) of the Act (29 U.S.C. 657(c)(3)).

Several commenters indicated that OSHA had erred in its proposal regarding appropriate sampling devices for cadmium. Mr. G. F. Stone, Manager of Occupational Health and Safety for the Tennessee Valley Authority, submitted that in section VIII (E) of the proposal, the Agency referred to passive dosimeters and charcoal tubes as monitoring devices for cadmium. Mr. Stone correctly indicated that this reference should be deleted because such sampling devices can only be used for vapors (Ex.19–5). It has been deleted.

Regulated Areas: Paragraph (e)

This final standard contains requirements that regulated areas be established whenever and wherever an employee's exposure to airborne concentrations of cadmium is, or can reasonably be expected to be, above the PEL. Access to these areas is to be controlled and limited to authorized persons. In accordance with performance criteria, regulated areas are to be demarcated in any manner that adequately alerts employees of the boundaries of these areas. No detailed specifications are required for demarcating regulated areas.

The requirement to establish regulated areas extends to temporary and to intermittent exposures above the PEL, as well as to more constant ones. Thus, for example, whenever it is reasonably expected that the PEL may be exceeded for an employee performing a maintenance operation, a regulated area shall be established for the area and for the length of time required to perform that operation and for any additional time that air cadmium levels may be expected to continue to exceed the PEL. For this cadmium standard, the existence of a hazard, and not the particular type of operation or work being performed, is the basis for determining the need for protective measures.

Access to the regulated area is restricted to "authorized persons". For purposes of this standard, these are persons who are authorized by the employer to be present in the area, generally because of their job duties, and persons authorized by the OSH Act or OSHA regulations to be in that area.

Areas where employee exposures are over the PEL need to be demarcated to warn employees who are not essential to the performance of tasks within the area to keep out. Demarcation is also necessary to warn employees required to be in the regulated area that respirators must be worn to avoid excessive exposures via inhalation and that good personal hygiene must be practiced to avoid exposures to cadmium via ingestion. Good personal hygiene practices include refraining from smoking, eating, drinking, chewing tobacco or gum, refraining from applying cosmetics in regulated areas, and refraining from carrying the products associated with these activities into regulated areas or storing such products there.

OSHA received specific comments from medical experts that employees should not carry food, tobacco products, gum, or such other products into cadmium contaminated areas since these products rapidly become contaminated themselves (Ex. 29). Consumption of heavily contaminated products contributes to cadmium accumulation in the human body. (ref. in Kjellstrom, Ex. 29). Other hygienic

practices associated with working in regulated areas also are required under paragraph (j) of this standard, which is discussed below.

The purpose of a regulated area is to assure that employers make employees aware of the presence and location of cadmium at levels above the PEL in the workplace. This minimizes the number of employees excessively exposed. The employer makes employees aware of this potential hazard by demarcating the area and posting warning signs. Since under paragraph (m)(1) of this standard the signs must state that only authorized personnel are allowed in the area and that respirators must be worn in the area, the signs and the demarcation of such areas should effectively warn employees not to enter these areas unless they are authorized to do so and only if they are wearing a respirator.

In this way, employees who work in other areas of the workplace will not be unnecessarily exposed to cadmium if they are required by their job to work in a regulated area for part of the workday. Due to the serious nature of the adverse health effects associated with excess exposure to cadmium, no one should be in a regulated area without proper personal protection.

This provision will reduce the overall cadmium exposure of many employees, thereby reducing their risks of contracting cadmium-induced illness. OSHA considers this to be necessary to further reduce the any remaining risk of disease at the PEL where risk is estimated without regard to the additional reductions in risk attributable to this requirement for regulated areas and to the other ancillary requirements.

The establishment of regulated areas is an effective means of limiting excess cadmium exposure to as few employees as possible. This is consistent with good industrial hygiene practice whenever exposure to a toxic substance can cause serious health effects. The requirement provides additional benefits to employers in that, by limiting access to regulated areas to authorized persons, the employer's obligation to implement other provisions of this standard for employees who are exposed above the PEL is limited to as few employees as possible.

Readily observable temporary sign(s) posted at the boundary of the area, which are consistent with the Hazard Communication Standard, will be sufficient to remind employees that respirators and good personal hygiene practices are needed and that unprotected people should not enter the area.

With two exceptions, these requirements for regulated areas are essentially the same as those proposed. One exception relates to the proposed EL. With the deletion of the proposed EL from this final standard, discussed above in the section explaining the PEL, all references to an EL also have been eliminated from the requirements for, and discussion of regulated areas.

The other exception relates to how to measure the exposure level that determines whether a regulated area should be established. The language of the proposal, that a regulated area shall be established "wherever airborne concentrations of cadmium are, or can reasonably be expected to be in excess of the permissible exposure limit * * *", might be considered ambiguous. It might be interpreted to mean that, regardless of employee exposure levels, a regulated area shall be set up wherever area sampling shows concentrations of cadmium to exceed the PEL. That was not OSHA's intention. In fact, OSHA does not prescribe or rely upon area sampling in determining compliance with the PEL. The language of this final standard clarifies OSHA's intention to require the employer to establish a regulated area only where an employee is or can reasonably be expected to be exposed to airborne concentrations of cadmium in excess of the PEL based on breathing zone samples.

Methods of Compliance: Paragraph (f)

With regard to methods of compliance, the final standard follows the proposal in its fundamentals except in three major ways. First, where the employer demonstrates that exposures are only intermittent, a 30-day exclusion is applied to the requirement to implement engineering controls to achieve the PEL. Second, for a small number of industries where it is not feasible to achieve the PEL by engineering and work practice controls, separate engineering (and work practice) control air limits (SECALs) of 15 $\mu g/m^3$ and/or 50 $\mu g/m^3$ are established at the lowest levels feasible above the PEL. (See Table F-1.) And third, OSHA in this final standard has set out in general terms the necessary elements of a compliance program.

Beginning with the fundamentals, paragraph (f)(1)(i) of this standard, like the proposal, requires employers to institute engineering and work practice controls as the primary means to reduce and maintain employee exposures to cadmium to levels at or below the PEL. Engineering controls include the installation of equipment, such as forced air ventilation, or the modification of a process, such as enclosing it, to control employee exposure levels. Work practice controls involve the manner in which a task is performed, such as how the worker positions himself/herself relative to the source of exposure and/or to the engineering controls, to control employee exposure levels.

Under paragraphs (f)(1) (i), (ii), and (iv) the employer is required to implement engineering and work practice controls even if feasible engineering and work practice controls are inadequate to lower exposures to or below the PEL or, where applicable, the SECAL. In such circumstances, the employer must implement engineering and work practice controls to reduce employee exposures to the extent possible and must provide supplemental respiratory protection in accordance with paragraph (g) to comply with the PEL.

Primary reliance on engineering controls and work practices is consistent with good industrial hygiene practice (NIOSH, Tr. 7/17/90, pp. 51–56; Exs. 57; 77; 19–8; 19–21). The Agency also relies on traditional adherence to a hierarchy of controls that prefers engineering and work practice controls over dependence upon respirators. Such reliance also is supported by some employers and company doctors (Exs. 19–31; L–19–57; 118; 19–2).

Engineering controls are preferred by OSHA for a number of reasons. Engineering controls are reliable, provide consistent levels of protection to large numbers of workers, can be monitored continually and inexpensively, allow for predictable performance levels, and can remove toxic substances from the workplace. Once removed, the toxic substances no longer pose a threat to the employee. Moreover, the effectiveness of engineering controls does not depend to any marked degree on human behavior, and the operation of equipment is not as vulnerable to human error as is the use of personal protective equipment.

Engineering controls can be grouped into 3 main categories: (1) Substitution, (2) containment and isolation, and (3) ventilation, both general and localized. Quite often a combination of these controls can be applied to an industrial hygiene problem to achieve satisfactory air quality. However, it may not be necessary or appropriate to apply all these measures to any specific potential hazard.

Substitution can be the appropriate solution to an industrial hygiene problem. One of the best ways to prevent workers from being exposed to a toxic substance is to stop using it entirely. Although substitution is not always possible, one should always consider whether a non-toxic or less

toxic material could be substituted for a more toxic one. OSHA received comments on the availability of cadmium substitutes for several industry segments (Ex. 8–706). Another kind of substitution that may provide effective control of an air contaminant is exchanging one type of process equipment for another, or in some cases, exchanging one process for another. For example, a process change in chemical production from powder to pellets or granules will usually reduce exposures. Similarly, automation of a process can further reduce the potential hazard to an employee.

In addition to substitution, there are two basic ways to effectively control employee exposure levels by separating workers from the source of the hazard. In one, containment (enclosure), the hazard is enclosed by a physical barrier, which contains it at its source, thereby separating the hazard from most workers. In the other, isolation, the hazard is not contained but the workers are isolated from the source of the hazard. Isolation can be accomplished, for example, by placing the employees in a clean room, in a properly ventilated cab, or at some distance from the source of the exposure.

Frequently containment maximizes the effectiveness of other engineering controls such as local exhaust ventilation. For example, where a chemical mixing operation is enclosed in a room, confining the airborne contaminants generated by the operation to a small area, the application of local ventilation to control the contaminant at the source is more effective.

Ventilation, general or local, is the most important engineering control available to the industrial hygienist. (See discussion below on mechanical ventilation.) Its principal application is to maintain airborne concentrations of contaminants at acceptable levels in the workplace. A local exhaust system is used to capture an air contaminant at or near its source and to carry it off before it spreads throughout the workplace. General ventilation, on the other hand, allows the contaminant to spread throughout the workroom but dilutes its concentration by circulating large quantities of air into and out from the workroom. A local exhaust system is generally preferred to ventilation-by-dilution (general ventilation) because it provides a cleaner and healthier work environment. Also, a local exhaust system requires a relatively small volume of air and uses a smaller fan and dust collector.

Work practices, as distinguished from engineering controls, involve the way a task is performed. The Agency has found that good work practices can be a vital aid in achieving compliance with the PEL. Some fundamental and easily implemented work practices are: (1) Following the proper procedures to minimize exposures in operating production and control equipment; (2) not eating, drinking, smoking, chewing tobacco or gum, or applying cosmetics in regulated areas or carrying products associated with these activities into regulated areas; and (3) good housekeeping.

Good housekeeping plays a key role in the control of occupational health hazards. Accumulations of cadmium dust increase the risk that workers' exposures will rise above the PEL or the AL. Dust in the workplace on overhead ledges, equipment, floors, etc., should be removed before some disruption, like traffic or random air currents, re-entrains the dust and makes it airborne again. A regular cleanup schedule using HEPA filtered vacuum cleaners is an effective method of removing cadmium dust from the work area. Similarly, immediate cleanup of any toxic spills is a very important work practice control measure.

Periodic inspection and maintenance of process equipment and control equipment, such as ventilation systems, is another important work practice control. In plants where total containment is used as an engineering control, the failure of the ventilation system for the containment area can result in hazardous exposures in the enclosure. Frequently, equipment which is near failure or in disrepair will not perform normally. Regular inspections can detect abnormal conditions so that timely maintenance can then be performed. If equipment is routinely inspected, maintained, and repaired, or replaced before failure is likely, there is less chance that hazardous exposures will occur.

In addition to the above work practice controls, workers must know the proper way to perform their job tasks to maximize the effectiveness of engineering controls. For example, if a worker inappropriately performs a task away from an exhaust hood, the control measure will be of no use. Failure to properly operate engineering controls may also contaminate the work area. Workers can be alerted to safe operating procedures through fact sheets, discussions at safety meetings, and other educational means.

Good supervision is another important work practice. It provides needed support for assuring that proper work practices are followed by workers. By directing a worker to position the exhaust hood properly or to improve work practices, such as weighing toxic materials or handling contaminated scoops or shovels, a supervisor can do much to minimize unnecessary exposure to air contaminants.

Employees' exposures also can be controlled by scheduling production and/or workers' tasks in ways that minimize employee exposure levels. For example, the employer can schedule operations with the highest exposures at a time when the fewest employees are present. Thus, clean-up operations in which toxic substances are involved might be performed at night or other times when the production staff is not present. Such methods of controlling worker exposures to contaminants are known as administrative controls. OSHA generally approves of the use of administrative controls. However, the Agency prohibits using one form of administrative control, worker rotation, as a method of compliance with this standard. Worker rotation circulates employees into and out of contaminated areas, thereby reducing the exposure to individual employees by increasing the number of employees exposed. Since even low cadmium exposure levels are associated with cancer and kidney damage, OSHA prohibits worker rotation, because it places more employees at risk of material impairment to their health (Ex. 19–57; Tr. 7/18/90 p. 252). For these reasons, OSHA finds comments to the contrary unpersuasive (Ex. L–19–57; Tr. 7/18/90, pp. 252–322).

Respirators are another, important method of compliance. However, to be used effectively, respirators must be individually selected; fitted and periodically refitted; conscientiously and properly worn; regularly maintained; and replaced as necessary. In many workplaces, these preconditions for effective respirator use are difficult to achieve with sufficient consistency to provide adequate protection. The absence of any of these preconditions can reduce or eliminate the protection the respirator provides to the employee.

Because there are so many ways that respirators can be rendered ineffective and so many potential problems associated with their use, OSHA has traditionally relied less on respirators than on engineering and work practice controls in the hierarchy of controls. For example, where work is strenuous, the increased breathing resistance of certain types of respirators may contribute to an employee's health problems and may reduce the acceptability of wearing a respirator to employees. Although

experience in industry shows that most healthy workers do not have physiological problems wearing properly chosen and fitted respirators, common health problems can cause difficulty in breathing while an employee is wearing a respirator.

Employees with respiratory system and cardiac diseases may have difficulties in wearing respirators. Cardiac or cardiorespiratory diseases that may affect respirator use include coronary thrombosis, any type of congestive heart disease, other ischemic heart diseases, and hypertension.

The amount of difficulty associated with respirator use will clearly depend both on the degree of cardiorespiratory inadequacy and on the amount of physical effort required by the work. Some people who may have difficulty wearing a negative pressure respirator, which increases the resistance to inspiration, should be able to manage well with a positive pressure type respirator.

The decision about the fitness of the individual to wear a respirator is a judgment that can best be made by a licensed physician, who must take into account the state of the individual's health as well as the physical requirements of the job (Bond; Tr. 7/18/90, pp. 199–200). Consequently, OSHA requires medical examinations under paragraph (l)(6) of this standard that target the main potential health problems for workers required by paragraph (g) to wear respirators. For any employee required by his/her job to wear a respirator who has not had a medical examination within the preceding 12 months to evaluate the employee's physical fitness to wear a respirator, such a medical examination is required prior to assignment to that job.

Safety problems created by respirators that limit vision and communication must always be considered. In some difficult and dangerous jobs, effective vision or communication is vital. Voice transmission through a respirator can be difficult, annoying, and fatiguing. In addition, movement of the jaw in speaking can cause leakage, thereby reducing the efficiency of the respirator and decreasing the protection afforded the employee. Also skin irritation can result from wearing a respirator in hot, humid conditions. Such irritation can cause considerable distress to workers and can cause workers to refrain from wearing the respirator, thereby rendering it ineffective. For all these reasons, OSHA has concluded once again that reliance upon respirators as the primary method to reduce a workers exposures should be minimized. This decision is consistent with the cadmium proposal and is based upon OSHA's experience and generally accepted principles of industrial hygiene. There is no evidence or data in the record that would justify OSHA changing its long-established position on this matter.

Respirator efficiency ultimately relies on the individual employee's good work practices, and respirator programs place the burden of protection on the employee. By contrast, engineering controls entail relatively high, front-end costs, but have the advantage that they can control toxic substances before employees are exposed to them. In any event engineering controls do not rely for their effectiveness so routinely on the individual employee's good habits. To date, therefore, OSHA is satisfied that respirators do not offer equal or better protection than engineering controls.

Because respirators are less reliable than engineering and work practice controls and may create additional problems, they are not the preferred method of compliance with the PEL. Accordingly, their use as a primary control is restricted to certain circumstances by paragraph (g)(1) of this standard. In those circumstances, where engineering and work practice controls cannot be used to achieve the PEL (e.g., certain maintenance and repair operations, emergencies, wherever an employee is exposed above the PEL in an industry to which a SECAL is applicable, or during periods when equipment is being installed), OSHA recognizes that respirators may be essential to reduce worker exposure, and provision is made in paragraph (g) for their use as primary controls. In other circumstances, where work practices and engineering controls alone cannot reduce exposure levels to the PEL, respirators also may be used for supplemental protection. In these situations, the burden of proof of infeasibility is appropriately placed on the employer.

Respirators also may be used when an employee exposed at or above the action level requests a respirator. In such cases, it is OSHA's intention that the employer comply with all provisions of the standard applicable to required respirator use; e.g. medical examinations under paragraph (l)(6) and other provisions in paragraph (g).

In all these ways, this final standard basically tracks the proposal in its approach to, and requirements for, methods of compliance. However, three significant changes have been made to the proposed standard in this regard.

(1) For a small number of processes in selected industries where it is not feasible to achieve the PEL by engineering and work practice controls alone, separate engineering (and work practice) control air limits (SECALs) of 15 and/or 50 $\mu g/m^3$ have been established as the lowest feasible levels above the PEL by paragraph (f)(1)(ii) of this standard (See paragraph (f)(1)(ii) and Table 1 in the standard and also see Section VIII—Regulatory Impact Assessment, in this preamble for those industries to which a SECAL is applicable). The result is that employers in these industries are not required to achieve the PEL exclusively by engineering and work practice controls but are instead only required to comply with the PEL by any combination of methods of compliance, including respirators, and to comply with the higher SECAL exclusively by means of engineering and work practice controls. Like the PEL for all other industries and occupations, the SECAL, where applicable, must be achieved by engineering and work practice controls, except to the extent that the employer can demonstrate that such controls are not feasible.

(2) A 30 day exclusion for intermittent exposure has been added to the general requirement in paragraphs (f)(1)(i) and (i) of this standard that the PEL and the SECAL must be achieved by engineering and work practice controls. Under the exclusion, the employer's obligation to implement engineering and work practice controls to comply with the PEL or the SECAL is not triggered if an employee is exposed only intermittently so long as the employee is not exposed above the PEL (SECAL) on 30 or more days during a year (12 consecutive months). Thus, if an employee is exposed to cadmium on only 29 days during a year, even if the exposure is above the PEL (SECAL) on all of these days, the employer is not required by this standard to implement engineering and work practice controls to control exposures to the PEL (SECAL). The burden is on the employer to prove the required elements of the exclusion from the obligation to achieve the PEL or, where relevant, the SECAL by engineering and work practice controls.

(3) In paragraph (f)(2)(ii), OSHA has set out in general terms the necessary elements of a compliance program. Similar elements were included in OSHA's health standards for arsenic (29 CFR 1910.1018).

OSHA discusses these changes in order. First, OSHA has decided to adopt a separate engineering (and work practice) control air limit (SECAL)

above and in addition to the PEL for a number of reasons, some quite general and others specific to conditions in the cadmium industries and occupations. The main reason OSHA has adopted this two-tier structure, which was repeatedly urged upon OSHA by the Cadmium Council (Ex. L-140-28), is that it is simultaneously more protective of workers' health and feasible.

Based upon the evidence in the record (Health Effects; QRA), the PEL for cadmium must be set at least as low as 5 $\mu g/m^3$. By implementing the new PEL in conjunction with the ancillary provisions of the standard, OSHA expects that cadmium exposed workers will be protected from significant risks of kidney damage and lung cancer (Ex. L-140-50; See Section VI—Quantitative Risk Assessment). In addition, (See Section VIII—Regulatory Impact Analysis), a PEL of 5 $\mu g/m^3$ is at or very near the limit that can be achieved by engineering and work practice controls for thousands of cadmium exposed employees. Consequently, the health science data requires OSHA to set the PEL at 5 $\mu g/m^3$, and the economic and technological data indicate that level is generally within the limits of feasibility.

However, for a relatively small minority of cadmium exposed workers, concentrated almost exclusively in easily identifiable and distinct industry segments, like the primary cadmium producing industries of cadmium refining and zinc smelting, Ni-Cd battery manufacturing, lead smelting, plastic stabilizer production, plating and cadmium pigment production, a PEL of 5 $\mu g/m^3$ does not appear to be achievable by engineering and work practice controls in a number of processes. (See Table 1 and discussion under Section VIII—Regulatory Impact Assessment.)

Under these circumstances, and focusing exclusively for the moment on policy issues, OSHA is faced with a choice. OSHA can set the PEL high enough that it can be achieved by engineering and work practice controls in most of the operations most of the time (*United Steelworkers of America* v. *Marshall*, 647 F.2d 1139, at 1272 [D.C. Dir. 1980], cert. denied, 453 U.S. 913 [1981]) in all or nearly all of the industries and in all of the occupations. But in that case, the relatively severe feasibility constraints in the primary cadmium producing industries might act as the limiting factor for protecting all cadmium exposed employees, and the vast majority of cadmium exposed workers outside these industries would be less protected than they can and need to be. For most cadmium exposed workers, a PEL of 5 $\mu g/m^3$ is feasible by engineering and work practice controls alone and would provide greater protection. Moreover, even for employees in industries that cannot control air cadmium levels to 5 $\mu g/m^3$, setting the PEL at a level no lower than the lowest level that can be achieved by engineering and work practice controls also would be less protective.

In general, setting the PEL at the lowest level achievable by engineering and work practice controls in cases where the health science data shows significant remaining risk at that level means that workers may not be adequately protected. Employers in those cases would not be required, as they would be if the PEL were set at the lower level indicated by the health science data, to provide additional, needed protection to workers through respirators and compliance with other provisions.

Although, as was stated above, the Agency does not believe that respirators are as effective or as safe as engineering controls in protecting workers, OSHA has no doubt that respirators are eminently better than no protection at all. Furthermore, although OSHA is reluctant to require workers to wear respirators routinely for extended periods of time, where the health science data indicate that additional worker protection is required below the level attainable by engineering and work practice controls, OSHA believes, on balance, that it is important to assure that additional protection be provided, even if this necessitates reliance upon routine use of respirators.

To the extent that OSHA in this standard is divorcing the PEL from the SECAL and is setting the PEL at the lower level indicated by the health science data, OSHA is establishing a protective policy. Some precedent for this may be found in the way OSHA responded to the recent non-ferrous foundry industry lead remand (55 FR 3146, Jan. 30, 1990).

However, the issues in the lead remand case were presented in such a different context that OSHA did not have the opportunity or the need to broadly reconsider the relationship between the health data and the PEL, on the one hand, and the feasibility data and the engineering control limit, on the other. In the lead remand, the PEL had been established more than a decade before. In that context, the only question for OSHA on remand was whether that PEL was feasible in particular remand industries and, if not, what was the lowest feasible PEL industry by industry.

By contrast, in this standard, OSHA is consciously deciding to set the PEL lower than the level achievable by engineering and work practice controls in a number of processes in the primary cadmium producing industries. OSHA is aware that there are arguments for and against this decision, and indeed this is the first time the Agency has decided so clearly to separate the PEL from the SECAL. After extensive consideration of the pros and cons, OSHA has decided that the added protection to cadmium exposed workers resulting from this decision outweighs the attendant disadvantages deriving from the need in certain industries with a relatively small number of exposed employees for greater reliance on respirators to supplement engineering and work practice controls.

OSHA believes this to be good policy, which is supported, and may under certain circumstances even be required, by law. Under section 6(b)(5) of the OSH Act the Agency is legally required to set standards that "to the extent feasible" best protect workers from significant risks of material impairment of health. As stated in the cadmium proposal (55 FR 4094), OSHA does not believe that this obligation can be satisfied by using a lowest-common denominator approach to protecting workers, i.e., by protecting all workers only to the extent that the most severe feasibility constraint on protecting any worker would allow. On the contrary, OSHA believes that if a minority of workers cannot be as effectively protected as the majority, that fact is not an adequate reason to forego protecting the majority to the extent feasible. The courts seem to agree.

In the recent decision involving OSHA's asbestos standard, the U.S. Court of Appeals for the District of Columbia Circuit appears to have held that, where there is continuing significant risk at a PEL of 0.2 fibers per cubic centimeter and a PEL of 0.1 fibers per cubic centimeter is achievable in an industry sector employing 93% of the exposed workers, then, absent some persuasive justification to the contrary, OSHA cannot legally impose the higher PEL on that sector even if the lower PEL could not be achieved in operations in other industry sectors. The court, therefore, remanded the case to OSHA "to address the issue of disaggregating the general industry standard to afford workers the benefits of more stringent standards in areas where they are feasible." *Building and Construction Trades Dept., AFL-CIO* vs. *Brock*, 838 F.2d 1258, 1272-73. OSHA considers its decision in this rulemaking to require

compliance with a SECAL and a PEL in certain industries to be in accordance with the asbestos opinion.

With regard to the second significant change in the proposed cadmium standard, OSHA in paragraph (f)(1)(iii) of this final standard has added an exclusion to the general requirement of paragraphs (f)(1)(i) and (ii) that the PEL and the SECAL must be achieved by engineering and work practice controls. The exclusion is for employees who are only intermittently exposed to cadmium and are exposed above the PEL on fewer than 30 days per year (12 consecutive months). OSHA received comments on the need for such an exclusion (e.g., EEI, Tr. 7/19/90, pp. 5–68).

OSHA is aware that this introduces an added element of complexity to the standard. However, the Agency believes the exclusion is one method of providing needed flexibility, in a standard that applies to multifarious industries and occupations, while protecting workers.

Under the exclusion, the employer's obligation to implement engineering and work practice controls to comply with the PEL or the SECAL is not triggered until an employee is exposed above the PEL on 30 or more working days during a year. Where the exposure is for fewer than 30 working days, the employer may use any mix of controls to achieve the PEL, including respirators. However, OSHA has qualified the exclusion by requiring the employer to demonstrate that the employee is only intermittently exposed. OSHA considered several options when reviewing the request for an exclusion to engineering controls. (See also Ex. L–144–28)

OSHA decided to add an exclusion to the final standard for several reasons. First, under current exposure conditions, the main threat from exposure to cadmium is cumulative. Thus, assuming stable exposure levels, the fewer the days the worker is exposed, the less cadmium will accumulate in the worker's body. At some point, the risk of adverse health effects from so few days of exposure per year is reduced to insignificance. Consequently, some exclusion is justified.

Second, in a number of the cadmium using industries (e.g., plastics manufacturers who use cadmium stabilizers), as distinguished from the cadmium producing industries, exposure to cadmium is typically intermittent and brief (e.g., Exs. 120; 8–716). Under such conditions of exposure, it may not be economically feasible, cost effective, or very beneficial to workers' health for employers to invest the monies needed to install engineering controls to control cadmium to the PEL.

Third, with regard to industries and occupations that are neither primary producers of cadmium nor routine users of cadmium, the 30-day exclusion broadly means that engineering and work practice controls need not be implemented and consequently that in this respect the standard is feasible.

The alternative to incorporating an exclusion in the requirement to implement engineering controls would require employers to implement engineering controls wherever employees are exposed to cadmium above the PEL, even if they are only exposed on one or several days a year. OSHA does not think that the expense for implementing engineering controls in such circumstances, which can be quite high, would be justified. Consequently, incorporating some sort of exclusion seems to make sense in controlling occupational exposure to cadmium.

The question, then, is what number of days should be selected as the maximum, above which engineering and work practice controls must be implemented. There is no simple, scientifically definitive answer to that question. OSHA chose fewer than 30 working days per year in part because the lead standard incorporated a similar exclusion and in part to make this exclusion congruent with the exclusion provided in paragraph (l)(1)(i) regarding medical surveillance. Since lead and cadmium are both heavy metals that accumulate in the body, it seemed appropriate to incorporate similar maxima as triggers. Furthermore, industry representatives indicated that 30 working days per year appeared to reasonably reflect the frequency patterns for intermittent exposures in their industries (Tr. 7/19/92, pp. 10–15). In any event, OSHA is assured that no number of days other than 30 per year would be more reasonable.

In providing this exclusion, OSHA wants to make clear its intention to provide relief exclusively to employers whose employees are exposed to cadmium only intermittently and otherwise are effectively not exposed to cadmium at all. If employees are only exposed to cadmium on fewer than 30 working days, with respirator use required to reduce exposures that are above the PEL, the cumulative exposure allowed under the exclusion is expected to be minimal. On the other hand, if employees are exposed to cadmium above the PEL on fewer than 30 working days, but also are exposed at or below the PEL on many, most, or all other days, then such an exclusion might allow employees to experience much higher cumulative exposures over a 12-month period, well above what would otherwise be considered acceptable exposure levels. That is not OSHA's intention. Consequently, the 30-day exclusion does not apply to employees who have more than nominal exposure to cadmium in addition to the exposure during the fewer than 30 days. Where the employee has such other exposure, regardless of whether the employee is exposed above the PEL on fewer than 30 days a year, the employer is obligated, to the extent feasible, to achieve the PEL or the SECAL, whichever is relevant, by means of engineering and work practice controls. The Agency hopes this 30-working-day exclusion will make the standard more flexible in the great variety of intermittent exposure conditions to which the standard will apply.

Under paragraph (f)(1)(iii), it is the employer's responsibility to demonstrate the existence of all the elements required for the employer to be able to take advantage of the exclusion. Thus, the employer must prove that: (a) the employee is exposed above the PEL on fewer than 30 days per year; and (b) the employee is effectively not otherwise exposed to cadmium. OSHA placed the burden of proof on the employer for several reasons. First, the employer is in the best position to demonstrate the existence of all the elements, because the employer has the best access to needed information about employee exposure levels and, where existing information is inadequate, the employer also is in the best position to develop the necessary information. The employer is best able to gather, develop, correlate and maintain the exposure data needed to assess an employee's exposure to cadmium. The employer, for example, can best determine how often to monitor a particular employee to satisfy the burden of proof for the exclusion. Second, by contrast, since OSHA generally only inspects individual workplaces periodically and relatively briefly, it would be extremely difficult for OSHA to develop or gather the information concerning the intermittency and intensity of employee exposures needed to determine whether the exclusion applies. Third, the employer has an interest in demonstrating the applicability of the exclusion to his/her employee(s). Employers generally believe that engineering controls are more expensive than other methods of compliance and therefore have a perceived economic incentive to assure that engineering controls are not implemented for any employee for whom this standard does not require them.

(3) The third significant change to the proposal is the requirement for specific elements in the written compliance program. As modified, paragraph (f)(2) requires an employer who has employees exposed over the PEL to establish and implement a written compliance plan which describes the methods to be used to reduce employee exposure within his/her workplace to or below the PEL. The 30-day exclusion in paragraphs (f)(1) (i) and (ii) does not apply to the requirement to develop a written compliance plan, because, regardless of the manner in which exposure must be controlled, a plan must be developed to show how it will be achieved. The plan must provide for compliance through engineering and work practice controls, where required by the standard, to the extent feasible. These written plans must be furnished upon request for examination and copying to representatives of the Assistant Secretary, representatives of the Director of NIOSH, and affected employees or their representatives; and must be reviewed and updated, as discussed elsewhere in this preamble.

The purpose of requiring an employer to establish a written compliance program and to annually review and update it is to effectively promote required compliance with the PEL and/or SECAL or, in the alternative, where reducing airborne cadmium levels to the PEL or SECAL is not feasible, to effectively aid the employer in reducing employee air cadmium levels to the lowest feasible levels. OSHA recommends that records of routine maintenance of equipment, required to achieve stability in the control of exposures, be maintained and be accessible for review by OSHA. If circumstances change significantly (e.g. process changes or advancements in engineering controls where it previously was infeasible to achieve the PEL or SECAL by engineering and work practice controls), the employer is required to review and update the compliance program as needed.

OSHA has set out in very general terms the required elements of a compliance plan. The elements are similar to those required under the lead and arsenic standards (29 CFR 1910.1025 (e)(3)(ii); 29 CFR 1910.1918 (g)(2)(ii)). OSHA believes that by requiring certain elements in compliance plans the Agency will direct the employer's attention to these elements and communicate a sense of what a compliance plan entails. OSHA further believes that requiring a detailed implementation schedule will facilitate timely compliance. The more effective the compliance plan, the more likely it is that the employer will achieve compliance within the standard's deadlines.

The required elements of the plan include a description of the relevant aspects of each operation in which cadmium is emitted; a report of the technology considered in meeting the air cadmium limit; a description of the specific methods that will be used to achieve compliance, including the underlying documents justifying the choice of methods; air monitoring data characterizing cadmium emission sources; a detailed implementation schedule, with progress documented by appropriate underlying documents; a work practice program; and a written plan for emergency situations.

OSHA has made another minor change to the proposal by adding paragraph (f)(3), which pertains to mechanical ventilation. The paragraph is basically the same as paragraph (e)(5) in the lead standard (29 CFR 1910.1025) and similar in part to paragraph (e)(4) in the cotton dust standard (29 CFR 1910.1043). Mechanical ventilation is generally the most important engineering control for controlling cadmium exposure. Consequently, the Agency has made it explicit under paragraph (f)(3)(i) that when ventilation is used to control exposure, measurements that demonstrate the effectiveness of the system in controlling exposure, such as capture velocity, duct velocity, or static pressure, should be made to ascertain and maintain the effectiveness of the ventilation equipment. This provision was included to facilitate understanding of good general maintenance practices. It is not expected that this provision will add additional costs to an employer's routine maintenance procedures.

The Agency further specifies under paragraph (f)(3)(ii) that measurements of the system's effectiveness in controlling exposure should be made within a reasonable time period, i.e., within five days, after any changes in change in production, process, or control that might result in a significant increase in employee exposure to cadmium. Under (f)(3)(iii), it is specified that if air from an exhaust ventilation system is to be recirculated into the workplace, the system shall have a high efficiency filter and be monitored to assure effectiveness. In addition, under (f)(3)(iv), OSHA requires that employers develop and implement procedures to minimize employee exposure to cadmium when maintenance of ventilation systems and changing of filters is being conducted.

OSHA believes that paragraph (f) of this standard, which requires the employer to give preference to engineering controls and work practices over the use of respirators, is protective and encourages employers to pursue a cost-effective approach to controlling cadmium exposure.

Respiratory Protection: Paragraph (g)

With regard to respiratory protection, this final standard adopts the proposed provisions with little or no substantive modification. The provisions of this standard are in keeping with requirements for respiratory protection in other OSHA health standards (Lead 29 CFR 1910.1025; Benzene 29 CFR 1910.1028), and with recent developments in the field.

Respirators are necessary as supplementary protection to reduce employee exposure when engineering and work practice controls cannot achieve the necessary reduction to or below the PEL. Respirators may also be necessary at other times: while such controls are being implemented, during emergency situations, during intermittent exposures under the 30-working day exclusion when engineering and work practice controls are not required, wherever an employee is exposed to cadmium above the PEL in an industry to which a SECAL is applicable, and for brief or intermittent exposures that cannot be controlled through engineering and work practice controls. A respirator also must be provided by the employer for all authorized employees in regulated areas.

Finally, OSHA in paragraph (g)(1)(vi), also requires employers to provide a respirator to any employee who is exposed to cadmium at or above the action level who requests one. This provision is the same in the final standard as in the proposal (55 FR 4052, at 4123). It also is similar to a provision in the lead standard (29 CFR 1910.1025 (f)(1)(iii)). The employer under paragraph (g)(2)(ii) is also required to provide a powered air purifying respirator (PAPR) to any employee entitled to be provided a respirator whenever that employee requests a PAPR and the PAPR will provide adequate protection to the employee. This provision clarifies the language in paragraph (g)(2)(ii) of the proposal to make it consonant with paragraph (g)(1)(vi) in the proposal and final standard.

Because of the risk of serious adverse health effects from cadmium exposures, OSHA accepts the need for requiring respirators in the above mentioned

circumstances in order to reduce an employee's cumulative dose of cadmium.

The final standard requires that whenever respirators are required to reduce employee exposures, the employer must provide the type of respirator appropriate to the exposure level at no cost to the employee. Employers must also assure that respirators are used properly when required. The standard contains specific requirements for the use, selection, maintenance, and fitting of respirators, which are derived from OSHA's experience and are consistent with widely accepted principles of industrial hygiene and with other OSHA health standards (Asbestos, 29 CFR 1910.1001; Lead, 29 CFR 1910.1025; Benzene, 29 CFR 1910.1028; Formaldehyde, 29 CFR 1910.1048).

Table 2 lists the type of respirator to be used at each airborne concentration of cadmium in the workplace. While the employer must select the appropriate respirator from the table on the basis of the airborne concentration of cadmium, the employer may always select a respirator providing greater protection, (i.e., a respirator prescribed for higher concentrations of cadmium than the concentration to which the employee is exposed). The standard further requires that the respiratory protection program implemented by the employer conform to that set forth in 29 CFR 1910.134, which contains the basic requirements for proper selection, use, cleaning and maintenance of respirators. Since OSHA's risk assessment indicates that cadmium is highly toxic, OSHA has required all air purifying respirators to be equipped with a HEPA filter, regardless of the exposure level. OSHA believes that HEPA filters provide an extra margin of safety at all levels of exposure. While other non-HEPA filters may perform efficiently at very high concentrations of cadmium in air, the HEPA is the most efficient, e.g., 99.97% removal at higher concentrations. Moreover, only the HEPA filter is efficient at lower PELs, e.g., PEL < 50 $\mu g/m^3$ (Asbestos, 51 FR 22695, June 20, 1986).

OSHA is especially concerned about efficiently filtering small size particles, i.e., the particles for which the HEPA filter is the most effective. Thus, OSHA, in requiring the use of HEPA filters is concerned especially to protect workers exposed to low levels of cadmium in the form of small particles. OSHA believes that the requirement for HEPA filters will provide a needed degree of safety for these workers, that cannot be provided as effectively by other filters. The requirement for HEPA filters is consistent with other OSHA health standards (Lead, 29 CFR 1910.1025; Asbestos, 29 CFR 1910.1001).

The standard also requires employers to permit employees to leave regulated areas to readjust the respirator facepiece for proper fit, to change the filters, or to replace the respirator. It also requires employers to permit employees to leave the regulated area to wash their faces or their respirators to avoid potential skin irritation associated with respirator use. These requirements encourage and facilitate the proper use of respirators by employees through authorizing employees to take specific actions to assure the effective functioning of the respirators and to reduce the probability of certain adverse side effects from wearing respirators. These requirements are consistent with provisions in other health standards (e.g., Inorganic Lead, 29 CFR 1910.1025) and with the proposed cadmium standard (55 FR 4123).

The standard requires fit testing of all respirators to assure at least a minimally acceptable fit. Quantitative fit testing requires the use of moderately sophisticated testing equipment and is more expensive to perform than qualitative fit testing. This may reduce its availability in some worksites. Also, testing services may not be available in all parts of the country to provide quantitative fit testing services for small employers. To tailor the respirator fit testing to the circumstances of the employer's establishment, OSHA permits the employer to choose either quantitative or qualitative fit testing if cadmium exposures are less than 10 times the PEL. Mandatory protocols for whichever type of testing the employer chooses are set forth in Appendix C to this standard.

OSHA is requiring quantitative fit testing of all tight-fitting air-purifying respirators (either positive or negative-pressure) when used at exposures exceeding 10 times the PEL, 50 $\mu g/m^3$, because proper fit is essential to the performance of these respirators. Quantitative fit testing is a procedure whereby the level of penetration of a test agent of known concentration is measured inside the facepiece of the respirator. Quantitative fit testing is generally recognized as the better method for determining how well a respirator fits a particular individual. It provides a quantitative assessment of the extent of the fit (i.e., the fit factor). It allows the employer to test various respirators on the employee until the optimum or best fitting respirator is identified and selected for the employee. Whenever quantitative fit testing is used to assess the fit of a negative pressure respirator, a fit factor of at least 10 times the protection factor for that class of respirators shall be achieved for an acceptable fit. This is a minimum requirement. Whenever quantitative fit testing is used to assess the fit of a positive pressure respirator, the employer shall test a negative pressure respirator made by the same manufacturer, which is the same model and size, to determine whether the facepiece-to-face seal is adequate. The seal is acceptable if the fit factor is at least 10 times the protection factor for the relevant class of negative pressure respirators.

The regulatory language in the proposal, which required that both negative and positive pressure air purifying respirators be fit tested, was not clear on this point. A commenter stated that the proposed requirement for quantitative fit testing for negative pressure air purifying respirators and powered-air-purifying respirators (PAPRs) should be extended to all tight-fitting respirators, including self contained breathing apparatus (SCBAs) and supplied air respirators (L19–53). Language has been added to paragraph (g)(4) to clarify the requirement to fit test tight-fitting supplied-air respirators and SCBAs.

Obtaining a proper respirator fit may require fit testing a variety of different mask sizes from several manufacturers to select the facepiece with the best fit (i.e., least leakage around the facesea) for each employee. A properly fitted facepiece helps to reduce inhalation leakage to a minimum. If the fit factor is not at least minimally acceptable, the respirator shall not be worn. With ill-fitting respirators, cadmium contaminated workplace air may enter the facepiece through gaps and leaks in the facepiece seal.

Qualitative fit testing does not provide a numeric measure of the tightness of the fit but simply determines whether a respirator "fits" or not. Qualitative fit testing is a technique whereby a person wearing a respirator is tested to see whether a test agent with a detectable odor or taste threshold can be detected inside the respirator. If the odor or taste cannot be detected, the respirator is said to "fit". Qualitative fit testing is more subjective than quantitative testing because it depends on the individual's ability to detect the test agent.

OSHA recognizes that quantitative fit testing may have some advantages over qualitative fit testing. However, for employees exposed to lower levels of cadmium, (10 times the PEL or less)

qualitative testing conducted in accordance with the protocols described in Appendix C can adequately assess the fit of the respirator to assure that each employee is assigned and wears the respirator that provides a proper fit with the least possible leakage. It is important that all employees who wear respirators be medically screened to determine employee fitness for respirator usage. Respirator use may constitute a burden on the employee's cardiopulmonary system. This burden may result in symptoms such as shortness of breath, chest pain, dizziness or fatigue. These symptoms may be exacerbated by pre-existing lung disease such as chronic bronchitis, emphysema, asthma or pneumoconiosis.

Paragraph (l)(6)(i) of this standard requires that limited medical examinations be made available to workers with a job that requires the use of a respirator. This differs from the proposal which required a full medical examination (55 FR 4125). The limited medical examination must be made available prior to the employee's assignment to a job requiring a respirator unless the employee has received a medical examination within the preceding 12 months that satisfies all the requirements of paragraph (l)(6)(i)(A)–(D). The medical examination is to assure that individuals who are incapable of wearing a respirator or who might suffer some adverse health effect from wearing a respirator are not required to wear one. The medical examination is made available to determine whether any health conditions exist that would affect the employee's ability to wear a respirator. If an examining physician determines that an employee will be unable to continue to function normally while wearing a respirator in a job where exposures exceed the PEL, then the employee shall be afforded the opportunity for transfer as set forth in paragraph (l)(11). This is consistent with OSHA's previous health standards (e.g., Asbestos, 29 CFR 1910.1001; paragraph (g)(3)(iv)).

This does not mean that medical removal protection (MRP) under paragraph (l)(11) applies to a new employee who is determined in a pre-employment medical examination for respirator use to be unable to wear a respirator. Nor does it mean that MRP applies to a worker determined to be medically unable to wear a respirator who seeks to transfer to a job for which a respirator is required. The MRP provisions relating to an employee's inability to wear a respirator apply only to a worker who already is functioning in a job where a respirator is required who is then determined to be medically unable to wear a respirator.

OSHA has not exempted occasional users of respirators from the medical evaluation requirement. OSHA believes such users need to be evaluated for their fitness to wear respirators as well. In addition, applying such an exemption might create administrative problems (Docket Number H–049, Respiratory Protection Revision).

The standard requires employers to provide a proper respirator at no cost to any employee with cadmium exposures at or above the action level who requests one. Due to the serious nature of the adverse health effects of cadmium exposure, workers exposed at or above the action level may choose to use respirators. OSHA generally agrees with the commenter who argued that OSHA should have a consistent medical surveillance policy for all respirator users, including voluntary users (Ex. 19–9). As stated, medical surveillance under paragraph (l) is triggered at exposure levels at or above the action level. Similarly, an employee exposed at or above the action level has the right to request a respirator. Therefore, workers who voluntarily request a respirator are likely to already be covered by medical surveillance.

In addition, unless otherwise indicated, all other relevant requirements apply equally to voluntary respirator users. Thus, under paragraph (l)(6), the employer must provide the voluntary user with a limited medical examination to determine the employee's fitness to wear a respirator prior to wearing one. Similarly, the employer must maintain the voluntary users' respirators in good repair and provide an adequate supply of filter elements. If employees entitled to be provided a respirator by the employer were treated differently, their entitlement might be compromised. For all workers covered by this standard who wear a respirator and for workers who are participating in medical surveillance under this standard, an examination for fitness to wear a respirator is effectively part of routine medical surveillance.

For a respirator program to be effective, the employee must be properly trained to wear the respirator, to know why the respirator is needed, and to understand the limitations of the respirator. An understanding of the hazards involved also is necessary to enable employees to take steps for their own protection.

Commenters and witnesses in the rulemaking raised several main points about OSHA's proposed requirements for respiratory protection. On the one hand, a number of commenters criticized these requirements for not being strict enough. NIOSH, for example, presented a very stringent approach to respirator usage (Exs. 57; 100). NIOSH had several recommendations regarding respirator protection for cadmium exposed workers. NIOSH opposed routine, full-time use of respirators and allowing the use of negative pressure respirators and instead recommended that only the most protective positive pressure supplied-air and SCBA respirators be used, since cadmium is an occupational carcinogen (Ex. 57; NIOSH, Tr. 7/17/90, p. 51). OSHA has never followed such a stringent policy on respirator use. If respirators other than the positive pressure respirators NIOSH recommended are permitted, NIOSH recommended that the assigned protection factors given in the NIOSH Respirator Decision Logic be used, in particular that tight fitting PAPRs be given a protection factor of 50 (OSHA proposed 250), and that loose fitting PAPRs be given a protection factor of 25, as OSHA proposed. (Tr. 7/17/90, pp. 57–58, 77, 83, 164–65, 212–14). In view of the disagreement regarding protection factors (see below), OSHA decided not to change its proposed protection factors and to allow further comments on this issue to be placed in the record of the proposed Respiratory Protection Revision standard (Docket Number H–049).

On the other hand, several commenters criticized OSHA's proposal for being too strict regarding respirators. Thus, one commenter argued that PAPRs and supplied air respirators should be assigned a protection factor of 1000 in the final standard (Ex. 19–20). Another commenter criticized OSHA for assigning a protection factor (PF) as low as 25 to loose fitting PAPRs, instead of the current PF of 1,000 or at least 100 (Ex. 19–39). Still another criticized the Agency for not assigning a PF higher than 10 to half-mask, negative pressure respirators, which it claimed might in some situations be more effective and safer than full facepiece, negative pressure respirators or PAPRs (Tr. 6/12/90, p. 7). Another commenter asked, in light of NIOSH's disapproval of disposable "high-efficiency" respirators for use against asbestos because of its carcinogenicity, whether such respirators were useable for cadmium exposures (Ex. 19–18). One questioned the need to provide PAPRs on request when exposures did not exceed the PEL (Ex. 19–22).

OSHA has extensively reviewed the respirator performance studies supporting the protection factor of 10 given to half mask respirators as part of the Respirator Standard Revision (Docket No. H-049). The concept of giving an increased protection factor to a respirator based on higher fit factors measured during quantitative fit testing has been discredited. Workplace protection factor studies (Docket H-049 Exs. 27-1; 27-2; 27-9; 38-2; 38-7) and laboratory fit testing studies (Docket H-049 Exs. 2; 38-3) that have been reviewed as part of the 29 CFR 1910.134 respirator standard revision show that the fit factors achieved during quantitative fit testing are not achieved in the workplace. While half masks can achieve fit factors greater than 10 during QNFT, they have not been able to demonstrate consistent workplace protection levels greater than 10. Consequently, the protection factors OSHA had listed for cadmium respirators in the proposal (55 FR 4123) are not being changed. The few comments on protection factors that were received do not justify changing the protection factors listed.

A question about the use of disposable high-efficiency respirators such as the 3M Model 9970 for protection against cadmium was raised by Bruce Crowell of the Duke Power Company (Ex. 19-18). OSHA is concerned that the effectiveness of such respirators against carcinogenic dusts and fumes (NIOSH, Tr. 7/17/90, p. 51; Ex. 57) is limited by problems in achieving an adequate fit. This concern has been addressed in several OSHA standards. The cotton dust standard allowed a protection factor of 5 for disposable dust/mist respirators due to problems with respirator fit. The asbestos standard prohibited the use of disposable respirators, with or without HEPA filters. However, there are HEPA disposable respirators on the market with elastomeric facepieces that do not have these problems with fit. For the time being, OSHA will accept the use of HEPA disposable respirators with cadmium. Nonetheless, caution is urged in using HEPA disposable respirators, particularly single use HEPA respirators without elastomeric facepieces.

Michael Dwyer of the McDonnell Douglas Corporation (Ex. 19-22) commented that employers should be required to provide PAPRs on request only if exposures exceed the PEL. Mr. Masaitis, testifying for the American Iron and Steel Institute, stated that it "is unreasonable to require that an employer provide a PAPR to an employee simply because one is requested" when other adequate protection is available (Tr. 7/18/90, pp. 282-283). The cadmium standard requires that respirators, including PAPRs, be provided by employers to employees exposed at or above the action level on request. PAPRs can minimize the physiological burden on lung function imposed by air purifying respirators. Dr. Tyner of Gates Energy Systems commented that lung function should not interfere with a worker's ability to wear a respirator as long as positive pressure respirators are available (Ex. 19-2). PAPRs can also provide added protection. OSHA, therefore, will continue to require that employers provide a PAPR to an employee exposed at or above the action level when requested.

Several other commenters criticized aspects of the protocols for fit testing in appendix C (Exs. 19-5; 19-7; 19-9; 19-20).

Mr. G.F. Stone of the Tennessee Valley Authority commented on the requirement in appendix C that the employer assign specific individuals to assume full responsibility for the qualitative/quantitative fit testing program (Ex. 19-5). He recommended that the employer be required to assign a single individual to be responsible for the entire respirator program, and that individual could then delegate the fit testing responsibilities to appropriate individuals. This cadmium standard permits an employer to designate one individual to be responsible for the entire respirator program. Such a requirement for a single respirator program administrator is being considered for inclusion as part of the respirator standard revision (29 CFR 1910.134). However, that proposed revision and this cadmium standard in their fit testing procedures require that individuals be assigned to be responsible for the qualitative and quantitative fit testing programs who are trained and experienced in selecting proper fitting respirators, performing fit testing, calibrating fit test equipment and interpreting fit testing results. This specialized knowledge and ability to perform fit testing goes beyond that normally expected of an overall program administrator. The purpose of this requirement is to be sure that the fit testing program is performed only by appropriately trained personnel.

In appendix C, the quantitative fit testing methods state that corn oil or sodium chloride are the only accepted challenge aerosols. Mr. G.F. Stone of the Tennessee Valley Authority (Ex. 19-5) urged OSHA to revise this to permit the use of Portacount fit testing instruments, which use ambient air particles as the challenge aerosol. The quantitative fit test methods in appendix C have been shown to be accurate through extensive validation testing. In addition, the use of the Portacount is currently permitted under other OSHA standards by a compliance interpretation that treats their use as a *de minimis* violation of the fit testing requirements (Ex. L-166). The cadmium standard will continue this interpretation of the Portacount. As part of the respirator standard revision (29 CFR 1910.134), the manufacturer of the Portacount has the opportunity to submit validation testing of its fit testing method and instrumentation to show that it is capable of determining fit factors as accurately as the corn oil and sodium chloride systems currently recognized, in order to become a validated fit test method. If the Portacount becomes a validated fit test method, the appendix C fit test methods will be revised to reflect this.

The Maryland Occupational Safety and Health program (MOSH) recommended that the grimace be deleted from the fit test exercises so that "workers will not fail otherwise acceptable fit tests" (Ex. 19-7). The purpose of the grimace exercise is to determine whether the respirator being fit tested will reseat itself on the face after the respirator seal is broken during the grimace exercise. In quantitative fit testing, the test instrumentation should show a rise in challenge agent concentration inside the mask during the grimace exercise and a drop once the respirator reseats itself. If the respirator fails to reseat, the subsequent test exercises will show excessive leakage and result in failing the test. Since even a properly fitting respirator may show increased penetration during the grimace exercise, the penetration measured during the grimace exercise is not to be used in calculating the fit factor. The language in appendix C has been modified to reflect this.

MOSH also recommended that the saccharin solution qualitative fit test protocol be deleted from appendix C (Ex. 19-7). MOSH pointed out that while the saccharin method is the only protocol used with disposable dust respirators, such respirators are not allowed by the proposed cadmium standard. The proposed and final cadmium standards require the use of HEPA filters, which means that the irritant smoke and isoamyl acetate protocols can be used for qualitative fit testing. The saccharin protocol, which uses a large particle size test aerosol, is not necessarily appropriate for cadmium exposure with that type of respirator.

OSHA agrees with MOSH that the saccharin solution protocol is not now needed for the respirators permitted under the cadmium standard, so it has been deleted from appendix C.

Frank Wilcher (Ex. 19–20) of the Industrial Safety Equipment Association (ISEA) questioned the requirement in Appendix C that employees be offered a range of respirator facepieces to choose from, in at least five different sizes, and from two manufacturers. These requirements were called "excessive and unnecessarily inflexible" since an adequate fit can be obtained without offering respirators from two different manufacturers. The number of sizes and models offered, the commenter declared, should be a function of the size of the workforce.

OSHA understands that in a particular workplace a limited selection of respirator sizes and models could possibly be made to fit all those who need one. However, such occurrences cannot reasonably be relied upon as a pretext for limiting respirator selection options. The increased numbers of individuals in the workforce, such as women and minorities, with facial types and sizes that are different from, say, those of white and black males means that a wide range of facepiece sizes is needed to assure adequate fits. The purpose of fit testing is to achieve the best possible fitting respirator and this is only possible when an adequate selection of models and sizes is available. There is no standardization on sizes among respirator manufacturers. Each manufacturer develops their own facepiece molds and none correspond identically. This means that one manufacturer's medium size facepiece may fit an individual, while another manufacturer's medium size facepiece may not. Respirators come in different sizes, some in three different sizes (small, medium, large) while others only come in two sizes (large, medium). Therefore, the cadmium fit testing protocols continues to require that a selection of at least five facepiece sizes from two different manufacturers be available to provide a wide range of possible facepiece fits. This requirement is the same as the one in Appendix C, paragraph I.B.1. in the asbestos standard (29 CFR 1910.1001).

Mr. Stephen Wilson of the Duriron Company (Ex. 19–9) commented that the requirements in section (g) and Appendix C are too detailed, and should be part of the respiratory protection standard (29 CFR 1910.134) and included in the cadmium standard only by reference. OSHA agrees that the ideal place for these detailed respiratory protection provisions is in the respirator standard. However, the respiratory protection standard revision will not be finalized until well after this cadmium standard is published. To achieve the level of respiratory protection appropriate for cadmium exposures it is necessary to include these provisions in the cadmium standard now. Subsequently it may be possible, once the respiratory protection standard revision is finalized, to remove these detailed provisions from the cadmium standard and incorporate by reference the respiratory protection standard provisions.

Emergency Situations: Paragraph (h).

The language in this final standard concerning emergency situations is basically the same as the language in the proposal. It requires the employer to develop and implement a written plan for dealing with emergencies involving substantial releases of airborne cadmium. The plan must include provisions for the use of appropriate respirators and personal protective equipment. In addition, employees not essential to correcting the emergency must be restricted from the area, and normal operations in the area must be halted until the emergency is abated. Examples of such emergencies may include ruptures of containers filled with cadmium in dispersible form and failures of control or operating equipment. Emergency plans are necessary to direct employees to act in ways that maximize their personal protection and minimize the hazards in the event of an emergency. To that end, employees not engaged in correcting the emergency must be prohibited from the area and normal operations in the area halted until the emergency is abated.

Protective Work Clothing and Equipment: Paragraph (i).

Protective clothing and foot coverings are required to prevent contamination of the employee's body and the employee's street clothing and shoes. Protective clothing, if provided and used properly, helps to prevent cadmium exposure beyond the workplace. By contrast, wearing contaminated street clothing outside the worksite would lengthen the duration of the employee's exposure and could cause cadmium to accumulate in employees' cars and homes, exposing other individuals to the hazard.

This final standard, with substantial modifications, adopts the requirements of the proposed cadmium standard regarding protective clothing and equipment. These requirements are typical of other OSHA health standards and are based upon widely accepted principles and conventional practices of industrial hygiene.

The final standard requires that the employer provide protective clothing and equipment to employees who are exposed to cadmium at levels above the PEL and to employees exposed at any level where skin or eye irritation associated with cadmium exposure occurs. This is a minor change from the proposal, which required protective clothing to be provided if "the possibility of skin or eye irritation exists from cadmium exposure * * *." (55 FR 4124). As the discussion in the preamble to the proposed cadmium standard (55 FR 4112) makes clear, OSHA did not intend that the mere "possibility" of associated skin or eye irritation should trigger the obligation for the employer to provide protective clothing and equipment to employees, because that possibility might exist in nearly all workplaces with exposure to cadmium dust. According to the preamble in the proposal it was the occurrence of such irritation that triggered the employer's obligation to provide protective clothing. This final standard follows that intention.

In addition, the language in paragraph (i)(1) of the final standard clarifies OSHA's ongoing understanding that appropriate protective work clothing and equipment must prevent contamination of the employee and the employee's garments. If they did not, they would not be "protective".

Personal protective clothing and equipment includes, but is not limited to, coveralls, shoe covers, head coverings, and goggles. Clean protective clothing and equipment are to be provided by the employer at least weekly, but OSHA recommends that they be provided daily to assure their effectiveness. Protective clothing and equipment is to be provided to each affected employee at no cost to the employee. This is consistent with similar requirements in the lead and arsenic standards, 29 CFR 1910.1025 (g)(2), and 1910.1018(j)(2), respectively. Removal of cadmium from protective clothing by blowing, shaking, or any other means that disperse cadmium into the air is prohibited.

The standard also requires that the employer be responsible for cleaning, laundering and disposing of the required protective clothing and equipment, to eliminate any potential exposure that might result if the clothing and equipment were laundered or cleaned by the employee at home. Like the proposal (55 FR 4124), the final standard requires that protective clothing and equipment be cleaned, maintained, and

replaced as needed in order to assure its effectiveness.

The standard provides that the employer shall assure that all protective clothing is removed at the end of each work shift and only in change rooms. The contaminated clothing and equipment that is to be laundered, cleaned, or disposed of is required to be stored in a closed container prior to laundering or disposal so that contamination of the change room is minimized and exposure of employees who later handle the clothing also is minimized. These employees are further protected by the requirement that they be informed of the potentially harmful effects of cadmium exposure and that warning labels be placed on the bags or containers. Since these containers are to be located in the change room, it is appropriate to limit workers' removal of their contaminated clothing to that area.

The standard obligates the employer to provide personal protective clothing at no cost to the employee. Since the employer is responsible for reducing exposures below the permissible exposure limit, the obligation to provide personal protective equipment properly rests on the employer. The employer also is in the best position to provide the correct type of clothing and keep it in the condition necessary to perform its protective functions.

Hygiene Facilities and Practices: Paragraph (j).

This final standard, like the proposal, requires employers to provide hygiene and lunchroom facilities for employees exposed to cadmium at levels above the PEL and to assure employee compliance with basic hygiene practices to minimize additional sources of exposure to cadmium that may accumulate on a worker's clothes or body. The final standard makes it clearer that all of these facilities must comply with the requirements of 29 CFR 1910.141. For all employees who are exposed above the PEL, the employer must provide adequate shower and washing facilities, clean rooms for changing clothes, and lunchroom facilities. In addition, employers must assure that employees use the facilities as required by the standard. Employers also must assure that employees exposed above the PEL must observe prohibitions on the availability and use of cosmetics, tobacco and chewing products, and food and beverages in regulated areas under paragraph (e). OSHA expects that strict compliance with these provisions will virtually eliminate several sources of cadmium exposure that substantially contribute to overall exposure levels.

Several of these facilities and practices are presently required under current OSHA standards for General Environmental Controls in subpart J of 29 CFR part 1910. For example, § 1910.141(e) states that if a standard requires employees to wear protective clothing, then the employer must provide change rooms with separate storage facilities for street and work clothing. In addition, § 1910.141(g) requires the employer to prohibit the consumption of food and beverages in areas where there is exposure to toxic substances. The hygiene provisions of paragraph (j) of this standard augment the requirements of 29 CFR 1910.141 with additional requirements that are specifically applicable to cadmium exposure and consolidate all related provisions.

OSHA believes it is essential for employees to have separate locker and storage facilities for street and work clothing to prevent cross-contamination of their street clothes. This provision will minimize employee exposure to cadmium after the work shift ends, because it reduces the period during which employees may be exposed to cadmium-contaminated work clothes.

Showering also reduces the worker's period of exposure to cadmium by removing cadmium which may accumulate on the skin and hair. Requiring employees to change out of work clothes, which are then segregated from their street clothes, to shower before leaving the plant, and to leave work clothing at the workplace significantly reduces the movement of cadmium from the workplace. These steps assure that the duration of cadmium exposure does not extend beyond the workshift and provide added protection to employees and their families.

The final standard also requires employers to provide employees whose airborne exposure to cadmium is above the PEL with readily accessible lunchroom facilities in which tables maintained for eating are free of cadmium and no employee is exposed at any time to a concentration of cadmium at or above 2.5 $\mu g/m^3$. This is the main change from the proposed provisions regarding hygiene facilities, which required employers to provide lunchrooms with a positive pressure and a tempered and filtered air supply. By contrast, the final standard is written in performance language. It is OSHA's intention, of course, that employees are not to be exposed to uncomfortable temperatures.

OSHA makes this change to provide more flexibility to employers while still assuring adequate protection to employees. Although the employer may, in any event, often have to provide the type of lunchroom specified in the proposal in order to comply with the performance requirement of the final cadmium standard, OSHA recognizes that there may be many instances where employers can comply without having to do so. OSHA agrees with the industry commenter who said that "where the lunchroom is not adjacent to cadmium contaminated areas" and there is no cross contamination of the lunchroom, a positive pressure, filtered air supply is unnecessary (Ex. 19–22). OSHA therefore sees no reason to require the provision of such lunch rooms where they are not needed.

OSHA believes that the requirements for lunchroom facilities in this final standard are at least as protective as the proposed requirements. For example, the final standard, unlike the cadmium proposal, requires that tables in the lunchroom facility must be maintained free of cadmium and that no employee there may be exposed to a concentration of cadmium at any time at or above 2.5 $\mu g/m^3$. The 2.5 $\mu g/m^3$ limit is not an 8 hour TWA PEL but is an absolute prohibition of levels that high or higher at any time.

OSHA feels it is imperative that employees have a clean place to eat to minimize the possibility of cadmium contaminated food and to reduce the likelihood of additional exposure to loose cadmium dust through inhalation or ingestion. Since OSHA believes that employers have several equally protective options to achieve these goals, the standard has not set specific requirements.

Employers must also assure that employees who work in regulated areas wash their hands and face prior to eating or smoking and that employees not enter the lunchroom wearing protective clothing unless it is properly cleaned beforehand. Employers are given discretion to choose any method for removing surface cadmium from the clothing that does not disperse the dust into the air. These requirements are basically the same as those in other OSHA standards (e.g., paragraph (i)(4) of the lead standard, 29 CFR 1910.1025).

Housekeeping: Paragraph (k)

Like other OSHA health standards dealing with toxic dusts (Asbestos, 29 CFR 1910.1001), the cadmium standard imposes the general housekeeping requirement to maintain all surfaces as free as is practicable of accumulations of cadmium. In the final standard the strong preference for vacuuming (or equally effective and protective methods

of cleaning) that is incorporated in the proposal is made more explicit. The standard requires that, where possible, surfaces contaminated with cadmium be cleaned by vacuuming or other methods that minimize the likelihood of cadmium becoming airborne. The standard allows shoveling, dry or wet sweeping, and brushing only if the employer shows that vacuuming or other methods that are usually as efficient as vacuuming are not effective under the particular circumstances. It also requires that vacuuming be done with cleaners equipped with HEPA filters to prevent the dispersal of cadmium into the workplace. The standard differs from the proposal (55 FR 4124) in that it allows the use of compressed air for cleaning when the compressed air is used in conjunction with a ventilation system designed to capture the dust cloud created by the compressed air. In addition, items contaminated with cadmium and consigned for disposal are to be collected and disposed of in sealed impermeable bags or other closed impermeable containers.

These housekeeping provisions are exceptionally important because they minimize additional sources of exposure that engineering controls generally are not designed to control. Good housekeeping is a cost effective way to control employee exposure levels by removing from the worksite cadmium dust that can become entrained by physical disturbances or air currents and carried into employee breathing zones.

Medical Surveillance: Paragraph (l)

(1) *General.* The medical surveillance provisions of this final standard were developed from the proposal in light of the entire record. More specifically these provisions are derived in no small part from the proposal and the responses to it, as further articulated in a July 2, 1990, memorandum sent by OSHA to all the hearing participants (Ex. 46). That memorandum summarized the comments and testimony in the rulemaking to date, indicated OSHA's then current thinking, and requested further information, comment, and testimony at the upcoming hearing in Denver. The response to that memorandum, which was substantial (e.g., cites), has also shaped the medical surveillance program in the final standard.

The medical surveillance provisions of paragraph (l) generally are aimed at accomplishing three main interrelated purposes: First, identifying employees at higher risk of adverse health effects from excess, chronic exposure to cadmium; second, preventing cadmium-induced disease; and third, detecting and minimizing existing cadmium-induced disease. The core of medical surveillance in this standard is the early and periodic monitoring of the employee's biological indicators of: (a) Recent exposure to cadmium; (b) cadmium body burden; and (c) potential and actual kidney damage associated with exposure to cadmium.

It is not yet known how to biologically monitor human beings to specifically prevent cadmium-induced lung cancer or certain other cadmium-induced lung diseases. By contrast, the kidney can be monitored to provide prevention and early detection of cadmium-induced kidney damage. Since, for non-carcinogenic effects, the kidney is considered the primary target organ of chronic exposure to cadmium, the medical surveillance provisions of this standard effectively focus on cadmium-induced kidney disease. Within that focus, the aim, where possible, is to prevent the onset of such disease and, where necessary, to minimize such disease as may already exist. The by-products of successful prevention of kidney disease are anticipated to be the reduction and prevention of other cadmium-induced diseases.

More specifically, for veteran workers, the aim of these medical surveillance provisions is to promptly identify employees with excessive, cumulative exposure to cadmium, especially those who were excessively exposed to cadmium before this standard takes effect. Once these employees are identified, the aim is to monitor them, ideally to prevent cadmium-induced kidney disease, or at least to minimize it. For cadmium exposed workers who have not yet been excessively exposed to cadmium, the aim is to identify those at higher risk and to prevent excess exposure and resulting disease.

In order to assure that biological monitoring results are accurate and reliable, an issue raised during the rulemaking (Ex. 19–29), OSHA in paragraph (l)(1)(iv) of this standard requires that the employer make sure that collecting and handling of biological samples is done in a manner that assures reliability and that analyses are performed in laboratories proficient in the particular analyte. OSHA has developed a non-mandatory protocol to guide employees and laboratories in these regards (See appendix F). An employer who follows this protocol will be in compliance with the performance requirements in paragraph (l)(1)(iv) of the standard. However, the employer is free to follow other procedures so long as they provide at least the same degree of accuracy and reliability.

As discussed below in connection with the medical surveillance program, the lowest biological triggers incorporated in this standard are above existing levels of detection and are distinguishable from lower levels that for purposes of this standard are treated as "normal" levels of these biological parameters in the general population.

In addition, the degree of accuracy and reliability described in appendix F for biological monitoring required by this standard is achievable with currently available equipment. As a result, OSHA feels comfortable with triggering enhanced medical surveillance and other actions from such biological monitoring results. To assure the necessary quality of results, OSHA recommends that laboratories that analyze levels of cadmium in urine (CdU), cadmium in blood (CdB), and Beta-2 microglobulin in urine (β_2–M) should demonstrate their proficiency in certain, specified ways.

The scope of medical surveillance in this standard is designed to accomplish the purposes set out above. OSHA in its proposed cadmium rule originally sought to include in medical surveillance all workers who are, or may in the future be exposed to airborne levels of cadmium at or above the action level or the excursion limit (55 FR 4124). The excursion limit has since been deleted, as discussed above. However, in the proposal, the use of the action level of 2.5 $\mu g/m^3$ alone was both too broad and too narrow. On the one hand, including all workers who are or will be occupationally exposed to airborne levels of cadmium at or above the action level would allocate scarce resources to monitoring many workers who may not be at significant risk of disease, because by the nature of their work their cadmium exposures are only intermittent and at very low levels (Exs. 8–732; 12–10–G; 148; 120). On the other hand, limiting coverage only to workers who may be currently exposed to cadmium mistakenly ignores the possibility of excess risk of cadmium-related illness among workers who were previously exposed but no longer are (Ex. 19–2). In the case of workers whose previous exposure occurred before the effective date of this standard, the levels of cadmium to which many workers were exposed probably were considerably higher than the new PEL. As a result, these previously exposed workers may have higher body burdens of cadmium and may be in particular need of medical surveillance. Kidney dysfunction arising from chronic, excess

exposure to cadmium, for example, occurs among workers with a certain minimum accumulation of cadmium in their kidneys (Ex. 144–3–C; Section VI—Quantitative Risk Assessment; Summary of Kidney Dysfunction).

Consequently, in response to comments (Exs. 19–18; 101) the scope of medical coverage in paragraph (l)(1)(i) of the final cadmium standard is defined both more narrowly and more broadly than in the proposal. Not every worker who is or will be exposed to cadmium at or above the action level at work is covered. Instead, a certain threshold of exposure to cadmium is required to trigger medical surveillance. An employee will be covered by medical surveillance if the employee is or may be exposed at or above the action level of 2.5 $\mu g/m^3$ on 30 or more days per year. This is in line with testimony in the record (Tr. 7/19/92, pp. 14–17) and with previous OSHA health standards. In those standards medical surveillance for currently exposed employees frequently is triggered by exposure at or above the action level, which typically is set at half the PEL, on 30 or more days per year (Benzene, 29 CFR 1910.1018 (n)(1)(A); Lead, 29 CFR 1910.1025(j)(1)).

In addition, certain workers who no longer are exposed to cadmium but who were previously exposed by the current employer also will be included in medical surveillance under this standard. They will be included if prior to the effective date of this standard they might previously have been occupationally exposed at or above the action level to cadmium by the current employer unless they did not in those years work in those jobs for an aggregated total of more than 60 months. Although OSHA is not requiring employers to provide medical surveillance to workers previously exposed for less than 60 months, OSHA recommends that employers provide the same medical surveillance to all workers who worked for the current employer in cadmium exposed jobs for a total of 12 months or more prior to the effective date of this standard (See Benzene; 29 CFR 1910.1028 (i)(1)).

With regard to these veteran workers, because cadmium is retained for so many years in the body and because it is a cumulative toxin that can cause chronic disease, workers who were excessively exposed to cadmium before this new standard took effect must also be medically monitored, at least for a time, even if they no longer are currently exposed or cease to be exposed. Employees who were not exposed before the effective date of this standard and new employees who begin cadmium exposed work under the new PEL are not likely to be exposed to such high cumulative levels. Under the new PEL, workers are not likely to be exposed above the critical air concentration for susceptible populations of 225 $\mu g/m^3$-years because the PEL is sufficiently low (Friberg *et al.*, ref. in Ex. 4–27).

Veteran workers, however, may have exceeded this dose. In the past, many highly exposed workers were exposed to cadmium concentrations ranging between 40–50 $\mu g/m^3$. Five years of exposure to these levels would result in a cumulative cadmium dose ranging from 200–250 $\mu g/m^3$-years. Thus, in order to protect susceptible populations from kidney dysfunction, OSHA chose 60 months (5 years) as the past total months of exposure to trigger medical surveillance for veteran workers. This provision of the standard is consistent with OSHA's approach in the benzene and arsenic standards. (See the benzene standard 29 CFR 1910.1028 under paragraph (i)(1)(i).) In the benzene standard, veteran workers were covered by the medical surveillance provisions if they had past exposure to 10 ppm for one month. One month of exposure to 10 ppm is equivalent to a cumulative dose of 0.83 ppm-years of benzene prior to the promulgation of the new benzene standard (i.e., 10 ppm $\times$ 1/12 = 0.83 ppm-years). Since the new benzene standard allows workers to be exposed annually to 1 ppm-years of benzene, 0.83 ppm-years represents about 80% of the annual allowed cumulative dose.

In the final cadmium standard, veteran workers would not be eligible for medical surveillance unless they have been exposed in the past to cadmium for five years. If veterans were exposed, for example for five years at or above the action level, they would have been exposed to more than 12.5 $\mu g/m^3$-years (action level of 2.5 $\mu g/m^3 \times 5$ years). This cumulative dose would constitute approximately 250% of the annual cumulative cadmium dose under the new PEL and proportionately is only about three times more than allowed in the benzene standard in order for veteran workers to qualify for medical surveillance.

In the arsenic standard, veteran workers were also included in medical surveillance. Under paragraph (n)(1)(i)(B) of the arsenic standard (29 CFR 1910.1018) all employees exposed above the action level for 30 or more days per year for a total of 10 years or more were covered by medical surveillance. Thus, OSHA considers the inclusion of medical surveillance for veteran workers, who have been exposed to cadmium for five years prior to the promulgation the new cadmium standard a reasonable basis to qualify them for medical surveillance.

Dr. Friberg stated in his written testimony (Ex. 29) that there are several reports of a high prevalence of kidney dysfunction observed after an exposure that would correspond to 45 years of exposure to 10 to 20 $\mu g/m^3$:

> * * * we should make clear that to equate such exposure with a safe threshold is to me a serious and irresponsible mistake * * * a considerable prevalence of kidney dysfunction can be expected when below such concentrations * * * (Tr. 6/6/90, p. 76)

The burden is on the employer to demonstrate that an employee previously or currently exposed to cadmium does not exceed any of the triggers in paragraph (l)(1)(i) of this standard and therefore need not be provided medical surveillance. OSHA believes the employer is in the best position to carry this burden. The employer has strong economic incentives to assure that medical surveillance is not provided to any employee who does not qualify for it. The employer also is best able to gather, develop, correlate and maintain the exposure data needed to assess an employee's current exposure and exposure history.

However, OSHA recognizes that it may be difficult at times for employers to sustain the burden of proof concering employees who were exposed before the effective date of this standard. Nonetheless, where the extent of the employee's cumulative exposure is unclear, the Agency chooses to err on the side of protecting workers. Thus, if the employer is uncertain whether a particular employee has in fact been previously exposed at or above the action level for more than 60 months, and especially where the employer may have some reason to believe the employee may have been so exposed, it is OSHA's intention that the employer resolve doubts in favor of worker protection and to provide at least some medical surveillance for that employee. As a result, for example, OSHA intends that workers who were exposed for indeterminate, substantial periods prior to the effective date of this standard, and who were not regularly monitored, or for whom exposure records were not kept, be initially screened to detect potential or actual kidney disease or other cadmium-related illness. Thereafter, if medical surveillance carried out over approximately one year shows no indications of cadmium related disease or of increased risk of such disease, periodic medical

surveillance for these veteran workers can be expeditiously terminated.

Paragraph (l)(1)(ii) of this standard requires that the employer provide the examination specified in paragraph (l)(6) to workers who are required to wear a respirator because their job exposes them to cadmium levels above the PEL. The purpose of the examination is to determine the employee's capacity to wear a respirator. This requirement, which is typical of other OSHA health standards, (e.g., Lead, 29 CFR 1910.1025; Benzene, 29 CFR 1910.1028; Formaldehyde, 29 CFR 1910.1046; and Asbestos Final Standards, 29 CFR 1910.1001) is to assure the identification of employees with medical conditions that make wearing a respirator a health risk.

Paragraph (l)(1)(iii) provides that all medical examinations and procedures required by this standard be performed by or under the supervision of a licensed physician and without cost to the employee. The licensed physician is required to read and be familiar with the health effects section of appendix A, the regulatory text of this section, the protocol in appendix F, and the questionnaire of appendix D. Although, a licensed physician is the appropriate person to supervise and evaluate a medical examination, certain required elements of the exam need not be performed directly by a physician and may be performed by another, appropriately qualified person under supervision of the physician.

OSHA received comments saying that medical examinations should be performed under physician supervision (Tr. 7/18/90, p. 160). The choice of the physician, and the physician's training, are extremely important factors in the medical evaluation of workers' health (Friberg, Tr. 6/6/90). For physicians who do not have a thorough knowledge of cadmium toxicology, preventing and treating cadmium induced disease can be very difficult (Ex. 29). Therefore, OSHA has provided documentation in the appendices to familiarize physicians and other medical personnel with the toxic effects of cadmium.

The standard also requires that all examinations and procedures be performed at a reasonable time and place. It is necessary that examinations and procedures be performed at a place convenient to the employee, during the workday, and without loss of pay, in order to maximize the likelihood that employees will participate. This provision is consistent with other OSHA health standards (e.g., Asbestos, 29 CFR 1910.1001; Arsenic, 29 CFR 1910.1018).

As mentioned above, paragraph (l)(1)(iv) requires that specimens for biological monitoring be collected and handled appropriately, and that laboratories be proficient, as specified in appendix F.

Paragraph (l)(2)(i) requires the employer to provide an initial or preplacement medical examination to all employees covered by medical surveillance within 30 days after initial assignment to a job with exposure to cadmium or no later than 90 days after this standard goes into effect, whichever comes last. The purpose of the initial medical examination is to:

(1) Establish the current health status of the employee and to determine whether it is appropriate to assign the employee to jobs with cadmium exposure;

(2) Initially determine what level of medical surveillance the employer must provide to the particular employee; and

(3) Establish essential baseline data for each employee as a criterion for assessing subsequent changes in health status attributable to cadmium exposure.

The initial medical examination includes biological monitoring and a detailed medical and work history, with emphasis on past exposure to cadmium, history of organ system dysfunction relevant to cadmium exposure, and smoking history and status. OSHA has decided to rely on biological monitoring as the primary screening device for identifying employees at elevated risk of cadmium related illness. OSHA believes that biological monitoring results showing levels of cadmium in urine (CdU), Beta-2 microglobulin in urine (β_2-M), and cadmium in blood (CdB), when used together, are the best indicators of cadmium exposure and of the risk of cadmium related illness (Dr. Friberg, Tr. 6/6/90, pp. 108–109).

OSHA has chosen to rely on these three biological parameters as the main medical screening device because they are the best indicators of present exposure, past exposure, and cadmium related kidney dysfunction. Generally, monitoring CdU levels is useful and needed to determine past exposure to cadmium and body burden of cadmium among workers without kidney disease. However, monitoring CdU levels is no longer reliable after the onset of disease because the kidney spills a large amount of cadmium. Then for a time no cadmium appears in the urine even though the kidney is damaged and the cadmium burden in the kidney cortex is continuing to increase (Friberg, Ex. 144–3–C).

Monitoring levels of CdB is generally useful as an indicator of recent exposure to cadmium. Elevated levels of β_2-M are indicative of the presence or absence of an early stage kidney disease.

In choosing to rely primarily on biological monitoring for medical screening, OSHA has dropped the proposed requirement that a full medical examination be included as part of the initial medical examination, as provided in paragraph (l)(2) of the proposal (55 FR 4124). The Agency believes requiring biological monitoring of the indicators for cadmium exposure, cadmium body burden and cadmium induced kidney disease eliminates the need for a full medical examination as a screening tool. The biological indicators will be sufficient to establish the employee's baseline health status for all employees covered by medical surveillance. Given the adequacy of biological monitoring and the limited resources and the high cost of full medical examinations, the Agency believes that in the initial phase of medical surveillance, full medical examinations should only be required for employees whose biological monitoring results are abnormal as specified in paragraphs (l)(3)(i)–(iv).

Paragraph (l)(2)(iii) provides that an initial examination is not required if adequate records show that an employee has been examined in accordance with the requirements of paragraph (l)(2)(ii) within the past 12 months. This reflects a change from the proposal (55 FR 4124) in which no recent examination could be used instead of an initial examination. This provision was included because OSHA believes that requiring an initial examination so soon after an adequate prior examination is medically unnecessary and would waste scarce resources.

Paragraph (l)(3) specifies the main elements of the medical surveillance program the employer must provide to eligible employees. This program is basically incorporated in paragraph (l)(4), concerning periodic medical surveillance. The program, at first sight, may appear to be quite complex, but it is based upon a few simple, fundamental principles.

At least a minimum of medical surveillance must be provided to all workers covered under paragraph (l)(1)(i) of this standard. In addition, enhanced medical surveillance is required for workers whose initial biological monitoring results are abnormally high. At the outset, the frequency and scope of medical surveillance depends directly upon the level of initial biological monitoring results. Thereafter, it depends upon the results of any subsequent biological monitoring and medical examinations. These results, if abnormal, may increase

the required frequency and scope of medical surveillance or, if within the "normal" range, may set the frequency and scope at minimum levels.

In the medical surveillance program required by paragraph (l) of this standard, an initial distinction is drawn between workers who are, or may be currently exposed by the employer on 30 or more days per year and workers who have been exposed by the employer prior to this standard for 60 months. For workers who have, or may have been excessively exposed prior to the effective date of this standard, the purpose of medical surveillance is twofold: First, to promptly identify those among them who have abnormal monitoring results, for whom further medical surveillance is required; and second to identify those among them who have biological monitoring results that are consistently within the "normal" range. Generally, employees in the latter group are not considered to be at excess risk of cadmium induced disease and, therefore, do not need further periodic medical surveillance. Thus, for workers in medical surveillance exclusively because of past exposure to cadmium, the results of initial and follow-up biological monitoring determine not only the frequency and scope of the ensuing medical surveillance but also whether the worker will continue to be provided with periodic medical surveillance at all.

Concerning currently exposed employees covered by medical surveillance under paragraph (l)(1)(i)(A), if an employee's initial biological monitoring results are confirmed to be within the range that for purposes of this standard is considered "normal", the employer must provide the employee with the minimum level of medical surveillance, as set forth in paragraph (l)(4)(i)–(iii) of this standard. However, if the employee's initial biological monitoring results are confirmed to exceed the normal range, then the employer must provide the enhanced level of medical surveillance that is appropriate to the level of the initial results, as set forth in paragraph (l)(3)(ii)–(iii). Basically, the higher the employee's monitoring results, the more frequent and comprehensive the medical surveillance required. A summary chart and Tables that outline these provisions have been provided in appendix A.

Concerning employees whose exposure to cadmium has been, or may have been prior to the effective date of this standard, who are covered by medical surveillance exclusively under paragraph (l)(1)(i)(B), their biological monitoring results will determine whether or not they will be provided periodic medical surveillance. If the initial biological monitoring results are confirmed to be within the normal range, and if follow-up biological monitoring results required within 12 months under paragraph (l)(3)(i)(B) also are within the normal range, then under paragraph (l)(4)(v) periodic medical surveillance may be discontinued.

However: (1) If the initial biological monitoring results for such previously exposed employees are within the normal range, but their follow-up biological monitoring results, taken within 12 months, exceed the normal range, then the employer must provide annual medical examinations as specified under paragraph (l)(4)(v)(C) until all the results of biological monitoring are consistently within the normal range specified by paragraph (l)(3)(i)) or the examining physician determines in a written medical opinion that further medical surveillance is not needed to protect the employee's health. Or (2) if the initial biological monitoring results for such previously exposed employees exceeds the normal range, then these employees shall be provided medical surveillance under the same regimen as currently exposed employees ((l)(3)(ii)–(iv)) unless and until the employee's levels of CdU, CdB, and β_2-M are all within the normal range on two consecutive tests over a period of no less than 12 months. At that point, as specified by paragraph (l)(4)(v)(B), the employer may terminate periodic medical surveillance for the employee.

In establishing this medical surveillance program, OSHA had to make a number of fundamental determinations. First, the Agency had to decide which biological parameters would be used to detect excess cadmium exposure and potential excess risk of cadmium induced disease. Second, OSHA had to assess the range that for the purposes of this standard will be considered to be the "normal" range for each of these parameters. Third, the Agency had to decide how to trigger enhanced medical surveillance. Fourth, OSHA had to decide when and how often to require biological monitoring, full medical examinations, and other related actions to be provided by the employer. Fifth, OSHA had to decide how the medical surveillance program should be applied to employees previously exposed to cadmium who no longer are exposed. Sixth, the Agency had to decide at what levels of the biological parameters, if any, workers need to be removed from exposure to cadmium at or above the action level and at what levels, if any, these workers could be returned to their normal cadmium exposed jobs. All of these decisions are based upon the health effects data in the record, including epidemiological and animal studies of cadmium induced disease and histopathological data, which are thoroughly summarized and analyzed in the Health Effects section of this preamble (Section V).

Concerning the choice of biological parameters, it is universally recognized that the best measures of cadmium exposure are measurements of cadmium in biological fluids, especially urine and blood. Of the two, CdU is conventionally used to determine body burden of cadmium in workers without kidney disease. CdB is conventionally used to monitor for recent exposure to cadmium. In addition, levels of CdU and CdB historically have been used by industry as triggers that require medical action (Ex. 14–6) and to evaluate the likelihood that workers will develop kidney disease (Thun et al., Ex. L–140–50; WHO, Ex. 8–674; ACGIH, Exs. 8–667; L–140–51).

The third biological parameter upon which OSHA relies for medical surveillance is Beta 2 microglobulin in urine (β_2-M), a low molecular weight protein. Excess β_2-M has been widely accepted by physicians, scientists, and industry experts, as a reliable indicator of functional damage to the proximal tubule of the kidney (Exs. 8–447; 144–3–C; 4–47; L–140–45; 19–43–A). Excess β_2-M is found when proximal tubules can no longer reabsorb this protein and essential elements in a normal manner. Given the fact that the employees monitored for β_2-M levels under this standard are in fact exposed to not inconsiderable amounts of cadmium, abnormal β_2-M levels in these employees are more likely to be related to excessive cadmium exposure than to other causes. (See Section V, Health Effects). Age alone cannot account for the excess of β_2-M observed in cadmium-exposed workers (Exs. 8–642; 8–668–B; L–140–45). Used in conjunction with biological test results that indicate the presence of abnormally high levels of CdU and CdB, the finding of excess β_2-M can establish for an examining physician that any existing tubular proteinuria is probably cadmium-related (Tr. 6/6/90, pp. 108–109, 135).

OSHA chose to rely on β_2-M as an early indicator of kidney disease because the Agency concluded that β_2-M is the most thoroughly studied of the various indicators that might be used. Although there may be some problems associated with handling β_2-M (e.g., the pH of the urine must be kept at or above

6.0; Exs. 8–086; 8–447; L–140–1); and with accurately measuring and characterizing the protein in the sample (Phadebas, Ex. L–140–1), most occupational, epidemiological studies of kidney disease among cadmium exposed workers have relied upon β_2-M measurements as the early marker of nephrotoxicity (Exs. 8–086; L–140–1; 4–47; 4–28; 4–27; L–140–45; L–140–50). Moreover, with few exceptions, the medical experts who testified at the OSHA hearings and provided comments in the cadmium rulemaking agreed that, all things considered, β_2-M currently is the best single, non-invasive test for screening for cadmium induced nephrotoxicity (Exs. 19–14; 55; 4–47; 4–28; 4–27; L–140–50; 8–670).

OSHA specifically considered alternative markers, such as retinol binding protein (RBP), metallothionein, and N-acetyl d glucosaminidase (NAG) in urine, and decided that experience with these alternatives was too limited and their biological significance and predictive value was less certain than β_2-M (Ex. 30). For example, "normal" levels for retinol binding protein were not clearly established in the record and do not appear to have been clearly established in the general medical literature. (See NIOSH, HHE Ex. 128; Mason, Ex. 8–669–A; Health Effects, Section V—kidney.)

Having chosen the biological parameters to be measured, OSHA then had to evaluate the record evidence to determine background levels of each parameter so that the Agency could determine what levels should be considered excessive. With regard to CdU, very low levels of cadmium are found in body fluids of non-occupationally exposed general populations, even though cadmium occurs in the general environment and can be taken into the body through the consumption of cadmium-containing food or by smoking cigarettes. It has been shown that urinary concentrations of cadmium minimally increase with age (Exs. 8–642; 8–86A).

In 1983, Kowal and Zirkes reported the concentration of CdU samples collected from almost 1,000 persons (males and females, CdU standardized to specific gravity) from nine states in the U.S. (Ex. 8–642). Ninety-five percent of the population had CdU levels less than 2.8 μg/g Cr, which is lower than the cadmium in urine trigger in this standard for enhanced medical surveillance. The overall geometric mean level of CdU for males was 0.55 μg/g Cr and for females was 0.78 μg/g Cr (Ex. 8–642). In other studies, median levels of CdU are about 0.5 to 1 μg/liter at the age of 70 (Exs. 8–068–B, L–140–31).

It was observed that the urinary excretion of cadmium was also influenced by smoking habits. Smokers have higher average levels of CdU compared to non-smokers of the same age, (Ex. 8–86–B) but CdU levels are not influenced by smoking to the same extent as cadmium blood levels. In a limited study of CdU levels among the U.S. population, among current and former smokers, arithmetic mean CdU levels ranged from 1.0 to 1.5 μg/1 urine for females and males, respectively (Ex. 8–86–B). While this study indicated some smokers could have CdU levels of 3.4 μg/liter urine, this is an upper range that has not been standardized to control for diuresis, i.e., standardized to grams of creatinine.

These levels are generally lower than the lowest CdU trigger levels included in the proposed cadmium standard (55 FR 4125, Feb. 6, 1990).

Several industry spokespersons held the opinion that a trigger level of 10 μg/g Cr urine (or 10 μg/l urine) would protect workers from unnecessary risk of cadmium-associated renal dysfunction (Exs. 19–30; 19–43; 8–201; 19–43; 120). However, as discussed below and in detail elsewhere in the preamble, OSHA's understanding of the relevant literature and risk assessments indicates that this is incorrect (Exs. 8–447; 19–14).

Dr. Tyner, Medical Director of Gates Energy Products, a major nickel-cadmium battery production facility, indicated that 10 μg/g Cr in the urine would be a practical and safe trigger for medical action (Ex. 19–2). Dr. Kazantzis who testified for the Cadmium Council stated that levels must be kept much lower than 10 μg Cd/g Cr (Tr. 6/8/90, pp. 150–200; Ex. 19–43–A).

The Cadmium Council submitted comments in support of medical action whenever CdU levels reach 10 μg/g Cr (Ex. 19–43) based on a study by Buchet *et al.* in 1980 (Ex. 8–201). However, OSHA notes that in the study by Buchet, the prevalence of kidney dysfunction among exposed workers whose CdU levels were above 10 μg Cd/g Cr was 15% (Ex. 8–201). In the total group, the prevalence of kidney dysfunction among exposed workers (18.2%) was statistically significantly elevated ($p < 0.025$) above the prevalence of kidney dysfunction among controls (6.8%).

Richard Bidstrup, Counsel for SCM Chemicals, Inc., submitted comments on SCM's behalf (Ex. 19–42A) to the effect that measuring the level of CdU is helpful and that if urinary cadmium is greater than 10 μg/l (with specific gravity adjusted to 1.020) or low molecular weight protein is greater than 300 μg/1, urine analysis should be conducted more often until levels are below these thresholds.

Leading world experts in the field of cadmium-induced kidney dysfunction, such as Drs. Thun, Friberg, and Elinder, were of the opinion that CdU levels had to be kept as far below 10 μg Cd/g Cr as possible in order to protect most workers from kidney dysfunction. Their opinions were based upon their own studies and their review of the medical literature (Ex. L–140–50).

In 1991, the American Conference of Governmental Industrial Hygienists (ACGIH) recommended lowering its biological exposures index (BEI) for CdU to 5 μg Cd/g Cr (L–140–51).

After testifying at the hearings and in response to a written request by OSHA for further information and comments on medical surveillance, David Volkman, of Big River Zinc, stated (Ex. 84) that medical surveillance monitoring should focus on micrograms of cadmium per gram creatinine (μg Cd/g Cr) and B_2-M. He stated that if a trigger level was set for medical action, 5 μg Cd/g Cr would be adequate (Ex. 46).

Dr. Bosken, a physician who provided comments for the Public Citizen Health Research Group and the International Chemical Worker's Union (HRG/ICWU), stated that HRG/ICWU supports a lower level of urinary cadmium (3 μg/g Cr) than that proposed by OSHA as the level to initiate a review of the employee's work practices, respirator use, and engineering controls (Ex. 123). The HRG/ICWU support 5 μg/g Cr as a trigger level for medical removal, noting that, at this level, "* * * a substantial amount of renal disease [is] to be expected in workers * * * [Ex. 123)" Thus, in summary, despite some differences in opinions, there is broad agreement that CdU levels must be well below 10 μg/g Cr. In addition, broad-based population studies show that CdU concentrations for the general population not occupationally exposed to cadmium average less than 1 μg/L and that 95 percent of individuals not occupationally exposed, including both smokers and non-smokers, exhibit levels of CdU less than 3 μg/g Cr. (See Appendix F).

OSHA, therefore, chose the level of CdU >3 μg Cd/g Cr as its lowest CdU trigger for enhancing medical surveillance. That level represents a clear cutoff point above which it may be assumed that workplace exposure to cadmium is affecting the biological monitoring test result. Dr. Elinder testified that while the medical

surveillance protocol for cadmium workers suggested by OSHA is more strict in comparison to the current Swedish protocol, it is better (Ex. 55). As Dr. Elinder stated in his testimony, dose-response analyses in the medical literature makes it clear that if CdU is allowed to increase above 5 μg/l about five percent of workers are likely to get cadmium induced tubular dysfunction.

In contrast to CdU levels, levels of cadmium in blood (CdB) reflect recent exposure to cadmium and do not appear to be significantly affected by the onset of kidney damage. Cadmium levels in blood are affected to some small degree by age, diet, and sex and to a larger degree by smoking habits (Jarup et al., Ex. 8–661). In studies of occupationally exposed workers it was found that age is not an important confounder (Ex. 8–661).

In 1988, Drs. Friberg and Elinder evaluated median CdB levels in males and females in different smoking categories. Ninety percent of female and male non-smokers had CdB levels less than 0.5 and 0.3 μg/liter whole blood (lwb), respectively. Ninety percent of female and male former-smokers had CdB levels below 0.8 and 0.9, respectively. Current smokers were divided into categories based upon the number of cigarettes smoked daily. Ninety percent of females and males who smoked less than a pack a day had CdB levels less than 2.0 and 2.5, respectively, while 90 percent of females and males who smoked more than half but less than a pack a day had CdB levels less than 3.0 and 3.7, respectively. Among female and male smokers who smoked more than a pack a day, 90 percent had CdB levels less than 3.5 and 4.5, respectively (Ex. 8–740).

A number of other studies provide data on the CdB concentration of non-occupationally exposed persons and indicate that non-smokers in countries where dietary cadmium intake is 10 to 20 μg/day have a median concentration in whole blood in the order of 0.4 to 1.0 μg/l, whereas smokers have a median concentration of 1.4 to 4.5 μg/l (Ex. 8–086–B). In the U.S.A. mean levels of CdB of non-smokers ranged from 0.4 μg Cd/lwb to 0.8 μg Cd/lwb. Mean levels of CdB among U.S. smokers were 0.9 in former smokers and ranged from 1.0 μg Cd/lwb to 3.4 μg Cd/lwb in current smokers (Ex. 8–086–B).

In 1980, for example, the World Health Organization, United Nations Environment Program (WHO/UNEP) launched a global biological monitoring program for the assessment of human exposure to heavy metals. Ten cities were included in the program. The program was initiated to enable valid comparisons of CdB levels for different countries. Until then, there were no accurate studies available and the normal concentration of CdB was not yet known (Ex. 8–86–B). In the WHO program, blood samples were obtained from similar groups of teacher-volunteers in cities from each participating country, including Baltimore, the only U.S. city for which such data were available. Different analytical techniques were used in different countries. Volunteers were divided into smokers and non-smokers.

In Baltimore, according to the WHO/UNEP study, the upper 90th percentile of CdB levels for non-smokers was about 1.0 μg Cd/lwb while the upper 90th percentile of CdB levels of smokers was about 2.6 μg Cd/lwb. A very high level of CdB was observed among smokers in Mexico City, i.e., the upper 90th percentile of CdB levels of smokers was 8 μg/l. However, the tobacco products, smoking habits of individuals, and environmental pollution problems in Mexico City are not readily comparable with those in Baltimore (Ex. 8–86–B).

In the final cadmium standard, OSHA has established a "normal" level of cadmium in blood as levels below 5 μg/lwb. This is based on OSHA's review of studies in which 95 percent of non-occupationally exposed worker populations which included both smokers and non-smokers exhibited CdB levels below 5 μg/lwb. (See appendix F.) By contrast, in studies that provided sufficient data on CdB levels among occupationally exposed workers who had greater than nominal levels of cadmium exposure, 95 percent of workers had CdB levels greater than 5 μg/lwb. (See Health Effects Section; appendix F.)

Several industry spokespersons held the opinion that a trigger level of 10 μg/lwb would protect workers from unnecessary risk of cadmium-associated renal dysfunction (Exs. 19–30; 19–43; 8–201; 19–43; 120). However, other participants in the rulemaking held the belief that 10 μg Cd/lwb is too high.

In 1991, the ACGIH recommended lowering its biological exposures indices (BEI) from 10 μg/lwb to 5 μg Cd/lwb (L–140–51). ACGIH justified this lowering of the BEI for CdB in its Notice of Intended Changes (Ex. L–140–51). ACGIH stated that recent studies indicate a higher incidence of renal dysfunction than previously estimated among workers with cumulative CdB concentration below 10 μg/lwb. The new BEI is intended to prevent the potential for increased urinary excretion of markers of renal dysfunction in almost all workers.

Dr. Elinder stated that from the dose-response analysis presented by Jarup, 1988, it is clear that if cadmium exposure continues, producing a cadmium concentration in workers' blood exceeding five micrograms per liter, a small percentage of the exposed workers will develop β_2-microglobulinuria (Ex. 55).

In summary, OSHA chose greater than 5 μg/lwb as the lowest CdB trigger for enhancing medical surveillance, because that level represents a clear cutoff point between exposed and non-exposed population. (See appendix F.)

OSHA received many comments regarding the use of β_2-M as a marker of kidney function. Dr. Lauwerys, the author of several studies on cadmium-induced renal effects and the guide for physicians, Health Maintenance of Workers Exposed to Cadmium published by the Cadmium Council (Ex. 8–447), stated that β_2-microglobulinuria occurs if levels of β_2-M exceed 200–300 μg/gram creatinine (g Cr) (Ex. 8–447). Other world experts who testified during the hearings agreed with the normal levels given by Dr. Lauwerys, standardized to grams of creatinine (g Cr) to correct for diuresis. Dr. Goyer testified that in the general population normal levels of β_2-M are less than 300 μ/g Cr (Tr. 6/6/90, p. 135). Dr. Friberg testified that levels of β_2-M above 200 μg/g Cr are rare in a population with "normal" kidney function (Ex. 144–3–C).

Although individual variations are great, most people's levels, are very low. Kowal et al. (Ex. 8–642) evaluated the levels of β_2-M in 1,000 non-occupationally exposed populations in the United States. The average level in the oldest group studied, aged over 70 years was 107 μg β_2-M/l urine. This was only marginally higher than in the age group 20–70, in which the average levels were 69 to 84 μg β_2-M/l urine (Referenced in Ex. 8–068–B).

Dr. Elinder, chairman of the Department of Nephrology at the Karolinska Institute, testified that the normal concentration of β_2-M has been well documented (Evrin and Wibell, 1972; Kjellstrom et al, 1977a; Elinder et al, 1978, 1983; Buchet et al, 1980; Jawaid et al, 1983; Kowal and Zirkes, 1983 referenced in Elinder, Ex. L–140–45). Elinder stated that the upper 95 or 97.5 percentile for the urinary excretion of β_2-M among persons without tubular dysfunction is below 300 μg/g Cr (Kjellstrom et al, 1977a; Buchet et al, 1980; Kowal and Zirkes, 1983). Elinder defined levels of β_2-M above 300 μg/g Cr as "slight" proteinuria (Ex. L–140–45).

According to Kjellstrom (Ex. 4–47), the upper 95 percent tolerance limit reported

in his paper (290 μg/l urine) was considered to be representative for large groups of subjects. According to Falck, the values obtained from the controls in his study were close to the levels that would be expected from unexposed people (Falck, Ex. 4–28). In the Falck study, normal kidney function was thus established at β_2-M less than 400 μg/l urine for 24 hour samples.

In six of the seven major epidemiological studies reviewed by OSHA in Section V—Health Effects, β_2-M was the marker of kidney dysfunction chosen by the authors. The "normal" levels of β_2-M was established based on samples taken from non-exposed controls and was about 300 μg/g Cr or less in all but two of the seven studies (Thun, Ex. 8–670; Falck, Ex. 4–28). (See Section VI—Quantitative Risk Assessment). In the two studies cited by the Cadmium Council, Buchet regarded β_2-M levels greater than 200 μg/g Cr as abnormal and Toffoletto regarded β_2-M levels greater than 260 μg/l urine as abnormal (Exs. 19–43–A, 8–201).

Furthermore, in studies of exposed workers, the geometric mean levels of β_2-M among workers without renal dysfunction, including both smokers and non-smokers, were lower than 295 μg/g Cr (Kjellstrom, Ex. 4–47; Roels et al., 1991, Ex. 149; Miksche et al., 1981, Ex. 12–10–E; and Thun, Ex. 8–670; see also appendix F). The fact that there is no clear statistical cutoff point between occupationally exposed and non-exposed individuals should not be surprising. Significantly elevated β_2-M levels are expected to correspond to the onset of kidney dysfunction. Only a certain number of cadmium exposed workers in the medical literature are likely to have developed kidney dysfunction, and this is likely to occur primarily among workers with high past exposures to cadmium. Consequently, the range of levels of β_2-M observed in most of occupationally exposed individuals are likely to be similar to the "normal" range observed among the unexposed. Despite the absence of a clear cutoff point between cadmium-exposed workers and non-exposed populations, such as with CdU and CdB, the range of levels of β_2-M that is considered abnormal is rather well established and generally agreed upon (Exs. 144–3–C, L–140–45).

The Agency recognizes that, although biological values lie on a single continuum with an infinite number of points between health and illness (Exs. 19–2; 19–14; 19–33; 19–34; 19–40; 19–42; 19–43; 77; 82; 84; 101; 106; 107; 120; and 123), OSHA had to select particular levels to indicate greater and lesser risk of cadmium-induced renal disease and to trigger appropriate medical responses. OSHA believes that its choice of triggers for enhanced medical surveillance based upon β_2-M levels represent cutpoints that are well established in the medical literature and widely used in practice.

Three issues were raised during the rulemaking regarding the use of β_2-M as a marker of kidney dysfunction and material impairment. First, there are other causes of elevated levels of β_2-M, not related to cadmium exposures (Ex. 19–14), and there are factors that can cause β_2-M to degrade so that low levels might be found even in workers with tubular dysfunction. For example, regarding the degradation of β_2-M, workers with acidic urine with pH<6 (Exs. L–140–1, 8–447) might have β_2-M levels that are within the "normal" range, when in fact, kidney dysfunction has occurred (Ex. 8–86–B; Friberg, Tr. 6/6/90, pp. 108–109). Second, there is debate over the pathological significance of proteinuria. Finally, detection of β_2-M at low levels is considered by some to be difficult. The issue of the levels of detection of β_2-M and proper handling of urine samples to prevent degradation of β_2-M has been addressed under "Specimen collection and preparation" procedures developed by Phadebas (Ex. L–140–1) and has also been addressed by OSHA in the section on specimen handling and lab standardization (See appendix F).

Regarding the first issue, the specificity of β_2-M as a marker of cadmium-induced kidney dysfunction is well established. The only other renal toxins or medical conditions which lead to elevated levels of β_2-M are anti-cancer drugs, aminoglycosides (antibacterial antibiotics such as streptomycin), anti-inflammatory compounds, myeloma, flu, and upper respiratory infections (Dr. Friberg, Tr. 6/6/90, pp. 108–109; Ex. L–140–1). As Dr. Thun stated:

> Low molecular weight proteinuria * * * does occur from other conditions but it's uncommon * * * part of the reason why the (kidney) data are so consistent is that the studies use a rather specific marker of cadmium renal effects * * *. (Tr. 6/7/90, p. 174)

Given the specificity of β_2-M, it is unlikely that other renal toxins would result in elevated levels of β_2-M (Exs. 4–47; 4–28; 4–27; L–140–50; and 8–670).

While a limited number of other non-cadmium related illnesses or factors may result in elevated β_2-M levels (Ex. 29), OSHA allows physician discretion as to the type of actions that must be taken when levels of β_2-M are only slightly elevated. For example, under paragraphs (l)(3)(ii)–(iv), physicians must provide a medical examination within 90 days if biological test results are "abnormal". This allows the physician time to evaluate and to rule out other etiologies. Moreover, medical removal for elevated levels of β_2-M is mandatory only when β_2-M is significantly elevated and either CdU or CdB also is elevated, specifically indicating excess cadmium exposure. β_2-M can also be degraded by bacterial infections, and in urine with pH less than 6, levels of β_2-M decrease. Bacterial infections and low pH levels occur normally in a proportion of the population. β_2-M can be degraded by low pH and bacterial infections while the β_2-M is stored in the bladder or urinary tract, and while urine is stored in sample collection bottles, leading to measured concentrations which are erroneously low (Ex. 8–086–B).

However, the bacterial infections are often accompanied by symptoms which can be diagnosed and treated. The acidity of the urine can be corrected *in vivo* by consumption of sodium bicarbonate and can be raised in the urine collection bottle by addition of an alkaline buffer. (See Ex. L–140–1, and appendix F.)

Regarding the remaining issue, pathological significance, it is clear from the testimony of world experts that elevated levels of β_2-M should be considered to be material impairment. Dr. Friberg testified that:

> * * * the beta-2 microglobulin proteinuria * * * should be regarded as an adverse effect * * * predictive of an exacerbation of the age related decline of the glomerular filtration rate * * * the proteinuria in cadmium poisoning is irreversible and is predictive of more severe effects even if the worker is removed from further cadmium exposure * * *. It is true that an increased excretion of low molecular weight proteins can be a very early indicator of kidney dysfunction. That's not immediately of the same clinical importance as an overt renal disease. Nevertheless, it is irreversible and the beginning of a process which has a high probability to lead to a progressive disease, a decrease in the glomerular filtration rate which clearly is a serious effect that easily may lead to overt disease. When discussing the kidney damage from cadmium, it is important that we make it clear that we are talking about serious, but often insidious effects on vital organs. The kidney has a considerable reserve capacity but once this is consumed symptoms may appear in swift succession and the condition of the patient then deteriorates rapidly, and the infection or other, in itself trivial disorder, could be a triggering mechanism. It is our responsibility to prevent this situation even among a small proportion of workers. (Tr. 6/6/90, pp. 73, 82, 86)

According to Dr. Lauwerys:

When increased excretion of proteins found (* * * β_2-microglobulinuria exceeding 200–300 μg/g Cr) and confirmed by a subsequent examination a few weeks later, it is recommended to perform a more extensive investigation of kidney function for evaluating the intensity of the biological disturbance * * *. Although the discovery of significantly increased excretion of proteins does not necessarily mean that renal insufficiency will occur, it is wise to remove definitively from cadmium exposure workers presenting any persistent signs of renal dysfunction" (Ex. 8–447).

Prolonged exposure to cadmium may lead to glomerular proteinuria, glucosuria, aminoaciduria, phosphaturia, and hypercalciuria (Exs; 8–86–B; 4–28; 14–18, p. 157) and kidney stones (Tr. 6/6/90, p. 106). These conditions are indicated by excess urinary amino acids, glucose, phosphate, or calcium, respectively. Each of these elements are essential to life, and under normal conditions their excretion is regulated by the kidney. Once low molecular weight proteinuria has developed, however, these elements may dissipate from the body. Loss of glomerular function may also occur, indicated by a decrease in the glomerular filtration rate and an increase in serum creatinine. Severe cadmium-induced renal damage may develop into chronic renal failure and uremia at which point some form of dialysis or kidney operation will be needed (Ex. 55).

Kidney dysfunction persists for years even after cessation of exposure. Loss of calcium and phosphorus may contribute to the increased risk of kidney stones observed in cadmium exposed workers (Ex. 4–29). Dr. Friberg testified that, in his opinion, kidney stones are a serious sequelae to cadmium-induced renal dysfunction. He and others originally thought that the increased prevalence of kidney stones observed in his studies of cadmium-exposed workers was confined to Sweden (Ex. 29). But later, the increased prevalence of kidney stones was observed in England, and in the U.S. the presence of kidney stones is a sign of a more generalized disorder of the mineral metabolism in the kidney (Tr. 6/6/90, p. 106).

Others held a different opinion about the prevalence of kidney stones among cadmium-exposed workers. For example, Dr. Spang stated that kidney stones are common in the general population of Sweden (20% in men and about 5% in women), and although he observed cases of kidney stones among cadmium-exposed workers, he did not know if the prevalence was different from that of the general population (Exs. 80 and 81).

Cadmium may also precipitate clinical osteopathy in persons with inadequate dietary calcium intake (Ex. L–140–50). Diets low in vitamin D and calcium may be a contributing factor to sequelae subsequent to cadmium-induced renal dysfunction.

There are at least two hypothesized scenarios by which cadmium-induced tubular proteinuria can cause other adverse health effects (Ex. 8–086). Under the first of these, cadmium-associated tubular dysfunction causes damage to the production of biologically active metabolites such as vitamin D which occurs primarily in the kidney. Under the second scenario, cadmium may cause atrophy of the gastrointestinal tract thereby reducing its ability to absorb essential elements such as calcium and phosphates. Both would lead to loss of essential elements and poor absorption of other minerals to replace those lost.

The gravity of cadmium-induced renal damage is compounded by the fact that there is no simple medical treatment such as chelation to prevent or reduce the accumulation of cadmium in the kidney without substantial risk (Tr. 6/6/90; p. 105). In contrast to other heavy metals, current chelation therapy does not reduce the body burden of cadmium without producing significant renal damage. When chelated cadmium arrives in the kidneys where the cadmium may still be toxic to renal cells. Thus, large amounts of cadmium may move from the liver or muscle storage sites, overwhelm the kidney's usual attempts to store cadmium in a less toxic form, and accelerate deterioration of renal function.

Regarding the pathological significance of proteinuria, OSHA believes that the loss of function of the proximal tubules with tubular proteinuria, as indicated by elevated levels of β_2-M, itself signifies damage that constitutes material impairment of health. OSHA acknowledges that the significance of the dysfunction as evidenced by elevated levels of β_2-M is controversial. Part of this controversy arises from the fact that a worker with elevated levels of β_2-M may not experience any symptoms.

Dr. Goyer testified that the confusion over the interpretation of pathological significance of elevated levels of β_2-M stems from the fact that injury to the tubuli ultimately affects the functioning of the glomerulus. According to Dr. Goyer, the confusion lies in part in the fact that cadmium's earliest effect is primarily in the tubule, while kidney function is usually measured in the glomerulus (Tr. 6/6/90, pp. 126–127).

OSHA believes that this confusion results from two misunderstandings. First, tubular proteinuria measured in micrograms per gram creatinine (μg/g Cr). Total proteins are measured in milligrams per gram creatinine in urine. Measuring total proteins is not useful for measuring the presence of tubular proteinuria. As Dr. Lauwerys stated in his guide to physicians:

When increased excretion of protein is found (total protein exceeding 250–350 mg/g creatinine, or beta 2 microglobulinuria exceeding 200–300 μg/g creatinine] * * * it is recommended to perform a more extensive investigation of kidney function for evaluating the intensity of the biological disturbances * * * (Ex. 8–447)."

Cadmium-related tubular damage usually precedes other kidney damage, but cadmium can cause other types of kidney damage, e.g., glomerular damage, at the same time as tubular damage (Ex. 4–50; Ex. 55). Once tubular proteinuria has developed, there is a greater likelihood that further damage to the kidney will result.

Second, leading world experts on cadmium-associated kidney dysfunction have stated that workers with tubular proteinuria will have a portion of the kidney's functional capacity compromised. This may not at first be manifested as "symptoms," because the kidney has a certain amount of functional reserve. However, the remaining functional portion of the kidney is needed at various times throughout one's life to deal with conditions or other illnesses that are likely to occur. If this reserve is reduced the remaining functional capacity of the kidney may rapidly succumb to a number of otherwise benign conditions. According to Dr. Elinder, Chairman of the Department of Nephrology at the Karolinska Institute in Stockholm, Sweden, workers with tubular proteinuria frequently deteriorate, with a significant decrease in renal function. Occasionally, severe cadmium-induced renal damage has progressed to become chronic renal failure and uremia (Ex. 55). At very low levels of β_2-M, however, a physician can determine that damage is occurring before it is "overt" illness that results in severe symptoms.

According to Dr. Goyer, Chairperson of the World Health Organization's Task Force on Cadmium, in his testimony at OSHA's hearing, fifty percent of workers with elevated levels of beta-2 microglobulin between 500–1,000 μg/g Cr will never revert to normal kidney function (Ex. 30). According to Dr. Friberg, Professor Emeritus, Karolinska Institute, this is because the tubules

contain lesions that can be observed in histopathology examinations (Ex. 29).

While most physicians would agree that glomerular effects and loss of GFR must be taken more seriously than a slight elevation in β_2-M, the finding of elevated levels of low molecular weight protein in the urine by itself indicates kidney dysfunction in the tubule (Ex. 8–447).

As Dr. Friberg stated in his testimony, each part of the nephron is dependent on every other part of the nephron. It is his expectation that if one part of the nephron suffers damage it is more likely that another part will suffer damage (Tr. 6/6/90, pp. 107–108). Ultimately then, cadmium-related tubular effects will be manifested as an effect on the function of the glomeruli, either subsequently to or in association with the onset of tubular proteinuria.

Because of the functional reserve of the kidney, the adaptive increase in a single nephron's glomerular filtration rate, after total or partial loss of other damaged nephrons, tends to obscure injury until a considerable amount of the functional elements of the kidney, the parenchyma, is irreversibly lost. This implies that under normal conditions, the basal GFR is submaximal. If as has been suggested, glomerular balance is very tightly maintained, reduction of tubular function may have repercussions on the glomerular level (Ex. 149). Early changes in glomerular function are not necessarily detectable by the measurement of basal GFR, but such changes may have a significant impact on health (Ex. 149). In a study by Roels (Ex. 149) it was found that a renal cadmium burden that had not yet caused microproteinuria did not impair the filtration reserve capacity of the kidney, but the age related decline of the baseline and maximal GFR is exacerbated in the presence of cadmium induced microproteinuria.

Not all participants in the rulemaking agreed that elevated levels of β_2-M signified damage that constitutes material impairment of health. Mr. Ken Storm, Senior Industrial Hygiene Specialist with Monsanto, stated that tubular proteinuria may result from a biochemical lesion of no clinical significance (Ex. 19–14).

Dr. Bond, medical consultant to SCM, testified that:

> * * * no histological abnormalities [are] seen in the proximal tubules * * * when there has been modest increase in urinary B2MG and Cd * * * [people with] * * * mild to moderate increases in urinary B2MG and Cd do not progress to renal failure if there are no other causes present such as infection, diabetes, etc. [Ex. 77]"

Dr. Kazantzis testified that in his opinion, tubular proteinuria alone is not accompanied by any specific histological change and that its pathological significance is unclear. Dr. Friberg, however, stated:

> It should be emphasized that tubular proteinuria may be accompanied by specific histological changes. Sometimes such changes have been reported before the functional changes. There are abundant data from animal studies showing early histological changes (Ref. by Kjellstrom, 1986, p. 38–43). Experiments from humans are more limited as only a small number of autopsies or biopsies are available. To the extent available, histologic changes were seen first of all in the proximal tubules (Ref. by Kjellstrom, 1986, p. 50–53). (Ex. 29).

Morphological changes are those that pertain to the form or structure of the organ. Histological changes are those that pertain to the minute structure and composition of the organ tissue. Twenty-three workers were evaluated for whom autopsy or biopsy data on morphological changes in the kidney were available (referenced in Dr. Friberg's written testimony). Of these, 18 workers had proteinuria. Of the 18 workers with proteinuria, all but three had morphological changes in their kidneys. There were no cases of workers with morphological changes without proteinuria (Ex. 144–3, p. 53). In five of the autopsy reports, the morphological changes in the kidneys were mainly confined to the proximal tubules, whereas the glomeruli were less affected.

These results demonstrate that functional changes in the kidney can occur before the microscopic structure of the kidney is severely damaged. The human data on pathological changes are limited, however, and animal data show that in some studies, morphological changes in the tubules emerge before measurable proteinuria (Ex. 8–086). In the absence of a better test, however, it appears that the use of proteinuria as a screening tool for morphological changes in the kidney will identify all cases of workers with histological or morphological changes in kidney tissue as well as identifying those with only functional changes that affect the kidney's ability to filter (Ex. 8–086 B).

These results show that elevated levels of β_2–M may indicate that kidney lesions of clinical significance have already occurred (Ex. 19–14). While a worker with elevated levels of β_2–M may not manifest any overt symptoms of illness, nonetheless, the tubuli and glomeruli have lesions that compromise the functioning of the kidney as a filtration mechanism. Any other minor kidney trauma may progress rapidly to serious kidney damage.

According to the American Conference of Governmental Industrial Hygienists (ACGIH):

> Persons excreting 290 $\mu g/L\beta_2$-microglobulin are not disabled: indeed they will not experience any symptoms. However, the lesion (from tubular proteinuria) is irreversible and represents a permanent loss of functional reserve. An infection or other condition which compromises renal function, but which would not normally lead to serious illness, could overwhelm the remaining kidney capacity. (Ex. 8–644)

While Dr. Kazantzis testified that renal stone formation has been rare in cadmium workers in recent years (Ex. 19–43A), and he went on to say that in a:

> * * * small proportion of long-term heavily exposed cadmium workers, tubular proteinuria has been followed by renal glycosuria, abnormal aminoaciduria, phosphaturia, and hypercalcuria. (Exs. 80 and 81)

Dr. Kazantzis continued that progressive decline in renal function is a slow process in workers with cadmium-induced nephropathy and that this decline is unlikely to progress to an increased mortality from chronic renal disease. In support of his opinion, he cited his study (Kazantzis and Armstrong 1982; Ex. 8–603) in which approximately 7000 cadmium-exposed workers with more than one year of cadmium exposure between 1942 and 1970 were followed up to 1979 (Ex. 8–684). He found an SMR of 65 for all deaths coded as nephritis and nephrosis; the five year update showed an SMR of 85. One worker classified as being in the "ever high" exposure subgroup died from nephritis and nephrosis.

Dr. Elinder indicated, however, that most workers in Dr. Kazantzis' study had such low cadmium exposures that cadmium-associated illnesses would not be induced (Ex. 4–25). By combining 199 workers with high exposures into a group with over 6000 workers with low exposures into one group, the power of the study to find an effect was reduced. Increased mortality from chronic nephritis and nephrosis has been observed in Swedish battery workers (Exs. 4–68 and 8–740). The difference between expected and observed deaths in the Kazantzis study may well be due to local differences in recording certain types of information on death certificates.

Three other epidemiological studies of cadmium exposed workers have shown increased mortality from kidney diseases, genito-urinary tract diseases, or kidney cancer. Thun observed an elevated SMR for genito-urinary cancer

(SMR=135, Obs=6) in his total cohort (Ex. 4–67); Dr. Elinder (Ex. 4–25) reported an elevated SMR for genito-urinary diseases in his total cohort (SMR=300, Obs=3.0); and Holden *et al.* (Ex.4–39) observed an elevated SMR for genito-urinary cancer in his total cohort (SMR=122, Obs=4.0). Because the number of excess cases in each study is too small to make these findings statistically meaningful, the relationship between cadmium exposure and risk of death from kidney dysfunction is not clear. These three mortality studies, however, provide consistent evidence of excesses of kidney illnesses among cadmium-exposed workers. This suggests the possibility that, at least in some cases, cadmium-induced kidney dysfunction may be associated with excess death.

Death from nephritis, nephrosis or end-stage renal disease is rare. Accurate death rates from kidney disease are difficult to ascertain, in part because such illnesses are uncommon and in part, because they are dramatically underreported by at least 50% (personal communication 4/30/92, National Institute of Diabetic, Digestive and Kidney Diseases). Dr. Thun indicated that impaired renal function is frequently underreported on death certificates even when the disease is sufficiently severe to require chronic hemodialysis (Modan referenced in Thun; Ex. 4–68). Under-reporting results because deaths from these diseases are coded as deaths due to complications arising from the treatment of these diseases or from sequelae to these diseases such as heart attack, stroke or diabetes.

Treatments for severe kidney diseases such as dialysis or a kidney transplant are available for those who can afford them. As Dr. Friberg indicated, several of his own patients had cadmium-induced uremia and died. If they had had the opportunity for dialysis or renal transplant, they could have been saved (Ex. 29). Such treatments, however, are grave, especially considering that early forms of kidney dysfunctions can be detected and more serious diseases can be prevented.

An additional part of the controversy over the significance of tubular proteinuria is the question of whether it is a reversible effect. Dr. Friberg testified that:

> The continuous release of cadmium from the liver, also after end of the exposure, means that the accumulation of cadmium will take place in the kidneys for a long time after end of exposure * * * there is much data showing that the proteinuria in chronic cadmium intoxication is irreversible * * * studies * * * show beyond doubt that several years after (medical) removal of the worker (due to proteinuria) there is either an increase of low molecular weight proteins in the urine or no change at all. (Tr. 6/6/90, pp. 74–75).

Drs. Bernard and Lauwerys conducted a follow-up study of workers who had been medically removed from occupational exposures due to cadmium nephrotoxicity (Ex. 35). Among male workers who had been removed from cadmium exposure because of elevated urinary excretion of β_2–M, retinol binding protein (RBP), or albumin, the evidence was that kidney dysfunction increased significantly over the five year period. Once it has appeared, Drs. Bernard and Lauwerys concluded, cadmium-induced proteinuria is in most cases irreversible. Bernard and Lauwerys demonstrated that proteinuria slowly progresses. Despite their finding that this evolution was slow, the authors concluded that the onset of proteinuria should be considered to be an adverse health effect, since such cadmium nephropathy may progress to renal insufficiency.

Dr. Bond stated that the clinical significance of slight increases in urinary β_2–M (for example, 350 μg/l) is uncertain, but that a repeated finding of β_2–M levels twice that of normal would more likely reflect a permanent effect, based on his experience and the literature. (Tr. 7/18/90, p. 169) Dr. Bond also agreed that cadmium-induced proteinuria must be prevented or minimized in order to prevent material impairment of health. (Tr. 7/18/90, pp. 150–258, 175–176). About 20% of the cadmium workers that Dr. Bond has medically evaluated have elevated β_2–M levels. Dr. Bond removed two of these workers from cadmium exposure in 1986 when their β_2–M levels in the urine were 3000 to 5000 μg/1. Annual testing after removal indicated that urinary β_2–M and cadmium levels did not decline appreciably. Dr. Bond stated that in his opinion, these two workers are not sick based on results from tests of their level of serum creatinine and alpha phosphatase which measure kidney function (Tr. 7/18/90, pp. 189–191). Dr. Bond did indicate, however, that he was "concerned" about the welfare of these two individuals because he did not know if they were likely to develop any further problems. (Tr. 7/18/90, p. 229).

According to Jarup *et al* (Ex. 8–661) during the ten-year period of follow-up in his study, none of the cases of elevated β_2–microglobulinuria (greater than 310 μg β_2–M/g Cr) discovered in the high dose groups were reversible. The authors concluded that it was unlikely that any of these cases of tubular proteinuria would disappear after such a long follow-up time and that it was quite possible that more cases of tubular proteinuria would develop with a longer follow-up.

It is clear from the record of the rulemaking that despite some controversy, there is general agreement that renal tubular and glomerular lesions represent permanent loss of kidney functional reserve and that the lesions are irreversible. A worker with elevated levels of β_2–M who does not experience overt symptoms of illness may succumb to other illnesses more rapidly. An infection or other condition which would not normally lead to serious illness but which compromises kidney function could overwhelm the remaining kidney capacity (Ex. 8–644). A worker who has only slightly elevated levels of β_2–M may later develop proteinuria, even after cessation of exposures, or the worker may develop more severe forms of renal dysfunction. Such dysfunction is of great concern to OSHA. Loss of kidney function and renal compromise, described above, meet the definition of material impairment as intended in the OSH Act and as defined in this final standard (Sec. 6(b)(5)).

In summary, various world experts and others take *200* μg β_2-M/g Cr either as the normal limit or as the lower limit of normal (Lauwerys, Ex. 8–447; Friberg, Ex. 29). The most widely used standard test for measuring concentrations of β_2-M, Phadebas, established levels above 300 μg/L urine as being abnormal (Ex. L–140–1). All of these data and expert opinion lead OSHA to believe that the Agency could reasonably set the lowest β_2-M trigger for enhancing medical surveillance from 200 μg to as high as 300 μg/g Cr. Both 200 and 300 μg/g Cr are considered to be very low levels.

On balance, OSHA has decided to set 300 μg/g Cr as the lowest β_2-M trigger for the following reasons. OSHA believes that the medical surveillance requirements in this cadmium standard are, of necessity, very strict. As Dr. Friberg testified:

> OSHA's document * * * when implemented, will have a major impact to protect the workers' health. The proposed changes in PELs and the strict control measures required by OSHA may seem drastic. They are not drastic from the point of view of the protection of the worker, however. They seem drastic only because so little has been done in the past (Tr. 6/6/90; pg. 86–87).

OSHA is aware that these requirements impose a substantial economic burden on employers. OSHA does not want to impose costs on employers for medical surveillance when it is uncertain

whether the lower trigger level of 200 μg β_2-M/g Cr will provide additional protection.

OSHA received comments on other medical surveillance protocols (Exs. 14–14–C; 77; 19–43–A; 107). The Agency believes that the essential elements for a sound medical surveillance protocol that were submitted by other hearing participants have been included in this program. However, OSHA chose to limit initial examinations as specified under (l)(2)(ii) to three biological tests (CdU, CdB, β_2-M) instead of routinely requiring the battery of tests some commenters requested (e.g., ASARCO, Ex. 107). OSHA also relies upon three biological monitoring results used in conjunction with each other, instead of only one parameter, as is the current practice in some industries (Ex. 14–6). The Agency has determined, based on record evidence, that one parameter, either CdU, CdB, or β_2-M, is less reliable by itself to evaluate an employee's health status. Thus, OSHA requires three tests, initially and periodically thereafter.

As indicated above, the final medical surveillance program included in this standard is based upon the proposal (55 FR 4124), the memorandum further articulating that proposal (Ex. 46, July 2, 1990), and the other record evidence. In that memorandum, OSHA: (1) Indicated that the proposed medical surveillance section, paragraph (l), had elicited substantial comment and testimony at the hearings in June, 1990, in Washington, DC; (2) summarized the submissions; (3) presented medical surveillance provisions that had been modified in response to the comments and testimony; and (4) requested participants to submit further testimony and comments on these provisions and related issues. The main change to the provisions incorporated in the memorandum is that in this final standard employers are required to monitor an employee's CdB as well as CdU and β_2-M. The change is based upon testimony and comments OSHA received on the proposal and memorandum (e.g. Exs. 19–2; 19–14; 19–33; 19–34; 19–40; 19–42; 19–43; 77; 82; 84; 101; 106; 107; 120; 123).

With the comments and relevant medical literature in mind, OSHA had to select particular biological levels to indicate greater and lesser risk of contracting cadmium induced disease and to trigger appropriate medical responses. Dr. Tyner, medical director of the Gates Nickel-Cadmium battery plant, stated, "The most important part of this proposed standard is the medical surveillance portion with the removal provisions * * *. Medical surveillance must be mandated." (Ex. 19–2)

Dr. Tyner stated that the proposed medical surveillance provisions are about right. "[Five] 5 μg/g Cr is a little low for removal * * *. Tubular proteinuria is definitely a good reason to remove someone from cadmium exposure" (Ex. 19–2). His company removes workers at 300 μg/Liter. Dr. Bond of SCM stated that an option to requiring each workplace to have a physician who knows about cadmium's toxicity is for OSHA to establish a medical surveillance protocol that would require proper medical examinations (Tr. 7/18/90, pp. 199–200, 244–248). Michael Coffman, manager of industrial hygiene for Federal-Mogul urges OSHA to "set objective, non-mandatory guidelines to assist physicians in determining under what circumstances medical removal is necessary" (Tr. 6/11/90; p. 126).

In response to such comments OSHA incorporated a significant degree of physician discretion into the final medical surveillance provisions, while specifying clear triggers for non-mandatory and mandatory medical actions, where needed.

OSHA believes that each of its choices of triggers for enhanced medical surveillance represents a cutpoint that is generally well established in the medical literature and is widely used in practice for assessing risk of cadmium induced disease and for initiating appropriate preventive or protective action. Of course, OSHA understands that one or more individual triggers might have been set somewhat above or below the particular level OSHA selected. However, the Agency is assured that the overall configuration of trigger levels makes sense as a program for protecting workers to the extent feasible from cadmium induced disease and also is internally consistent.

Take CdU as an example; if CdU biological monitoring results are within the so called "normal" range, at or below 3 μg/g Cr, the employer must provide currently exposed employees who are covered by medical surveillance with the minimum level of surveillance delineated in paragraphs (l)(2), (l)(3), and (l)(4). This minimum includes an initial medical exam (biological monitoring and work history), followed within 12 months by a periodic (biennial) full medical examination which includes biological monitoring, and then within the following 12 months by biological monitoring also on a biennial schedule. Thus, the minimum level of surveillance involves annual biological monitoring, either independent from, or as part of full medical examinations and biennial, full medical examinations.

However, if the employee's CdU are >3 but <15 μg/g Cr, the employer under paragraphs (l)(3)(ii) and (l)(4)(iv) of this standard must take a number of additional, limited steps to locate the source of the exposure problem, control the potential sources of overexposure in the workplace, and more closely monitor for potential changes in any of the employee's biological indicators. Furthermore, the employer is also required to provide the employee with a full medical examination within 90 days after receipt of the biological monitoring results.

To be more specific, for example, if the employee's biological monitoring results show CdU to be in excess of 3 μg/g Cr but at or below 15 μg/g Cr, then the employer is required to:

(a) Provide semi-annual biological monitoring;

(b) Provide annual full medical examinations;

(c) Reassess the employee's work practices, personal hygiene, respirator use, if any, and smoking history and status;

(d) Reassess the respirator program, hygiene facilities, maintenance and effectiveness of relevant engineering controls; and

(e) Take reasonable steps to correct deficiencies found in the reassessments that may be responsible for the employee's excess exposure to cadmium.

In addition, due to the potential for disease associated with CdU levels above 3 μg/g Cr and especially above 5 μg/g Cr. (See Health Effects Section V). OSHA also is requiring the examining physician to consider and determine in a written medical opinion whether or not the employee, in light of all the medical evidence, should be medically removed from exposure to cadmium at or above the action level. If the physician determines that the employee need not be medically removed, the employer must:

(1) Continue to provide semi-annual biological monitoring of potential changes in the employee's biological indicators;

(2) Provide annual medical examinations; and

(3) Make periodic efforts to locate and control the workplace sources of the employee's problem until the CdU levels return to within the "normal" range.

Moreover, if the level of CdU exceeds 15 μg/g Cr, then under paragraphs (l)(3)(iii) and (l)(4)(iv) of this standard the employer must provide a full

medical examination within 90 days after receipt of the results. The physician continues to be required to determine in a written medical opinion whether the employee should be medically removed from exposure to cadmium at or above the action level. If the physician determines that the employee need not be medically removed, the employer must continue to provide the same level of enhanced medical surveillance as is required at the next lower trigger level, except that biological monitoring must be conducted quarterly and periodic medical examinations must be provided semi-annually. The employer also must periodically continue his/her efforts to locate and control the workplace sources of the employee's problem.

More than that, if the biological monitoring results obtained during the medical examination confirm the initial (or periodic) monitoring results, that the employee's level of CdU exceeds 15 μg/g Cr, or CdB exceeds 15 μg/lwb, or β_2-M exceeds 1500 μg/g Cr and in addition to the elevated β_2-M level, CdU levels exceed 3 μg/g Cr or CdB levels exceed 5 μg/lwb, then the physician is required to medically remove the employee from exposure to cadmium at or above the action level.

With this provision for mandatory removal, OSHA is effectively eliminating the examining physician's discretion as to whether to remove the employee from cadmium exposure at or above the action level. OSHA believes that the risk of the employee having or developing kidney disfunction and perhaps other diseases is so high at these biological levels that the employee must be removed as soon as it is established by retesting that the earlier monitoring results are confirmed (Bernard and Lauwerys, Ex. 35; NIOSH, Ex. 128; Lauwerys, Ex. 8–718; Roels, Ex. 57–K; Buchet, Ex. 8–201).

However, to avoid the possibility that a cadmium exposed worker's confirmed, very high β_2-M levels might be attributable to something other than cadmium exposure, OSHA is requiring that, for mandatory medical removal based on high β_2-M levels, the β_2-M levels must be supplemented by abnormal levels in one of the two cadmium-specific biological parameters, CdB or CdU, as well. Thus, OSHA seeks to assure that removal for elevated levels of β_2-M be carefully restricted to employees with high risks of adverse material impairment of health associated with exposure to cadmium.

Medical evidence in general would support mandatory removal at lower levels than established in paragraph (l)(3)(iii) (Exs. 8–644; L–140–51; 35). However, OSHA is mindful of other important considerations that tend to weigh against currently requiring medical removal at lower biological levels. First, medical removal is a dramatic intervention that may have potentially dire, unintended life consequences for the employee and could be very costly to the employer as well. Even as medical removal provides one reasonable way to deal with an employee's medical problem, it may contribute to, or create other problems. For example, if a veteran worker is removed because of high biological monitoring results and his/her subsequent results do not fall to or below the "normal" level, which would allow return of the employee to his/her former job status, the employee thereafter might be terminated and become, practically speaking, unemployable in today's cadmium exposed jobs. Second, individuals' vulnerabilities and susceptibilities to cadmium toxicity vary somewhat, especially at lower levels of exposure such as those under the new TWA PEL of 5 μg/m³. The numerical mandatory removal limits have been selected using Agency judgement as to the need to protect the sensitive portion of the worker population without removing too many workers who will not develop kidney impairment. And third, veteran cadmium-exposed workers, who were occupationally exposed to much higher levels of cadmium in the past, still are employed in the workplace. For veteran workers near retirement, a complex decision that is at once medical, social and economic has to be made concerning medical removal. This decision is best made by the examining physician and the individual worker in consultation. Fourth, with large numbers of veteran workers still in the workforce, mandatory removal at relatively low levels may create feasibility problems for many employers.

Considering the pros and cons for setting lower mandatory removal triggers, OSHA recognized compelling arguments on both sides. In light of this reality, OSHA tried to take reasonable account of legitimate, conflicting concerns by steering a middle course. To protect worker health, the Agency set lower removal triggers at the discretion of the physician. OSHA believes that while the final standard allows for discretionary medical removal at low levels (e.g., using CdU as an example, as low as just above 3 μg Cd/g Cr), physicians generally will not remove workers at these levels. OSHA does not expect physicians to remove workers when they first exceed "normal" levels or at low levels. Before 1999, workers need not be medically removed at or near these levels, unless in the physician's opinion and after full review of all the pertinent medical information the physician deems it necessary to do so in the interests of the health of a particular worker.

Nonetheless, by providing the option of discretionary removal at these low levels, OSHA believes that the physician and the employee will become aware that increased risk of kidney dysfunction exists at these levels, and they will consider other actions short of medical removal to minimize or avoid permanent damage, e.g., diet, use of certain broad-spectrum antibiotics and other prescription medications, use of other non-prescription medications. The physician and the employee should be aware of the risks in order to mitigate the influence of other factors that might rapidly overwhelm the worker's remaining functional capacity in cases where some dysfunction has already occurred even though the worker's test results are below the mandatory removal levels.

In further recognition of the countervailing factors listed above, the Agency phases in lower levels for mandatory requirements over nearly six years. Thus, in paragraphs (l)(3)(iv) and (l)(4)(iv) mandatory medical removal is required after January 1, 1999 whenever biological testing during a physical exam confirms earlier results that CdU is >7 μg/g creatine, CdB is >10 μg/lwb, or β_2-M> 750 μg/g Cr and in addition to elevated β_2-M levels CdU levels exceed 3 μg/g Cr or CdB levels exceed 5 μg/lwb. Support for the particular levels chosen for removal can be found in the health effects section earlier in this preamble and in the record of the rulemaking. For example, Dr. Bond, who testified on behalf of SCM, stated that the clinical significance of slight increases in β_2-M (for example, 350 μg/L) is uncertain, but that a repeated finding of β_2-M levels twice that of normal would more likely reflect a permanent effect, based on his experience and the literature (Tr. 7/18/90, p. 169). Dr. Bond also agreed that cadmium-induced proteinuria must be prevented or minimized in order to prevent material impairment of health. (Tr. 7/18/90, pp. 150–158, 175–176).

By phasing in mandatory removal requirements at lower levels, OSHA expects that most of the problems associated with immediately imposing such lower levels will be avoided. For example, employers' efforts over the intervening years to comply with this standard, especially in the face of

prospects of still lower mandatory removal triggers, are likely to control cadmium exposures in the workplace to the extent feasible. Moreover, the normal infusion of new workers not previously occupationally exposed to cadmium in conjunction with normal levels of turnover and the retirement of veteran workers will produce a workforce most of whose members have considerably lower body burdens of cadmium. Taken together, these developments should make mandatory removal at lower levels generally feasible for employers and less potentially burdensome for employees.

OSHA's tiered structure for progressively enhanced medical surveillance incorporates a parallel structure for progressively reduced surveillance, which is triggered at each tier by sufficiently lowered biological test results. At each level of enhanced medical surveillance there is a mechanism for reducing medical surveillance when levels of all three biological parameters fall below specified trigger levels. Thus, for example, the enhanced medical surveillance triggered by paragraph (l)(3)(ii), where levels of CdU > 3 μg/g Cr, β_2-M > 300 μg/g Cr, CdB > 5 μg/lwb, is no longer required once the employee's levels of CdU fall to or below these levels. Thereafter, as long as the employee's biological monitoring results all remain within the "normal" range, the employer is required to provide only the minimum level of medical surveillance.

These medical surveillance provisions were developed with a primary focus on currently exposed employees. However, under paragraphs (l)(1)(i)(B), (l)(2)(i), (l)(3)(i)(B), (l)(3)(ii)–(vi), (l)(4)(v), and (l)(8), they apply as well to employees who may no longer be exposed to cadmium. Thus, the employer must provide medical surveillance to any employee who was exposed to cadmium prior to the effective date of this standard, unless the employer can demonstrate that the employee did not work for the employer in jobs with cadmium exposure for an aggregated total of more than 60 months in the years prior to the effective date of this standard.

OSHA understands that it may be difficult at times for the employer to demonstrate that the employee did not work for the employer in cadmium exposed jobs prior to the effective date of this standard for a total of 60 months or less. Consequently, the Agency does not require the employer to provide a certain proof to satisfy the employer's burden of proof. Rather, OSHA expects the employer to provide sufficient evidence to make it unlikely that the employee was exposed for a total of 60 months. The evidence must be reasonably persuasive in light of the protective purposes of medical surveillance. The evidence may be probablistic or circumstantial where direct evidence is neither available nor easy to develop.

Thus, on the one hand, for the reasons presented above, OSHA has placed the burden of proof on the employer to show that a currently or previously cadmium-exposed employee need not be provided medical surveillance under the criteria supplied in paragraph (l)(1) of this standard. And OSHA intends that these criteria should be interpreted in a manner that best assures medical protection to employees who appear potentially in need of it. On the other hand, OSHA does not intend to impose an unsustainable burden on the employer. On the contrary, the kind of proof that a reasonably conscientious employer could present generally should be viewed as satisfying the employer's burden of proof.

For employees to whom the employer must provide medical surveillance because of exposure to cadmium prior to the effective date of this standard, the main aim of initial medical surveillance, as previously indicated, is to identify as quickly as possible those with abnormally high biological test results. Once identified, these employees are then tracked through paragraphs (l)(3)(ii)–(iv) and (l)(4)(iv) into the same level of enhanced medical surveillance as currently exposed workers with similar test results. By contrast, for past exposed employees whose initial biological monitoring results are all within the normal ranges, the aim is to phase out periodic medical surveillance as expeditiously as prudence will allow. Consequently, under paragraph (l)(3)(i)(B) the employer is required to retest the employee within one year (12 months) of the initial exam. If the results of that retest confirm that all the levels remain normal, then under paragraph (l)(4)(v) the employer need not provide further medical surveillance to the employee.

The tiered structure of triggers for progressively enhanced and progressively reduced medical surveillance, outlined with regard to CdU, is utilized in paragraphs (l)(3) and (4) of this standard for CdB and β_2-M > levels, as well. Paragraph (l)(3) provides the required, tiered actions the employer must take in response to the initial biological monitoring results. Paragraph (l)(4) provides the requirements for periodic medical surveillance, which generally replicate the tiered requirements for biological monitoring in paragraph (l)(3). These parameters are required to be monitored on the same schedule as CdU.

In order to assist the employer, employee and the physician in understanding and implementing the medical surveillance provisions in this standard, OSHA has provided a Summary Chart of the provisions in the regulatory text and an example of a form for employee-notification-of-results in appendix A.

In addition to biological monitoring, periodic medical examinations also are required. Paragraph (l)(4)(ii) sets out the required contents of those examinations. The examination must include a detailed medical and work history and a conventional physical examination, with specific emphases on potential cadmium induced diseases and their biological indicators. Thus, particular attention is given to the respiratory and urinary systems, the same biological monitoring that is part of the initial examination, and additional blood and urine analyses.

Based upon numerous comments in the record indicating that OSHA should focus the content of the medical exam on potential lung and kidney disease as the critical effects, the Agency in this final standard has eliminated certain requirements from the proposed standard and added others (NIOSH, Ex. 19–26; Bond, Ex. 77; ASARCO, Ex. 107). For example, OSHA eliminated the proposed requirements for liver enzyme testing. While cadmium is regarded as a late-stage toxin to the liver, at least one commenter stated that there are no reports of cadmium-induced hepatocellular damage, therefore, medical tests for liver function are unjustified (Exs. 8–86, Ken Storm; 19–14, Monsanto). Dr. Friberg stated that there was no reason to include liver enzyme tests unless they are normally performed (Ex. 29).

A complete blood count is required as part of the full medical examination under paragraph (l)(4)(ii)(F). This test is expected to identify cases of anemia. According to Dr. Stopford, a physician with the Duke University Medical Center, a platelet count, which is already part of most commercially-available complete blood count panels, would help detect the toxic effects of cadmium on the spleen and liver, with associated anemia (Exs. 14–14B, 14–14–D). Dr. Stopford submitted comments to the record which included a case report on a worker with severe liver dysfunction (Ex. 14–14). Dr. Stopford

considered this case history to be cadmium related.

The proposed microscopic examination of urinary sediment was eliminated in the final standard, because comments were submitted that this test would provide little useful information (Ex. 29). Evaluation of the musculoskeletal system was eliminated from the physical exam but not from the medical history because commenters stated that musculoskeletal damage is seen only as a result of cadmium-induced kidney failure and probably will not be seen in the U.S. occupational environment (Exs. 19–14, 29; Tr. 6/6/90 pp. 112).

On the other hand, OSHA added other requirements to the final standard, for measuring urinary pH and creatinine in urine, as specified under paragraph (l)(2)(ii)(B)(2), because the Agency learned that they are needed to standardize and control the accuracy of measurements of cadmium and β_2-M (Friberg, Ex. 8–86, Vol. I, pp. 83; Phadebas, Exs. L–140–1, 4–47, L–140–45). Several commenters supported the requirement to measure creatinine in urine to control for diuresis if they do not do so at present (Exs. 84, 19–40).

Specifically, OSHA requires the following elements in the periodic medical examination for the following reasons. First, under paragraph (l)(4)(ii)(A) the Agency requires a detailed medical and work history to provide the physician with information, including employee reported symptoms, to be used in conjunction with a complete physical examination and biological monitoring. This information can assist the physician in determining the employee's health status, possible past exposures to cadmium or other toxic substances that may have damaged organs or systems susceptible to cadmium toxicity, and suitability for work in a job where cadmium exposure may occur. Questions 3–11 and 25–32 in appendix D are a required part of the medical history because they relate to the increased risk of kidney disease, lung cancer, bronchitis, fibrotic lung changes, and emphysema-like changes in the lung that can occur as a result of cadmium exposure (Ex. 19–26). The information about the respiratory system is also important for evaluating an employee's fitness for respirator use.

Second, a complete physical examination is required to enable the physician to directly and more broadly assess the health status of the employee and to pursue any other indications of potential medical problems that may be relevant to cadmium exposure. In the physical examination, the physician can assess other potentially serious adverse effects associated with cadmium exposure, like dermatoses, eye irritation and elevated blood pressure, which are beyond OSHA's primary focus on kidney and lung disease. A complete physical examination is particularly useful to the physician when exercising his or her discretion to determine whether the employee must be medically removed from exposure to cadmium under paragraphs (l)(3)(ii)–(iv).

Third, under paragraph (l)(4)(ii)(C) a chest X-ray is required at the first periodic medical examination, at the termination of employment examination (paragraph (l)(8)), and periodically as determined by the examining physician. An initial chest X-ray, although not useful for preventing lung cancer, can be useful for diagnosing lung cancer and other non-malignant lung diseases which are caused by cadmium exposure (e.g., Kazantzis Tr. 6/8/90, pp. 156–157), such as bronchitis, fibrosis and emphysema-like changes in the lung. It also provides baseline data upon which to assess any subsequent lung function changes (Ex. 19–26–F). OSHA is leaving the determination of frequency of chest X-rays to the discretion of the physician and is not requiring periodic chest X-rays because of the potential risk of adverse effects to the employee from too frequent X-rays (Ex. 19–14).

Fourth, pulmonary function tests are required to provide specific information about the employee's lung capacity and respiratory flow rate. This information is useful to diagnose bronchitis and emphysema, to provide baseline data on lung function, to evaluate any loss of lung function, and to provide baseline information of lung function status upon which to assess any subsequent lung function changes. This information may also be useful in assessing the health of employees who wear respirators. It is recommended that pulmonary function testing be conducted in accordance with the American Thoracic Society's criteria (Ex. 8–663).

Fifth, since a central purpose of the medical examination is to provide further information on the critical organs and critical effects associated with cadmium exposure, OSHA has included in the examination additional analyses of blood and urine and, for males over 40 years of age, prostate palpation or other at-least-as-effective diagnostic test(s). Specifically, OSHA has included a determination of the blood urea nitrogen (BUN) and serum creatinine levels and a complete blood count. Elevations in BUN and serum creatinine levels are indicative of kidney disease. For example, BUN and serum creatinine levels increase with the loss of glomerular filtration. Although BUN and serum creatinine tests are not cadmium specific, they do provide additional information about kidney function and kidney disease that is important for physicians to know in determining an employee's suitability for work in a cadmium-exposed job (Ex. 107). Regardless of whether the kidney disease is caused primarily by cadmium from occupational sources, and indeed regardless of whether the kidney disease is cadmium induced at all, the very existence of kidney disease in a cadmium exposed worker is serious cause for concern. OSHA in the final standard also has required a complete blood count, which most industry representatives stated was a very useful test for cadmium exposed workers (Dr. Bond, Ex. 77; Dr. Hine, ASARCO, Ex. 107; but see Ex. 19–14).

With regard to additional urine analysis, OSHA is also requiring a determination of the albumin, glucose and total and low molecular weight protein levels. While albumin and glucose tests are not cadmium specific, they can provide additional information about kidney function and kidney disease, which also is important for physicians to know in determining an employee's suitability for work in a cadmium-exposed job (Ex. 8–669–A). Elevated levels of albumin and glucose in urine may be indicative of a loss of glomerular function. In addition, the increased urinary excretion of low molecular weight proteins and total proteins (i.e., low and high molecular weight proteins combined) is associated with early renal damage.

Prostate palpation or other equally effective diagnostic tests are required to diagnose prostate cancer. Cancer of the prostate has been observed among cadmium exposed workers and was the first indication that cadmium exposure is associated with cancer. Although recent studies do not confirm the association between cadmium exposure and death from prostatic cancer, OSHA believes it would be premature and imprudent at this time to act as if exposure to cadmium did not increase the risk of prostatic cancer. Indeed, many scientists and physicians attribute the reduction in cadmium induced prostate cancer death rates not to a lack of association between cadmium exposure and prostatic cancer but to two other factors: The improved early diagnosis and treatment of prostate cancer, which has reduced the death rates from this disease, and the reduced levels of cadmium exposure (Ex. 19–42b; Environ Report, Ex. 12–39, ATSDR, Ex. 8–689). OSHA therefore, as prudent public health policy, requires inclusion

of prostate palpation or other equally effective diagnostic tests for prostate cancer in men over 40, the primary target group for prostatic cancer.

Finally, OSHA has authorized the physician to require any additional tests deemed medically necessary. OSHA believes that it is important that the examining physician have such discretion because, notwithstanding statistical probabilities, individual susceptibilities to, and tolerance levels and thresholds for, cadmium toxicity differ. The physician is in the best position to specifically determine which additional tests, if any, would be useful in evaluating the health status of the individual employee.

Paragraph (l)(5) provides for additional actions triggered by any unspecified but generally accepted abnormal findings consistent with cadmium toxicity that are identified through medical examinations. For example, in his guide for physicians who medically evaluate workers exposed to cadmium, Dr. Lauwerys indicates that levels of total protein in urine above 250–350 mg/g Cr may require additional medical attention and referral to a nephrologist (Ex. 8–447).

In devising paragraph this medical surveillance program, OSHA sought to provide objective markers for action while recognizing that single monitoring results generally should not be used in isolation from other results or other biological parameters or a holistic evaluation of the worker's health to determine a worker's fitness for cadmium exposed work. OSHA tried to provide a significant role for physician discretion in this evaluation, without leaving the physician devoid of boundaries on his/her discretion and guidelines to action.

Paragraph (l)(6)(i) requires the employer to provide a limited medical examination prior to the employee using a respirator to determine the employee's fitness for wearing a respirator. This is a change from the proposal, where a full medical examination, including elements designed to test the employee's fitness to wear a respirator, was required within 30 days after the employee was assigned to a job requiring the use of a respirator. Based on record evidence (Exs. 57, 19–22, 106), OSHA believes that a full medical examination is not necessary to determine the employee's fitness to wear a respirator and therefore in this final standard has only retained those elements of the full medical examination that are useful to such a determination. Based on comments to the record (e.g., ASARCO, Ex. 107), OSHA also believes that the examination to determine an employee's fitness to wear a respirator should be performed prior to the employee using a respirator. The examination must include a detailed medical and work history, with emphasis on questions 3–11 and 25–32 in appendix D, a blood pressure test, and any other tests or procedures, such as pulmonary function tests or a physical examination, that the examining physician deems appropriate. OSHA is requiring a detailed medical and work history with specific questions about past respiratory and cardiovascular problems, smoking history, and other medical problems that might either interfere with, or be exacerbated by the employee wearing a respirator, because this information should be gathered and medically assessed prior to the employee using a respirator.

In addition, the examining physician under (l)(6)(ii) should review the results of any biological monitoring of the employee's CdU, CdB and β_2-M. OSHA believes that the examining physician should assess these biological data indicating whether the employee has been overexposed to cadmium, has an abnormally high body burden of cadmium, or has kidney disease before the physician certifies the employee as fit to wear a respirator in a job in which the airborne cadmium levels are above the PEL.

Where the employee has actually exhibited difficulty in breathing during a respirator fit test or while using a respirator, then, under paragraph (l)(6)(iii), the employer is required to provide a full medical examination in accordance with paragraph (l)(4)(ii). The examination is required to determine the employee's fitness to continue wearing a respirator and his or her health status relative to further exposure to cadmium.

If the results of the medical examination under paragraph (l)(6)(i) or (iii) are abnormal, medical limitation of respirator use, including prohibition of such use or requiring that the employee be provided with a more appropriate respirator (e.g., a PAPR), shall be considered. If the employee is allowed to continue to wear a respirator the physician is required to periodically evaluate the employee's continuing fitness to wear a respirator as often as medically necessary. If the employee is found unable to wear a respirator, he or she shall be medically removed under paragraph (l)(11) of this standard from any current job where the employee is exposed to cadmium above the PEL.

In addition to the medical surveillance required in paragraphs (l)(2)–(6), paragraphs (l)(7) and (8) provide for further medical examinations in the event of acute exposure to cadmium because of an emergency or upon termination of employment, respectively. Emergency examinations are required because it would be imprudent to delay evaluating the effect of acute exposure to cadmium on the employee until the next periodic medical examination. Indeed, in an emergency, immediate medical attention may be necessary.

The employer, with one exception, is required under paragraph (l)(8) to provide a medical examination at the termination of employment to all workers to whom the employer at any time was required under paragraph (l)(1)(i) or (l)(7) to provide medical surveillance. Thus, for example, all workers who in any 12 month period after the effective date of this standard were exposed to cadmium at or above the action level on 30 or more days by the employer and all workers who had emergency medical examinations would be entitled to the examination required by paragraph (l)(8). In addition all workers exposed prior to the effective date of this standard who were covered by medical surveillance also would be entitled to a medical examination at termination of their employment, unless under paragraph (l)(8)(ii) the employer discontinued periodic medical surveillance as authorized under paragraph (l)(4)(v).

This requirement is somewhat different from the proposal. Under the proposal the employer would have had to provide a termination of employment examination to all employees who at any time had been eligible for a full medical exam under proposed paragraph (l)(3). However, under the proposal employers were not obligated to provide a full medical exam, or indeed any medical surveillance at all, to employees who had been exposed by them to cadmium exclusively prior to the effective date of this standard. The effect of the proposal, then, would have been to require employers to provide examinations at termination of employment only to employees who were exposed by them to cadmium at or above the action level after the effective date of this standard.

Unlike the proposal, the final standard does cover employees who may have been excessively exposed to cadmium prior to the effective date of this standard. However, the employer would not have to provide these employees with a termination of employment examination if their biological monitoring results had previously returned to "normal" levels and periodic medical surveillance of them had been

discontinued in accordance with paragraph (l)(4)(v).

The requirement for a medical examination at the termination of employment is in keeping with other OSHA standards (e.g., Asbestos, Coke Oven Emissions, Arsenic, Acrylonitrile, and Ethylene Oxide). The need for this requirement in the cadmium standard is due, in part, to the way cadmium is transported, distributed, and stored in the body. After absorption, cadmium is transported via the blood stream to other body parts, where it is bound to proteins and stored. Low excretion rates lead to a very efficient retention of cadmium in the body. The biological half-life of cadmium in various compartments of the body ranges from 20–37 years or more (Ex. 8–86–B). It is not surprising, then, that even after cessation of exposure to cadmium in the workplace, growing evidence indicates that cadmium stored in one body compartment can be transported to the kidney. In this way, cadmium proteinuria may develop years after exposure in the workplace has ceased. There is, therefore, little tendency for proteinuria (e.g., β_2-M>1000 μg/g Cr; Ex. 30), to decrease after removal from external cadmium exposure if past cadmium exposures were high (Ex. 35). Instead there can be an increase, which is substantial for some workers, and kidney damage can progress to a more severe stage of disease (Ex. 8–668). Consequently, it is important that the employee's health status regarding cadmium accumulation in the body be once again assessed at the employee's termination of employment.

Failure to find evidence of cadmium toxicity in the examination at termination of employment should not be viewed as a "clean bill of health." Physicians should use the opportunity of the examination to once again advise the employee of his/her cadmium body burden and prognosis, and to make recommendations for medical management and follow up. For the worker, this information allows him/her to determine the courses of action necessary to sustain health.

As part of the medical surveillance program established in this standard, the employer is required by paragraph (l)(9) to provide the examining physician with the following information: A copy of the standard and its appendices; a description of the affected employee's former, current, and anticipated duties as they relate to the employee's occupational exposure to cadmium; the employee's former, current, and anticipated future levels of occupational exposure to cadmium; a description of any personal protective equipment and respirators used, or to be used by the employee, including when and for how long the employee has used that equipment; and results from previous biological monitoring and medical examinations that were provided by the employer to the employee. Making this information available to the physician will aid in the evaluation of the employee's health and fitness for particular cadmium-exposed job assignments. This provision is essentially the same as in the proposal (55 FR 4126).

Under paragraph (l)(10), the employer is required to obtain a written opinion from the examining physician promptly after a medical examination of an employee. The written medical opinion must contain the results of the medical examination as they relate to occupational exposure to cadmium, any detected medical conditions relevant to further cadmium-exposure, any recommended restrictions upon the employee's exposure to cadmium or upon the use of protective clothing or equipment, and other elements of (l)(10)(i)(A–E). This written opinion by the physician, which is given to the employer, must include a statement indicating that the physician has provided the results of the tests, the medical examination, any diagnoses, and an evaluation of the employee's prognosis to the subject employee in a manner that appropriately informs the employee of the results of the tests. A suggested format for such a statement is included appendix A. The physician is not to reveal to the employer orally or in his/her written medical opinion specific findings or diagnoses unrelated to occupational exposure to cadmium. Under paragraph (l)(15)(i), the employer must give a copy of the written medical opinion to the affected employee within two weeks after receipt thereof.

The purpose of requiring the examining physician to supply the employer with a written opinion is to advise the employer of the medical basis for determining placement of employees in cadmium-exposed jobs. The requirement that a physician's opinion be in written form will assure that employers have had the benefit of this information which can be referred to as needed. The requirement that the written medical opinion from the examining physician include the physician's diagnosis and prognosis for the employee and other elements stated in paragraph (l)(10)(i)(A–E) is to assure that the employer and the employee are apprised of all medical information that is meaningful and relevant to the employee's initial or continued exposure to cadmium in the workplace. The requirements that the written medical opinion be promptly provided after the examination to the employer and that the employer, in turn, provide a copy of the physician's written opinion to the employee within two weeks of its receipt (paragraph (l)(15)(i) is to assure that notice of potential adverse health effects is promptly communicated to the employer and employee so as to minimize potential risk to the employee's health.

A requirement has been included in paragraph (l)(10)(i)(E) that the employer obtain a statement from the examining physician that the employee has been informed of the results and medical implications of the medical examination. It is the employer's responsibility to assure that the employee has been so informed. A suggested format for such a statement is provided in appendix A. In conjunction with the requirement that the employee must be provided with a copy of the physician's written opinion, OSHA is assured that the employee will be informed of the results of the medical examination. The requirement that the physician sign the opinion is to assure that the information that is given to the employer has been seen and read by the physician and that the physician has personally determined whether the employee may continue to work in cadmium-exposed jobs.

The purpose in requiring that specific findings or diagnoses unrelated to occupational exposure to cadmium not be included in any oral or written opinion provided by the physician to the employer under paragraph (l)(10)(iii) is to encourage employees to take the medical examination by removing any concern that the employer will obtain adverse information about their health status that has no relation to occupational exposures. This provision has been included in prior standards (e.g., final arsenic standard, 43 FR 19621).

Medical Removal Protection (MRP)

Paragraphs (l)(11) and (l)(12) provide for medical removal protection and medical removal protection benefits, respectively. These paragraphs apply only to workers who are exposed to cadmium at or above the action level. Paragraph (l)(11) generally requires the employer to remove workers from exposure to cadmium on each occasion that the risk of material impairment to the employee's health or functional capacity from continued exposure to cadmium is considered too high. More specifically, the employer must remove

the employee from excess exposure to cadmium in three cases. First, the employee must be removed from exposure at or above the action level on each occasion that a physician determines in a written medical opinion that medical removal is required under paragraphs (l)(3) and (l)(4). In accordance with these paragraphs, this determination may be based upon elevated levels of the employee's CdU, CdB or β_2-M. Alternatively, the determination may be based on evidence of illness, other signs of cadmium-related dysfunction or disease, or any other reason deemed medically sufficient by the physician. Second, the employee must be removed from exposure at or above the action level where medical removal is mandatory under paragraphs (l)(3)(iii) and(iv)(C) and(l)(4)(iv)) if the employee's levels of CdU, or β_2-M or CdB are confirmed to be in excess of the trigger levels specified in those paragraphs. Third, the employer must remove an employee from cadmium exposure above the PEL whenever a physician determines in a written medical opinion that the employee cannot wear a respirator. The MRP provisions apply only to such an employee when he/she already is functioning in a job where a respirator is required and it is then determined that the employee is unable to wear a respirator and therefore must be removed. MRP does not apply to a new employee who is determined in a pre-assignment medical examination for respirator use to be unable to wear a respirator. Nor does it apply to a worker found to be medically unable to wear a respirator that is required in a job to which the worker seeks to transfer or to a worker who has volunteered to wear a respirator.

Each time the employee is medically removed under paragraph (l)(11), paragraph (l)(12) requires the employer to provide medical removal protection benefits for up to a maximum of 18 months, thereby maintaining the employee's total earnings and other employment rights for that period as if the employee were not removed.

Medical removal protection (MRP), in paragraph (l)(11) of the cadmium standard, is a protective, preventive health mechanism that is integrated with the medical surveillance provisions of this standard. MRP requires employers to temporarily remove from jobs with significant exposure to cadmium those employees who are discovered through medical surveillance to be at the highest risk of sustaining material impairment to health from continued exposure to cadmium. The medical removal protection benefits (MRPB) provisions in paragraph (l)(12) of the standard require employers, on each occasion that an employee is medically removed under paragraph (l)(11), to provide temporary economic protection to the removed employee.

MRP and MRPB have previously been included in OSHA's Lead and Benzene standards, 29 CFR 1910.1025 and 1910.1028, respectively. The MRP and MRPB provisions of this standard are modeled upon similar provisions incorporated in the lead standard. The lengthy discussion and justification for MRP and MRPB provided in attachment C to that standard (43 FR 54440–73, Nov. 21, 1978) are, to the extent relevant, hereby adopted in this preamble to the cadmium standard.

MRP, contributes directly to achieving one of the aims of the OSH Act, assuring to the extent feasible "that no employee will suffer material impairment of health or functional capacity even if such employee has regular exposure to the hazard dealt with by the standard for the period of his working life" (Sec. 6(b)(5)). The term "material impairment" is not defined in the cadmium standard since it encompasses multifarious conditions. However for purposes of this standard, "material impairment" is intended to be interpreted as broadly as is necessary to achieve the preventive purposes of the Act. "Material impairment," thus, is intended to include early stage diseases and medical dysfunctions and is not intended to necessarily imply the existence of overt illness, irreversible damage, or clinical symptoms. In practice, the term will be defined in a manner consistent with sound medical practice through the physician determination mechanisms in the cadmium standard.

MRP and MRPB, separately and in combination, serve three main interrelated purposes. First, together, they increase employee participation and confidence in the standard's medical surveillance program. Second, by requiring the employer to remove employees with the highest risk of suffering cadmium induced disease from significant exposure to cadmium and to provide removed employees with enhanced medical surveillance, MRP serves both to prevent the onset of disease and to detect and minimize the extent of existing disease. Third, MRPB allocates the costs of medical removal protection to employers. The medical surveillance program in the cadmium standard represents a major element in OSHA's integrated approach to preventive health under the OSH Act. The success of the preventive approach crucially depends on voluntary and meaningful worker participation in medical surveillance.

Medical surveillance can only be effective in preventing (and minimizing) disease where workers: (1) Voluntarily seek medical attention when they feel ill; (2) refrain from efforts to conceal their true health status; and (3) fully cooperate with examining physicians to facilitate accurate medical diagnoses and effective treatment. This sort of employee participation and cooperation cannot be evoked by coercion. It will occur only where no major disincentives to meaningful worker participation exist. Without such participation, it would be much more difficult, if not impossible, to adequately monitor workers' health and to identify workers who need temporary medical removal. And without effective medical surveillance, the overall protection afforded by the cadmium standard would be substantially diminished.

MRP is a logical and natural culmination of medical surveillance. In order to protect the health of workers identified by the medical surveillance program as most in need of protection, MRP mandates temporary removal from significant cadmium exposure and enhanced medical surveillance. Without MRP, employers would be free to maintain high-risk workers in their current, high-exposure jobs, which would not be sufficiently protective of their health. Alternatively, employers could choose to terminate, temporarily lay off, or transfer those workers from higher-paying, cadmium-exposed jobs to lower-paying, less-exposed jobs. This might be protective enough but it could seriously damage workers' livelihood.

Under such conditions, workers would be faced with a painful dilemma: They could decline to participate in medical surveillance at substantial risk to their health, or they could agree to participate in medical surveillance at substantial risk to their livelihood. In either case, the effectiveness and integrity of the medical surveillance program would be compromised. In such circumstances, countless workers doubtless would be very hesitant to participate in medical surveillance. Consequently, in part to safeguard the medical surveillance program, both MRP and MRPB have been included in the standard.

With MRP, workers are assured of being removed to low exposure jobs when necessary to protect their health. And with MRPB, workers are assured that, if they fully participate in medical surveillance and if the results of medical surveillance require removal from their high-cadmium-exposure jobs, their

wages and job status will be protected for an extended period. During that period, the examining physician can determine whether the removed workers' health has sufficiently improved so they may be returned to their previous jobs, or they must be permanently removed from further exposure.

Viewed as a means to achieve the health goals of the standard, temporary medical removal is a method of control, not so different in this respect from engineering controls, which control airborne cadmium emissions. Implementing MRP, like other controls, necessarily entails certain costs. The employer, for example, might incur certain costs due to the temporary loss of a trained and experienced employee. Without MRPB, a removed worker might lose substantial earnings or other rights or benefits by virtue of the removal. These costs are a direct result of reliance on MRP to protect worker health.

OSHA considers the costs of protecting worker health to be an appropriate cost of doing business since employers are obligated by the OSH Act to provide safe and healthful places of employment. Consequently, the costs of MRP, like the costs of providing respirators and engineering controls, are placed on employers rather than on the shoulders of individual workers unfortunate enough to be at risk of sustaining material impairment to health due to occupational exposure to cadmium. Nevertheless, MRP should not be understood as an alternative to primary control of workers' exposure to cadmium. Rather, MRP is intended by OSHA to be used exclusively as fall-back protection, where other, primary methods of controls have proven to be insufficiently protective.

Precisely because MRP will impose additional costs on employers, MRP can increase the protection afforded workers by the cadmium standard not only directly by improving medical surveillance but also indirectly by providing employers with economic incentives to comply with other provisions of the standard. The costs of MRP are likely to decrease as employer compliance with other provisions of the standard increases. Employers who comply with other provisions of the standard should have to remove relatively few employees. With only a small number of employees requiring removal, complying employers are more likely to be able to find positions available to which removed employees can be transferred. By contrast, employers who make only cursory attempts to comply with the central provisions of the cadmium standard are likely to find that the greater their degree of noncompliance, the greater the number of employees requiring medical removal and the greater the associated MRP costs. Thus, MRP serves as a strong stimulus for employers to protect worker health and rewards employers who through innovation and creativity derive new ways of protecting worker health not contemplated by the cadmium standard.

One limiting factor on the potential of MRP to prevent disease is that, once an employee has developed proteinuria (e.g., β_2-microglobulinuria), in many cases medical removal can only slow and minimize the progression of the disease or dysfunction but cannot necessarily prevent the development of more serious disease. Medical removal, by severely restricting the intake of cadmium on the job while providing time for natural excretion to eliminate from the body previously absorbed cadmium that has accumulated in various body compartments, will effect a net decrease in the body's cadmium burden. However, the very process that reduces the overall body burden of cadmium leads to an increase in the kidney burden of cadmium (though generally to a smaller increase than if the employee had not been removed at all from significant exposure to cadmium). This is because the decrease in overall body burden of cadmium is achieved through the excretion of CdU, which passes through the kidney, thereby increasing the amount of cadmium in the kidney, where it continues to cause damage.

Thus, temporary medical removal can protect a removed employee from additional cadmium exposure but may not in some cases be a mechanism for restoring normal kidney function where cadmium-related proteinuria, or more severe cadmium-related kidney disease is already present. For workers who have already developed cadmium induced kidney disease, the primary purpose of temporary medical removal is to provide intense medical surveillance while minimizing both further exposure to cadmium and further progression of the dysfunction/disease during the period in which diagnosis and prognosis of the individual's particular cadmium-related dysfunction/disease can be fully evaluated. Consequently, early detection of excess exposure to cadmium through medical surveillance and early action to prevent excess exposure is critical. The medical surveillance program and the MRP provisions in the cadmium standard were devised with early detection and early action in mind.

Cadmium is naturally excreted very slowly from the body. It is excreted slowly because rapid elimination of cadmium would risk overburdening and damaging the kidney. This fact has two implications. First, because of the risk of kidney damage arising from the rapid elimination of cadmium from the body, current methods of chelation are unsafe for reducing cadmium in the body. Second, since there is no safe way to accelerate the excretion of cadmium, natural elimination is the only means that can be relied upon to reduce body burden and even this may not be "safe" (Friberg, Ex. 29).

Temporary medical removal is an indispensable part of the cadmium standard for two major reasons. First, workers who have not already developed irreversible kidney damage can be protected by temporary medical removal. Second, more specifically in operations and industries where engineering controls cannot reduce airborne cadmium levels to the PEL and during the period when industries are in the process of implementing engineering controls, workers with higher exposures to cadmium will have to place increased reliance on respirators for protection. The protection afforded by respirators often will be less than would have been afforded by engineering controls and MRP may become necessary. Thus, MRP can provide additional protection when it is especially needed.

As indicated above, temporary medical removal is mandated in three sorts of cases. First, under paragraphs (l)(3)(ii)–(iv) and (l)(4)(iv), the employer must remove the employee whenever a physician, in his or her medical discretion, determines in a written medical opinion that the employee shall be removed. The requirement that the physician make such a determination is driven by biological monitoring results, but the determination itself may be based upon biological monitoring results, other evidence of illness, or any other reason deemed medically sufficient by the physician. However, as stated previously, it is not OSHA's intention that workers should be removed under the physician's discretionary removal authority simply because their biological monitoring results exceed the minimum trigger provided in paragraph (l)(3)(ii). Second, under paragraphs (l)(3)(iii)–(iv) and (l)(4)(iv), the employer also must remove the employee whenever:

(i) The employee's CdU exceeds 15 μg/g Cr; or CdB exceeds 15 μg/lwb; or the level of β_2-M exceeds 1500 μg/g Cr

and, in addition, the employee's CdU exceeds 3 μg/g Cr or CdB exceeds 5 μg/lwb, and these levels are confirmed as specified in paragraph (l)(3)(iii); or

(ii) Beginning on January 1, 1999, the employee's CdU exceeds 7 μg/g Cr, or CdB exceeds 10 μg/lwb, or the level of β_2-M exceeds 750 μg/g Cr and, in addition, the employee's CdU exceeds 3 μg/g Cr or CdB exceeds 5 μg/lwb, and these levels are confirmed as specified in paragraph (1)(3)(iv).

Thus, under paragraphs (l)(3)(ii)–(iv) and (l)(4)(iv) removal may be effected by a written medical determination in which the physician exercises medical discretion to decide whether to remove an employee. However, where the employee's biological monitoring results are confirmed to exceed the trigger levels set out in paragraphs (l)(3)(iii)–(iv) and (l)(4)(iv), that alone triggers mandatory medical removal, and there is no latitude within which the physician may exercise discretion.

The third case in which temporary medical removal is mandated is where the employee is exposed to cadmium above the PEL and a physician determines in a written medical opinion that the employee cannot wear a respirator (paragraphs (l)(6)(iii)-(iv) and (l)(11)(ii)). For any employee who is removed because of the employee's inability to wear a respirator, the employer under paragraph (l)(11)(i)(D) is required to provide follow-up medical examinations at least every six months until the examining physician in a written medical opinion determines that the employee either may be returned to his or her normal job or must be permanently removed from exposure to cadmium above the PEL. The follow-up examinations are to monitor the health status of the employee insofar as it may be relevant to the employee's ability to wear a respirator and to reassess that ability so that the decision to return the employee to his or her normal job or to permanently remove the employee from work with exposure to cadmium above the PEL can be made as expeditiously as is medically prudent.

For employees who are removed because they experience difficulty breathing during use of, or fit testing for, respirators, additional tests are required to medically evaluate the reasons for the employee's inability to wear a respirator, such as changes in cardiopulmonary function. For these workers, who were exposed to cadmium above the PEL prior to being found to be unable to wear a respirator, it is also prudent to monitor their possible overexposure to cadmium.

The specific requirements of MRP, set out in paragraph (l)(11) of this standard, are written to achieve all the purposes discussed above. Under paragraph (l)(11)(i), the employer must remove any employee from work where exposure to cadmium is at or above the action level on each occasion that the employee's relevant biological monitoring test results exceed any of the mandatory medical removal triggers specified in paragraphs (l)(3) or (l)(4) of the standard and on each occasion that a physician determines in a written medical opinion that the employee should be removed from such exposure. As stated above, the physician's determination may be based on biological monitoring results; evidence of illness, other signs or symptoms of cadmium-related dysfunction or disease; or any other reason, except inability to wear a respirator, deemed medically sufficient by the physician to indicate that the employee has a medical condition that places the employee at increased risk of material impairment to health from further exposure to cadmium at or above the action level.

The biological monitoring test results that provide the central criteria for removal are established in paragraphs (l)(3)(ii)–(iv) based on medical evidence that workers with results above these levels are at substantially increased risk of cadmium-induced illness and dysfunction. The levels that were selected as triggers for each of the progressively enhanced tiers of medical surveillance, and ultimately for medical removal, generally must be avoided to prevent an increasing risk of cadmium related dysfunction and disease. The decision to remove an employee with CdU, CdB or β_2-M at or below the mandatory removal levels is left to the discretion of the examining physician because he/she is best able to make that judgment based upon all the available medical evidence concerning the particular employee. However, when the employee's biological monitoring results are confirmed to exceed these trigger levels, the accompanying risk of significant adverse effects to the employee's health is enhanced, and the decision to medically remove becomes mandatory.

In most cases in which a worker is removed for medical reasons, the standard provides for removal from work having an exposure to cadmium at or above the 2.5 μg/m^3 action level on any day. This limitation on the level of cadmium to which a removed worker can be exposed was selected for three reasons: First, to assure that the removed worker would not be exposed to cadmium at a level high enough to further increase the risk to his or her health; second, to assure that the level of cadmium to which the removed worker might be exposed would be low enough to facilitate a net decrease in the employee's body burden of cadmium, with the aim of restoring normal levels of cadmium in the measured compartments of the body, so that the employee could be returned to his or her former job status; and third, where cadmium-induced disease or dysfunction has already occurred, to minimize further progression of the existing condition. Nevertheless, OSHA recognizes that situations may arise in which removal of workers to jobs with airborne cadmium exposure just below the action level would be inadequate to protect the worker's health. These situations can and should be dealt with by the examining physician on an individual basis in the course of a thorough medical examination conducted pursuant to the standard. Although the standard embodies the judgment that, at a minimum, all removed workers must be removed from work having an exposure to cadmium at or above the action level, it does not restrict a physician from recommending actions more protective than the standard's requirements where necessary to protect the health of individual workers.

As stated above, under paragraph (l)(11)(i)(D), employees who are medically removed must be given follow-up medical examinations every six months until in a written medical opinion the examining physician determines that the employee either may be returned to his/her former job status or must be permanently removed from cadmium exposure at or above the action level. It is important that employees on medical removal receive semiannual medical examinations. Because cadmium is excreted in the urine, which must pass through the kidney, the burden of cadmium in the employee's kidney is likely to increase for a time while the employee is on medical removal. Therefore, it is imperative that the employee's health, and in particular the employee's kidney function, diet, smoking habits, use of medication, and water intake, be strictly monitored throughout the natural process of reducing the amount of cadmium accumulated in the employee's body.

In general, the medical basis for returning the employee effectively is a finding by the physician that the employee no longer has a medical condition that places him or her at increased risk of material impairment to health from exposure to cadmium at or above the action level. However, for

employees who were removed because of abnormally high biological monitoring results, with the single exception set out in paragraph (l)(11)(v) which is discussed immediately below, no employee may be returned to a job where he/she will be exposed to cadmium at or above the action level until his/her biological monitoring results fall to or below the return trigger levels specified in paragraph (l)(11)(iv), that is, until CdU falls to or below 3 μg/g Cr, CdB falls to or below 5 μg/lwb, and β_2-M falls to or below 300 μg/g Cr. These levels are below levels at which the standard requires the examining physician to consider discretionary removal. Return of a removed employee is generally not permitted until the employee's biological monitoring results have fallen to low levels in order to assure that workers who have been removed because of overexposure to cadmium are not returned to significant exposure to cadmium until their body burden of cadmium is sufficiently low.

However, in paragraph (l)(11)(v), the standard does provide one narrow exception to this requirement. In rare cases, where in the physician's professional opinion continued exposure will not pose an increased risk to the employee's health (e.g., the potential decrements to the employee's kidney function are not projected to be any greater if the employee were permitted to continue on the job than they would be if the employee were removed) and there are special circumstances making continued medical removal particularly problematic for the employee, the examining physician in a written determination may return a worker to his or her former job status despite what would otherwise be unacceptably high biological monitoring results. OSHA recommends that the physician consider the use of this narrow exception for particular employees only after two quarterly biological monitoring results have been obtained after medical removal (i.e., no sooner than six months after the worker has been medically removed due to elevated biological monitoring results). Six months will provide a minimum period of time during which a physician must try to determine if existing damage is cadmium related, and if so whether such damage is permanent. In cases where the employee is permitted to return to work under this exception, the employee should continue to be medically monitored as if he/she were still on medical removal until such time as the employee's biological monitoring results have decreased to or below levels of CdU of 3 μg/g Cr, CdB of 5 μg/lwb, and β_2-M of 300 μg g Cr.

The purpose of this exception, which OSHA intends to be used with extreme care, is to provide some flexibility where it is reasonably clear that returning the worker to his/her normal job is unlikely to adversely affect the employee's health and the alternative to return is, for all practical purposes, much more drastic for the employee; e.g., termination of the employee from his job with loss of pension benefits. Depending upon the particular circumstances, a decision to return a worker with high biological monitoring results might be justified, for example, when an employee has been on medical removal for 18 months, is about to retire, and the time that the employee will continue to be occupationally exposed at or above the AL is very limited; e.g., a few months. When the physician does authorize return of the employee in such cases, the physician may require the employer to provide the employee with additional protection, such as a supplied air respirator operated in a positive pressure mode. In any event, the decision to return the employee should be made only after the physician has fully explained the relevant facts and prognoses to, and fully consulted with the employee.

As discussed above, under paragraphs (l)(6)(ii) and (l)(11)(ii), medical removal also is required whenever an examining physician determines in a written medical opinion that an employee cannot wear a respirator and must be removed from a job with exposures to cadmium above the PEL.

Under paragraph (l)(11)(i)(B), an employer who is required to medically remove an employee must do so regardless of whether at the time of removal a job is available into which the removed employee may be transferred. If no such job is available, the employer must, nonetheless, pay full MRP benefits to the employee even though the employee is effectively medically laid off. Initially, this might be costly to employers. However, after the initial adjustment period during which workers who were excessively exposed to cadmium prior to promulgation of this standard will have to be medically monitored and, where necessary, removed in accordance with the medical surveillance and MRP provisions of this standard, MRP costs should be quite low. The provisions of this standard requiring employers to control workplace airborne cadmium levels to the PEL, in conjunction with the tiered structure of enhanced medical surveillance and other ancillary provisions should prevent the vast majority of workers from being excessively exposed to cadmium. Consequently, on the one hand, employers who promptly come into compliance with the provisions of the standard should encounter very few workers who require temporary medical removal at any one time, and on the other, exposure levels in most jobs should be controlled to levels low enough so that removed workers may be transferred into those jobs. OSHA, therefore, expects employers to experience only a minimal economic impact from MRP after the initial adjustment period.

Paragraph (l)(11)(vi) deals with "voluntary" medical removals and limitations by employers. Where an employer, although not required by the standard to do so, removes an employee from exposure to cadmium or otherwise places limitations on the employee's exposure to cadmium because of the effects of cadmium exposure on the employee's medical condition, the employer must provide the employee with the same MRP benefits (MRPB) as if the removal had been required under paragraph (l)(11). The purpose of this paragraph is to prevent employers from avoiding the requirements of paragraphs (l)(11) and (12) by voluntarily removing employees for medical reasons before those paragraphs would otherwise require removal and payment of MRP benefits. Without this provision regarding voluntary removal, MRP, MRPB and medical surveillance might be subverted by the actions of unscrupulous employers.

Paragraph (l)(12) of this standard deals with MRP benefits. Under that paragraph, the employer is required to provide up to 18 months of MRP benefits to a worker on each occasion that he or she is medically removed from exposure to cadmium in accordance with paragraph (l)(11). As stated above, OSHA is requiring that MRP benefits be provided in response to workers' understandable fears that participating in the medical surveillance program required by the cadmium standard otherwise might lead to a loss of their jobs and job benefits. Although MRPB cannot entirely eliminate that possibility (e.g., where a worker has suffered irreversible damage to his or her health that requires permanent removal from exposure to cadmium), workers will be protected for a considerable time from loss of income, job, seniority and all other employee rights and benefits due to temporary medical conditions that may require their removal from exposure to cadmium at or above the

action level. Moreover, even for workers who must be permanently removed, MRPB protects the workers' wages and rights and benefits during the period needed to determine that permanent removal is required. Thus, MRPB largely removes an important disincentive to voluntary participation by employees in medical surveillance.

OSHA selected 18 months as the maximum period during which MRPB might have to be paid for several reasons. First, OSHA wanted to provide benefits for a period that was long enough so that the vast majority of removed employees who could be returned to their former job status would be able to be returned before their MRPB ran out. Second, the 18-month period for MRP benefits appears to have worked well in the lead standard (see 29 CFR 1910.1025 (k)(2)). Cadmium, like lead, is a heavy metal with a long half-life in the body.

OSHA believes that, with medical removal, elevated levels of CdU, CdB and β_2-M can be reduced over time to safe levels in many employees who have not been so overexposed to cadmium that they have suffered resulting permanent damage to their health. However, how long it will take for employees with elevated levels to return to safe levels is not precisely known. The amount of time needed will depend upon three interrelated factors: the employee's current burden of cadmium or level of β_2-M; the employee's rate of excretion of cadmium; and the extent of any continuing exposure to cadmium. The exact rate of natural excretion of accumulated cadmium from an employee's body, in turn, depends upon several factors, e.g., past and recent exposures, and body burden (Ex. 29). Since the half-life of cadmium in some compartments of the body is very long, and in most compartments is even longer than the half-life of lead in bone, i.e., 20 years (Ex. 8-668), OSHA has concluded that nothing less than the 18-month-MRPB period provided in the lead standard should be applied to cadmium exposed workers. This is a change from the cadmium proposal, which authorized a maximum of six months for MRP.

Based on its experience with MRP in practice in the lead standard, the toxicological similarities between lead and cadmium, and the best available evidence on cadmium, OSHA believes that most workers removed from significant exposure to cadmium who can be returned to their former job status because of "normal" biological monitoring results will be returnable within considerably less time than 18 months. According to De Silva, when exposures end, CdU and CdB levels fall during the first year (Ex. 8-716). Dr. Friberg stated that after cessation of exposure, cadmium concentrations in blood rapidly decrease with a half-time of two to three months (Ex. 29). This decrease is related to body burden. After the rapid decrease, CdB levels decrease more slowly depending upon recent and past exposures. Furthermore, in some cases a high urinary cadmium excretion may be seen after short-term exposures that have been very high, even without renal dysfunction (Ex. 29).

If examining physicians seek to prevent the onset of kidney disease by prudent early responses to protect workers, e.g., by temporarily removing a worker whose CdU level is well below, say, 10 $\mu g/g$ Cr from exposure to cadmium at or above the action level, nearly all such workers should be returnable well within 18 months. For those workers whose levels have not fallen into the "normal" or safe range within 18 months, OSHA expects that continued temporary removal typically will serve no useful medical purpose since the damage done to their health is likely to be beyond restoration.

More generally, the medical determination as to whether a removed employee may be returned to his or her former job status can only be made after a medical examination, which the employer is required to provide. The employer must continue to provide MRP benefits until a final medical determination is made that either the worker can be returned to his or her former job status and the worker is returned or the worker is incapable of ever safely returning to his or her former job status and the worker is permanently removed by a written medical determination from exposure to cadmium at or above the action level.

Former job status refers to the position the worker would likely be occupying if he or she had never been removed. For example, if, but for a temporary medical removal, a worker would now be working at the same position held just before removal, then the employer must return the worker to that job. Otherwise, the employer may return the worker to a job that is consistent with whatever job assignment discretion the employer would have had if no removal had occurred.

The standard also provides in paragraph (l)(12)(iv) that the employer may condition the provision of MRP benefits upon the employee's participation in medical surveillance. Thus, the standard does not directly mandate worker participation in medical surveillance, but rather permits the employer to deny economic protection to employees who are unwilling to participate in medical surveillance.

This may constitute a modification of a similar provision in paragraph (k)(2)(iii) of the lead standard. In that standard, the employer is expressly authorized to condition provision of MRP benefits upon an employee's participation in follow-up medical surveillance while the employee is medically removed. The express authorization in the cadmium standard authorizes the employer to condition provision of MRP benefits on an employee's participation in medical surveillance provided pursuant to this standard, whether that surveillance is prior to or during medical removal.

OSHA provides this authorization for several reasons. First, as indicated, one of OSHA's primary purposes in requiring the employer to establish a medical surveillance program pursuant to this standard is to prevent occupational disease associated with exposure to cadmium. This can be most effectively accomplished when all employees participate in medical surveillance, which can provide early warning signals and thereby minimize the risk of disease. If an employer conditions the availability of MRP benefits upon an employee's participation in medical surveillance generally, the employee will have strong incentive to participate. Within the bounds of reason and what is lawful under the OSH Act, OSHA supports efforts to encourage and facilitate employee participation in medical surveillance.

Second, since the employer must bear the financial burden of medical removal, the employer has a legitimate interest in minimizing the need for medical removal. But, unless employees participate in medical surveillance, the employer may not be able to identify who among them may require additional protective measures to reduce their exposure to cadmium before medical removal is indicated. Thus, if an employee does not participate in medical surveillance, an employer may not learn that the employee's absorption of cadmium is approaching dangerous levels until, for example, the employee becomes symptomatic or learns from some other source that certain of his biological parameters are elevated. At that point, the employer may be left with no alternative but to medically remove the employee.

In authorizing the employer to condition provision of MPR benefits upon an employee's participation in the medical surveillance required by this standard, OSHA does not intend to authorize the employer to deny MRP benefits for insignificant or irrelevant lapses in such participation. The employee's actions should be assessed reasonably, in light of the goal of prevention of disease and the employer's interest in minimizing the need for medical removal. So long as the employee's lapses in participation do not frustrate the goal of disease prevention and the employer's interest in gaining early warning that an employee may need to be medically removed if steps are not taken to reduce the employee's absorption of cadmium, the lapses do not constitute grounds for denial of medical removal protection benefits. Thus, for example, if an employee did not show up once or twice for scheduled medical surveillance or even if the employee did not participate for a substantial period of time in medical surveillance, so long as the employee's participation was timely enough for the employee and employer to be on notice that the employee's biological monitoring results and/or other signs and symptoms are indicative of an increased risk of cadmium associated disease, the employer is not authorized to deny MRP benefits. The point is that the authorization provided by this paragraph is not intended to be used as an excuse to wrongfully deny employees MRP benefits.

In paragraph (l)(12)(ii) of the standard, the MRP benefits that the employer is required to provide are the "total normal earnings, seniority, and all other employee rights and benefits" of a removed or medically limited worker as if the worker had not been removed or otherwise limited. The purpose of this requirement is to assure that a removed worker suffers neither economic loss nor loss of employment opportunities due to the removal. Thus, for example, if a removed employee typically earned overtime pay on the job from which he or she was removed and would have continued to do so during the removal period, then MRPB must include the amount of that overtime as part of the employee's "total earnings."

Under paragraph (l)(13), a multiple physician review (MPR) mechanism is included in the medical surveillance provisions of the final cadmium standard, which gives workers the opportunity to obtain a second and possibly a third opinion regarding medical findings, recommendations or determinations made pursuant to the standard. Although MPR was not included in the proposed cadmium standard, OSHA in that proposal expressly stated that it believed MPR "might be necessary and appropriate" and requested comments on the matter (55 FR 4115). Written comments and testimony were received on this issue (Ex. 29, Tr. 6/6/90, pp. 110–111; Exs. 19–43; 123). Most of the testimony and comments supported the need for including MPR in the final cadmium standard.

According to Dr. Friberg:

> * * * it would be very difficult for the industrial physician to come up with wise decisions * * * in all circumstances * * * a multi-medical evaluation could be of value as soon as there is any * * * decision that is of consequence for the worker (Tr. 6/6/90).

Opposition to MPR was based primarily on the assumption that the physician doing the examinations would be trained and experienced in occupational medicine and thus would be able to perform adequately (Ex. 77). However, if the first physician were not so trained and experienced, this commenter stated that MPR should be used as described by OSHA (Ex. 77, p. 6). OSHA agrees that MPR is needed in the final standard.

Under paragraph (l)(13), an employee may designate a second physician to review any findings, determinations or recommendations of an initial physician chosen by the employer and to conduct such examinations, consultations, and laboratory tests as the second physician may deem necessary. If a disagreement arises between the two physicians, the employer and employee are to assure that efforts are made to get the physicians to resolve their disagreement. However, should they be unable to agree, a third physician selected by the disagreeing physicians is authorized to review the evidence and conduct such tests, consultations and discussions as are necessary to resolve the disagreement. The employer is then required to act consistently with the decisions of the third physician, unless the employer and employee agree that the employer should act consistently with the decisions of one of the other two physicians.

OSHA recognizes the importance attached to medical surveillance by the OSH Act (Sec. 6(b)(5)) and views multiple physician review in the cadmium standard as an important element in the standard's medical surveillance program. That program, in turn, plays a crucial role in the operation of the standard's medical removal protection program. OSHA has three main reasons for providing MPR: First, to strengthen and broaden the bases for medical decisions made under the standard in situations where a worker questions the findings, recommendations, or determinations of an initial, employer-retained physician. Second, to increase employee confidence in the soundness of medical findings, recommendations and determinations made pursuant to this standard. And third, thereby, to increase employee acceptance of, and participation in the standard's medical surveillance program.

OSHA expects the provision of MPR, in interaction with other provisions of the cadmium standard, to strengthen and broaden the bases for medical decisions made under the standard. The requirement in paragraph (m) of the cadmium standard that the employer provide employees with appropriate information and training gives workers a basic opportunity to become knowledgeable about the nature and symptoms of the main cadmium-related diseases and about their rights under the cadmium standard. The availability of MPR, in turn, provides workers with an opportunity to put that knowledge to use through the informed exercise of their rights under MPR. MPR thus provides incentives to workers to take advantage of available health education and training to protect their own health. Consequently, when a worker questions the conclusions of the initial physician, a reasonable basis is likely to exist for seeking a second medical opinion.

Moreover, with the severe shortage of trained and experienced occupational physicians in this country and since cadmium-related diseases are not often encountered among persons not occupationally exposed to cadmium, it cannot be assumed that physicians performing examinations or consultations under the cadmium standard will provide error-free diagnoses. Under the medical surveillance program, physicians are often expected to exercise professional judgment and discretion, for example, in determining whether to remove a particular employee from exposure to cadmium at or above the action level. Although physicians are required by the standard to review its preamble and to be familiar with cadmium-related signs and symptoms of illness, these two provisions cannot guarantee that examining physicians will, in fact, be adequately trained or provide error-free diagnoses of cadmium-related diseases.

For many reasons, accurate medical determinations under this standard are vital for the proper functioning of the preventive medical removal protection

program and more generally for the success of the medical surveillance program as a whole. The standard's PEL by itself may not be low enough to assure that all employees will be free of a risk to their health from occupational exposure to cadmium. In addition, many cadmium exposed workers will have had years of exposure to high levels of cadmium by the time the standard is promulgated. Furthermore, some cadmium related diseases may be reversible if detected at an early stage.

In the interest of accuracy, it would not be inappropriate to provide multiple physician review in all cases of medical surveillance under the standard where there might be any question about the validity of the initial physician's findings, recommendations or determinations. However, rather than requiring additional medical opinions in all such cases, which would be very expensive and potentially wasteful, OSHA is providing an opportunity for the person primarily affected by the initial physician's medical opinion, the employee/patient, to seek the opinion of another physician if the employee seriously questions the findings, determinations or recommendations of the initial, employer-selected physician.

OSHA's choice of the multiple physician review mechanism, as distinct from other mechanisms, is based in part on the common and increasing use of multiple physician review in the formation of medical determinations in the society at large. For example, MPR is frequently relied upon in the determination of a worker's eligibility for a disability pension and as a precondition for coverage in insurance policies to confirm certain diagnoses. Multiple physician review also has been incorporated into other standards promulgated by OSHA, such as the lead and benzene standards (29 CFR 1910.1025 and 1028, respectively).

The multiple physician review mechanism incorporated in the cadmium standard shares characteristics in common with many of these other examples of MPR. The worker has an opportunity to select a second physician if dissatisfied with the opinions of the first employer-selected physician, and if the two physicians disagree, the employee and the employer, through their respective physicians, may select a third physician to resolve the difference of opinion.

OSHA's second reason for providing employees with the opportunity for multiple physician review is to enhance employee confidence generally in the medical surveillance program and specifically in the soundness of medical determinations made pursuant to this standard. The cadmium standard's ability to prevent material impairment to worker health and functional capacity, particularly with respect to kidney damage in long term cadmium workers, will depend substantially on workers' trust and confidence in examining physicians. OSHA adopted the multiple physician review mechanism as a means of providing workers with an opportunity to obtain independent review of the findings, recommendations, and determinations of physicians whose opinions they do not trust.

Over time, this independent review, where implemented, is likely to show either that distrust of the employer-retained physician is unwarranted or that the employer should improve the quality of the employer-provided medical surveillance. Unless the employer fails to adequately respond, in either case confidence in medical surveillance and in the examining physician is likely to be increased. For example, if workers distrust a company doctor and therefore repeatedly seek other physicians' opinions, but the diagnoses of the other physicians repeatedly confirm the opinions of the company doctor, then workers will be much more likely to trust the employer-retained doctor in the future. On the other hand, if the choice of second and third physicians repeatedly results in medical determinations greatly at variance with the opinions of the employer-retained physician, then the employer is put on notice that the employer-provided medical personnel may need to be changed. In both cases, the multiple physician review mechanism will have served a beneficial purpose, either by dispelling an unfounded distrust of the company doctor or by correcting inadequate medical determinations while exposing major deficiencies in the employer's medical surveillance program and generating pressure on the employer to make needed changes. With employee involvement in MPR, resulting improvements in the medical surveillance program, and increased employee confidence in that program, OSHA expects increased employee participation in medical surveillance.

The inclusion of multiple physician review in the cadmium standard is not intended as criticism of the general medical community. Based on the rulemaking record, OSHA has no cause to conclude that most employer-retained physicians are not sincerely devoted to the good health of their workers. However, there is evidence in the record indicating that more than a few doctors retained by companies may not be sufficiently protective in light of recent developments concerning the potential carcinogenicity of cadmium and the levels of CdB, CdU and β_2–M that are considered toxic or indicative of the existence, or high risk, of cadmium associated disease (Exs. 29; 77).

Multiple physician review is directed at problems presented by a minority of physicians, whose relevant medical knowledge may not be up to date, who may not be sufficiently sensitive to the health risks posed by excess exposure to cadmium, or who, in a limited number of cases, may not put the health of the workers first. In such cases, the opportunity for a second medical opinion is appropriate to protect the employee's health. On the other hand, where employer-retained physicians have a close doctor-patient relationship with employees and employees have confidence in the physicians' abilities and devotion multiple physician review will be seldom used (Swick, Tr. 7/18/90, p. 333).

The multiple physician review mechanism operates in a simple and straightforward fashion. It is applicable to all forms of medical surveillance provided under the standard after any initial examination or consultation provided by a physician chosen by the employer. If an employee's past, present, or future cadmium exposure is a relevant consideration in the examination or consultation being provided by the employer, then the opportunity for an additional medical opinion must be provided.

OSHA recognizes the value to employers and employees alike of the MPR mechanism operating in an expeditious fashion, and has established explicit requirements to that end. After an initial physician conducts an examination or consultation pursuant to the standard, the employer must promptly notify the employee of his or her right to seek a second medical opinion. This notification need be no more than an oral reminder of the existence and content of the right. After this notification has been given, an employer may condition its participation in, and payment for, MPR upon the employee, within 15 days after receipt of the employer's notification or receipt of the initial physician's written opinion, whichever is later, both informing the employer (orally or otherwise) that the employee intends to seek a second medical opinion and initiating steps to make an appointment with a second physician. These steps would include actually arranging an appointment or contacting a physician with the request

that a referral to a specialist be arranged.

The standard contains no limitation on an employee's choice of a second physician, except the implicit requirement that the second physician, like the initial physician, must be licensed to practice medicine. Since cadmium can adversely affect numerous systems of the body, it would be inappropriate to limit the choice of doctors to any one specialty. Because it is in the employee's interest to choose an informed and competent physician, OSHA relies on employee self-interest to assure the value of the second opinion. Where, for example, an employee's disagreement with the initial physician's opinion revolves around a particular organ, e.g., the kidney, the employee would be likely to choose a specialist in that area. Where, however, the dispute revolves around several health effects or the employee cannot identify one specific problem, the employee would be likely to choose the general practitioner or internist most familiar with the employee's medical history and current health status. The employer must provide all relevant materials to the second physician.

The standard provides that the second physician shall review any findings, determinations or recommendations of the initial physician, and may conduct such examinations, consultations and laboratory tests as the second physician deems necessary to facilitate this review. While the standard does not expressly require the employer to supply the second physician with the same information that must be supplied to the initial physician, as well as the first physician's findings, determinations or recommendations, that is the intention. Indeed, the employer's obligation under paragraph (l)(9) of this standard to provide information to the examining physician is intended to extend beyond the first examining physician to all physicians who may be involved in multiple physician review or alternate physician determination under paragraphs (l)(12) and (13), respectively. All of these physicians, thus, would be provided with the same background information supplied to the initial physician and, as a result, would have as good an opportunity to assess the employee's health status.

If the second physician's findings, determinations, and recommendations are the same as those of the initial physician, then the multiple physician review process comes to an end. If, however, the opinions of the two physicians are in conflict, then the employer and the employee shall assure that efforts are made for the two physicians to resolve any disagreement. OSHA expects that the two physicians, as professionals, will communicate with each other to resolve their differences, but the standard requires the employer and employee to encourage such a resolution. In most cases, this professional interaction among peers should resolve any differences between the two physicians.

In cases where differences of opinion remain, these differences are likely to be genuine and substantial. Where the first two physicians have been unable to expeditiously resolve any differences of opinion with respect to an employee, then it is necessary for a third qualified physician to resolve the dispute. It is important that this third physician have the confidence of those concerned and be competent to resolve the dispute. Consequently, the standard provides that the third physician shall be designated by the employer and the employee jointly through their respective physicians. It is the responsibility of the employer and the employee to assure that a third physician is selected, but the selection is to be made by the two physicians. Since the third physician is chosen by the joint endorsement of the two physicians, confidence in the professional competence of the third physician should be assured.

The standard provides the third physician a full opportunity to review the findings, determinations, and recommendations of the two prior physicians by conducting such examinations, consultations and laboratory tests as the third physician deems necessary. The standard incorporates the expectation that the third physician will consult with the other two physicians. The third physician should provide a written medical opinion to the employer, which will normally operate as a final medical determination to resolve the disagreement between the other two physicians. The employer, then, is required to act in a manner consistent with the findings, determinations, and recommendations of the third physician, unless the employer and the employee reach an agreement that is otherwise consistent with the recommendations of at least one of the other two physicians.

Medical surveillance pursuant to section 6(b)(7) of the Act must be provided by employers without cost to employees. Since multiple physician review will be one means by which medical surveillance is provided to an employee, employers must bear the expense of this mechanism when it is used. In practice, and based partly on experience with MPR in other OSHA standards, OSHA does not expect the costs of MPR to be burdensome to employers. Employers will have substantial control over the frequency of its use. Where employers establish and administer medical surveillance programs that merit, engender, and maintain worker confidence, workers will see little or no need to seek second medical opinions.

As with many of the provisions of the final cadmium standard, the success of the multiple physician review mechanism will largely depend upon employers and employees acting in a reasonable manner and with good faith.

The requirement for MPR, however, is not intended to preclude an employer from establishing and implementing medical protocols for its employees that are expeditious and at least as protective. In paragraph (l)(14) a provision for alternate physician determination is expressly included in the standard. Under that paragraph, the employer and employee or designated employee representative may agree upon the use of any expeditious alternate physician determination mechanism instead of the multiple physician review mechanism provided. The only condition is that the alternate mechanism be no less protective of the employee's health than MPR. For example, the parties might decide in cases of dispute for an employee to go directly from an initial physician chosen by the employer to an agreed upon final physician, thus dispensing with the need for a second physician. Alternately, a jointly-agreed-upon physician might be used in the first instance without recourse to other physicians. Or, an employee might be given the opportunity to choose the final physician. OSHA encourages employers and employees to adopt medical determination procedures in which all parties have trust and confidence. Paragraph (l)(14) of the standard embodies this intention.

Under paragraph (l)(15) of this standard, the employer is required to provide the employee with certain information. The employer, within specified time periods, must provide the employee with a copy of the physician's written medical opinion, a copy of the employee's biological monitoring results, and, upon request, a copy of the information the employer is required to provide to the examining physician under paragraph (l)(9) of this standard. In addition, as discussed below in connection with the summary and explanation of paragraph (n)(5), the employer is required to make the

employee's medical records available upon request to other specified individuals.

OSHA believes that, for the good of the employee, facts, findings and decisions regarding the employee's occupational exposure to cadmium and medical status generally should be provided to the employee in written form. This is to assure that the employee is aware, and has a record of the results of exposure assessments and medical examinations that reflect his or her workplace experience. Making this information available to the employee will enable the employee to better understand the central facts concerning his occupational exposure to cadmium, including the extent of his cumulative exposure, the effect of that exposure on his health status, and the employee's rights under the cadmium standard. Being better informed, in turn, will enable the employee to more effectively participate in decisions about his/her health. It will also enable the employee to better inform physicians who, years after the employment has terminated, may need to know such facts to correctly interpret, and make proper decisions to protect or improve the employee's health status.

Under paragraph (l)(16), the employer is required to report on the OSHA Form No. 200, The OSHA Injury and Illness Log, any abnormal condition or disorder caused by occupational exposure to cadmium. This reporting requirement is consistent with the reporting requirements of the Bureau of Labor Statistics in the Department of Labor, as specified in Chapter (V)(E) of the Reporting Guidelines for Occupational Injuries and Illnesses. Although not included in OSHA's proposed regulation, OSHA indicated in that document that a provision for such reporting might be useful and appropriate (55 FR 4115).

Requiring employers to report occupational illnesses on the OSHA Form No. 200 and to post on that form for one month a year the annual summary of occupational illnesses is authorized under sections (8)(c) (1) and (2), (8)(g)(2), and (24) (a) and (e) of the OSH Act and is mandated by 29 CFR part 1904. The required reporting on the OSHA Form No. 200 and posting of the annual summary of the year's total from that form provides employers and employees with an additional opportunity to review the relevant record of illnesses among cadmium-exposed workers.

For the employer, for example, it is an opportunity to review all the cadmium-related removals during the year as a group, in order to ascertain whether there are patterns to the removals. For example, employers might use such information to determine the number of removals in various areas of the plant to see if the particular removals are correlated with higher exposures. In this way, employers may be able to identify and focus attention on certain areas of the plant where medical removals due to cadmium over-exposures are especially frequent. For the employer, it also is a reminder of those workers who require medical follow-up. For employees who have been removed for cadmium-related illness, this is an opportunity to confirm that the information provided to them individually is correct and has been reported to OSHA.

In addition, reporting on the log abnormal conditions and disorders that are occupationally caused and cadmium related will facilitate the development of occupational health statistics that are useful to the employer, the employee, and to OSHA, and in turn may facilitate the development of improved medical care. It will also provide OSHA with information and data helpful in assessing the effectiveness of the cadmium standard and in considering what, if any, modification should be made to the standard in the future. For all of these reasons OSHA believes that this requirement is pursuant to the OSH Act.

OSHA also believes that compliance with this requirement will be simple for employers. OSHA further believes that requiring the reporting of such removals may contribute to the prevention of more serious kidney damage.

Communication of Cadmium Hazards to Employees: Paragraph (m)

In this final cadmium standard, OSHA includes provisions entitled: "Communication of Cadmium Hazards to Employees". These provisions incorporate many requirements from OSHA's Hazard Communication Standard (HCS) and address the issue of transmitting information to employees about the hazards of cadmium through the use of: (1) Signs, (2) labels, (3) material safety data sheets, and (4) information and training. Previous OSHA health standards generally included separate paragraphs on employee information and training and on signs and labels. The hazard communication provisions of this standard, consistent with the HCS, incorporate both of those areas, along with provisions on material safety data sheets (MSDS), into paragraph (m). The hazard communication provisions in this standard are very similar to those now being included in other OSHA health standards (e.g., paragraph (j), Benzene Final Standard, 29 CFR 1910.1028) and are basically the same as those in the proposed cadmium standard.

OSHA's HCS (29 CFR 1910.1200) for general industry requires all chemical manufacturers and importers to assess the hazards of the chemicals they produce or import and to develop appropriate information about those hazards, which they are required to communicate in various ways to their own exposed employees and to relevant downstream employers, as specified under paragraphs (d)–(h) of the Hazard Communication Standard (29 CFR 1910.1200). Downstream employers, in turn, are required to communicate the information concerning the hazards of such chemicals in various ways to their own employees. The transmittal of hazard information to employees is to be accomplished by means of comprehensive hazard communication programs, which must include container labeling and other forms of warning, material safety data sheets and employee training.

Since the HCS is intended to comprehensively assess the potential hazards of chemicals and to communicate the needed information concerning hazards and appropriate protective measures to employees (52 FR 31877, August 24, 1987), OSHA includes paragraph (m) entitled "Communication of Cadmium Hazards to Employees" in this standard while referencing and requiring compliance with 29 CFR 1910.1200. In paragraph (m), OSHA also proposes additional particular requirements that are needed to protect employees specifically exposed to cadmium.

Paragraph (m) of this standard has been designed to be substantively as consistent as possible with the HCS requirements for employers. While avoiding a duplicative administrative burden on employers attempting to comply with the requirements of several different applicable OSHA health standards, the requirements nevertheless provide the necessary protection for employees through provisions for signs and labels, material safety data sheets, and employee information and training.

The standard requires that regulated areas be posted with signs stating: "Danger, Cadmium, Cancer Hazard, Can Cause Lung and Kidney Disease, Authorized Personnel Only, Respirators and Protective Clothing Required in this Area". The posting of these signs will serve as a warning to employees who may otherwise not know they are entering a regulated area. Such warning signs are required to be posted at all

regulated areas, that is, whenever an employee is exposed above the permissible exposure limit. The signs are intended to supplement the training that employees are to receive under other provisions of paragraph (m), since even trained employees need to be reminded of the locations of regulated areas and of the precautions necessary to be taken before entering these dangerous areas.

For some work sites, regulated areas are permanent, because air cadmium exposures there cannot be reduced below the PEL by means of engineering controls. In those situations, the signs are needed to warn employees not to enter the area unless they are authorized, wearing respirators, and there is a need to enter. Regulated areas may also exist on a temporary basis, such as during maintenance and/or emergency situations. The use of warning signs in these types of situations is also important since a maintenance or emergency situation is by nature a new or unexpected exposure to employees who are regularly scheduled to work at or near these sites.

The standard requires that the signs comply with paragraph (f) of the HCS and specifies the wording of the warning signs for regulated areas in order to assure that the proper warning is given to employees. OSHA believes that the use of the word "Danger" is appropriate, based on the evidence of the toxicity and carcinogenicity of cadmium. "Danger" is used to attract the attention of workers in order to alert them to the fact that they are in an area where the permissible exposure limit is exceeded and to emphasize the importance of the message that follows. The use of the word "Danger" is also consistent with other recent OSHA health standards dealing with carcinogens. The standard also requires that the legend, "Respirators and Protective Clothing Required in this Area", be included on the warning sign. Although OSHA recognizes that some employees entering the regulated areas may not be exposed above the PEL, as an eight-hour time weighted average, many employees who are assigned to work in these areas may remain in these locations for long enough periods of time so that they would be needlessly overexposed to cadmium if they did not wear respirators and protective clothing.

In addition, it would be quite confusing and administratively complex to allow certain workers in the regulated areas to work without having to wear respirators while others were required to do so. Moreover, to the extent that some workers in regulated areas who may not be exposed on a particular day above the PEL are nonetheless required to wear respirators, this should further reduce any risk that may appear to remain at the PEL of 5 before the effects of the ancillary provisions are considered. To assure that all employees who work in regulated areas are adequately protected, it is necessary that the sign alert them to the need to wear respirators and protective clothing.

The standard also requires that warning labels be affixed to all shipping and storage containers (including bags) containing cadmium, cadmium compounds, or cadmium-contaminated items such as clothing and equipment. The labels must be in compliance with paragraph (f) of the HCS and must state: "Danger, Contains Cadmium, Cancer Hazard, Avoid Creating Dust, Can Cause Lung and Kidney Disease". Containers leaving the workplace must carry such labels. The purpose of this requirement is to assure that all affected employees, not only those of the primary employer, are apprised of the potentially hazardous nature of cadmium exposure where exposure could exceed the action level.

In addition to being consistent with the requirements of the HCS, these requirements carry out the mandate of section 6(b)(7) of the Act which requires OSHA health standards to prescribe the use of labels or other appropriate forms of warning to apprise employees of the hazards to which they are exposed.

In this final standard in accordance with the requirements of 20 CFR 1910.1200(g), OSHA also requires the manufacturer or importer of cadmium or cadmium compounds to develop and distribute MSDSs and requires downstream employers with employees potentially exposed to cadmium to maintain and provide access to a material safety data sheet (MSDS) for cadmium. OSHA feels that a properly completed MSDS, if readily available to employees, can serve as an excellent, concise source of information regarding the hazards associated with cadmium.

OSHA's main purpose in this section of the final standard, as stated in the Agency's recently promulgated HCS, is to assure that employees will receive as much information as they need concerning the hazards posed by chemicals in their workplaces. The MSDS assures that this information will be available to them in a usable, readily accessible and concise form. The MSDS also serves as the central source of information for downstream employers who must be provided with an MSDS if cadmium or a product containing cadmium in a toxic or potentially toxic form is produced and shipped to them. Lastly, the MSDS serves as the basic source of information on the hazards of cadmium essential to the training provisions of this standard.

Producers and importers of toxic substances have primary responsibility under the HCS to develop or prepare the MSDS. The manufacturer or importer is most likely to have the best access to information about the product and is therefore responsible for disseminating this information to downstream users of the material. For employers whose employees' exposure to cadmium is from products received from outside sources, the information necessary for a complete MSDS or the MSDS itself is to be obtained from the manufacturer and made available to affected employees. The requirements for the information that is to be contained on the MSDS are explained in detail at 29 CFR 1910.1200(g).

Paragraph (m)(4) of this cadmium standard requires employers to provide all employees who are exposed to cadmium with information and training on cadmium prior to or at the time of initial assignment to a cadmium exposed job and at least annually thereafter. A record shall be maintained of the contents of such programs (paragraph (n)(4)). The training program is to be in accordance with the requirements of the HCS paragraphs (h) (1) and (2), and to include the specific information required to be provided by that standard, as well as those items stipulated in paragraph (m)(4)(iii) of this standard. In particular, as several hearing participants have pointed out (Exs. 82, 84, and 107), training should explain how smoking cigarettes can increase an employee's total exposure to cadmium, either directly through inhalation of the cadmium in cigarettes or indirectly through ingestion of cadmium dust from the workplace that may accumulate on cigarette tips. Employers should also seriously consider whether to include information about smoking cessation programs in their training.

In addition, employees are to be provided with an explanation of the contents of appendices A (Substance Safety Data Sheet, Cadmium) and B (Substance Technical Guidelines, Cadmium) to this standard. Employees also are to be informed where a copy of the final cadmium standard is accessible to them and to receive an explanation of the purpose and a description of the medical surveillance program required under paragraph (l) of this standard.

OSHA has determined during other rulemakings that an information and training program, as incorporated in the

inclusive "Communication of Cadmium Hazards to Employees" paragraph of this standard, is essential to inform employees of the hazards to which they are exposed and to provide employees with the necessary understanding of the degree to which they themselves can minimize the health hazard potential. As part of an overall communication program for employees, training serves to explain and reinforce the information presented to employees on signs, labels, and material safety data sheets. These written forms of information and warning will be successful and relevant only when employees understand the information presented and are aware of the actions to be taken to avoid or minimize exposures.

Training is essential to an effective overall hazard communication program. Active employee participation in training sessions can result in the effective communication of hazard information to employees, which can stimulate workers to take conscientious protective actions on their jobs, which, in turn, can reduce the risk off occupationally-related illnesses and injuries.

The training provisions of this standard are in performance-oriented, rather than specific, detailed language. The standard requires training to be in accordance with the requirements of 29 CFR 1910.1200 and lists the categories of information to be transmitted to employees. However, it does not specify the ways that this is to be accomplished. The use of such performance-oriented requirements will encourage employers to tailor their training programs to the needs to their specific workplaces, thereby resulting in the most effective training program suitable for each specific workplace.

OSHA believes that the employer is in the best position to determine how the training he or she is providing is being received and absorbed by the employees. OSHA has therefore laid out the objectives to be met and the intent of training, to assure that employees are made aware of the hazards in their workplace and how they can help to protect themselves. The specifics of how this is to be accomplished are left up to the employer.

Comments by participants in the rulemaking on the hazard communication provisions of the proposed standard focused on three aspects of the proposed training requirements. The first is the need to train cadmium exposed workers about the dangers of smoking cigarettes. The second is the requirement that the employer provide training to all employees who are potentially exposed to cadmium, however low the level to which they might be exposed, instead of only to employees exposed above an action level. The third concerns the relationship between the training requirements in this standard and the MSDS provisions of the hazard communication standard.

The first concern is that all employees potentially exposed to cadmium be trained about the special hazards of smoking (Ex. 29). OSHA shares this concern and is requiring that employers train cadmium exposed employees about the additional exposure to cadmium from cigarette smoking. OSHA also suggests that employers seriously consider taking other steps, as well.

The second concern is that there should be an action level to trigger the employer's training requirement (Exs. 19–9; 19–36; Tr. 7/19/90, p. 284). OSHA disagrees with this position for several reasons. As demonstrated above, at very low levels of exposure cadmium is a probable human carcinogen and appears to cause kidney damage. If there is a threshold level below which exposure to cadmium does not cause kidney damage and below which it is not associated with lung cancer, that threshold must be extremely low, its exact level is unknown, and it undoubtedly varies from individual employee to individual employee. Moreover, OSHA's Hazard Communication (Haz Com) standard (29 CFR 1910.1200) already requires employers to provide employees with information and training on hazardous chemicals in the workplace without regard to any action level.

Nonetheless, for reasons set out above in the relevant sections of this preamble, OSHA has placed threshold exposure levels on the employer's obligation to implement engineering and work practice controls to achieve the PEL and to provide medical surveillance. However, since exposure to cadmium is not associated with any positive health effects and even at low levels has the potential for adverse health effects in some workers, OSHA believes that all potentially exposed employees should be informed about the nature of the hazard and about ways to minimize their exposure to it in order to facilitate their voluntarily taking preventive steps to protect themselves. In addition, training is needed at exposure levels below the action level since even at those low levels the possibility of skin or eye irritation caused by such cadmium exposure may exist.

Consequently, OSHA believes that it is good public health to require employers to train all employees potentially exposed to any level of cadmium. In imposing this obligation on employers OSHA is mindful of the fact that in most of the relevant workplaces the required training typically will involve adding elements to existing training programs and will not be very burdensome.

The third concern is that products containing less than .1% of cadmium, which are below the level that in the hazard communication standard would trigger the requirement that the producer or importer of a product containing a chemical identified as a carcinogen must develop and distribute companion MSDSs (29 CFR 1910.1200 (g)(2)(i)(C)(1)), might nonetheless produce downstream exposure levels above 1 $\mu g/m^3$ without the downstream employer being notified or even aware that his/her workers are exposed to cadmium (EEI, Tr. 7/19/92, pp. 19–20). This concern was articulated in response to OSHA's cadmium proposal, which proposed alternative PELs of 1 $\mu g/m^3$ or 5 $\mu g/m^3$ and alternative ALs of .5 $\mu g/m^3$ or 2.5 $\mu g/m^3$, respectively. However, this final standard adopts the higher of the proposed alternatives, 5 $\mu g/m^3$ as the PEL and 2.5 $\mu g/m^3$ as the action level. No commenter has claimed that products with a cadmium content of less than .1% can produce exposure levels at or above this action level or above this PEL.

Consequently the concern that employers who are not notified of the presence of cadmium by upstream producers or importers and are not aware of its presence in their workplace might still be subject to obligations triggered by cadmium exposures does not appear to be relevant to obligations triggered by the AL and PEL of this standard. The concern, thus, would be limited to the training requirement, which is the only obligation in this final standard that can be triggered by exposure to cadmium below the action level.

OSHA recognizes that there may appear to be some grounds for concern on this point. Under particular circumstances it might indeed be possible for an employer, while exercising due care, to be unaware of potential employee exposure to cadmium in the workplace and nonetheless vulnerable to citation for failure to train exposed workers under the cadmium standard. However, OSHA believes such situations will be very rare. The Agency is assured that in the vast majority of situations where workers are potentially exposed to cadmium, the employer will be aware or at least on notice of the existence of the hazard. The Agency is further assured

that in most of the remaining situations, when inspections do occur, OSHA inspectors will weigh all the circumstances and generally refrain from citing unknowing employers who in good faith and in the exercise of reasonable care failed to provide required training. In any event, OSHA concludes that the small risk that an unknowing and blameless employer might be cited for failure to provide required training is outweighed by the need for the Agency to be conservative in protecting workers' health in the face of potential exposure to a highly toxic substance like cadmium.

Recordkeeping: Paragraph (n)

The recordkeeping provisions of this final standard are essentially the same as those in the cadmium proposal, which received little or no public comment (55 FR 4117). These provisions generally are similar to recordkeeping provisions in other OSHA health standards.

The standard requires employers to maintain exposure monitoring records and medical surveillance records. This requirement is in accordance with section 8(c) of the Act, which authorizes OSHA to require employers to keep and make available such records as the Secretary may prescribe "as necessary or appropriate for the enforcement of this Act or for developing information regarding the causes and prevention of occupational accidents and illnesses." The recordkeeping provisions of this standard are also in keeping with the regulation governing access to employee exposure and medical records (29 CFR 1910.20).

Medical and monitoring records are also maintained for employee disclosure and are designed to provide valuable information to both the employee and the employer. The medical and monitoring records required by this standard will aid the employee and his/her physician in determining whether or not treatment is needed for occupational exposure to cadmium and what level of treatment is necessary. Also, the employer benefits by keeping these records, since the information will enable the employer to better ensure that employees are not being over-exposed to cadmium; such information may alert the employer that steps must be initiated in order to reduce exposures.

The standard requires that records be kept of the results of environmental monitoring and the contextual information required by paragraph (d) of this standard to determine the airborne concentration of cadmium to which an employee has been exposed. Specifically, records must include the following information:

(a) The date, duration, and results in terms of an 8-hour TWA of each sample taken;

(b) The name, social security number, and job classification of the employee monitored and of all other employees whose exposures the monitoring is intended to represent;

(c) A description of the sampling and analytical methods used and evidence of their accuracy;

(d) The type of respiratory protective device, if any, worn by the monitored employee and by any other employees whose exposures the monitoring is intended to represent; and

(e) A notation of any other conditions that might have affected the monitoring results.

The standard requires that exposure monitoring records be maintained for each measurement taken. The monitoring and record may represent the exposure of more than one employee if representative sampling, as described in paragraph (d), is conducted. In that case, the record should clearly provide the same information about the employees whose exposures the monitoring is intended to represent as is required by paragraph (n) of this standard for the monitored employee.

A provision for the use of objective data in place of initial monitoring is included in this standard in paragraph (d)(2)(iii). Objective data are defined in paragraph (n)(2)(i) as information demonstrating that a particular product or material containing cadmium cannot release dust or fumes in concentrations at or above the action level even under conditions of worst-case release. Employers might use data from an industry-wide survey to estimate maximum cadmium exposure levels that could occur if that survey pertains to workplace conditions that, to the extent relevant and significant, are all very similar to those in the employer's worksite. Employers may also use laboratory product test results to demonstrate that airborne concentrations must be below the action level.

In addition to being required to keep records on monitoring of employee environmental exposure levels, the employer is required by paragraph (n)(3) to establish and maintain an accurate medical surveillance record for each employee to whom the employer must provide medical surveillance under paragraph (l) of this standard. As indicated above in this preamble, medical records are necessary for the proper evaluation of the employee's health. Furthermore, medical records, like exposure monitoring records, are necessary and appropriate both to the enforcement of the standard and to the development of information regarding the causes and prevention of occupational illnesses.

The records of the employee's prior medical and work history are useful to the examining physician in the examination at termination of employment as an aid in determining the status of an employee's health and in identifying adverse health effects associated with cadmium exposure. Good medical records, including the record of the examination at termination of employment itself, also can be useful to the Agency and others in enumerating illnesses and deaths attributable to cadmium, in evaluating compliance programs, and in assessing the accuracy of the Agency's risk estimates. Such records are useful, as well, to assess the adequacy of the standard in preventing disease. Provisions for collection of such information, including medical examinations at the end of employment, have been included in other OSHA standards (e.g., Arsenic, Benzene, and Lead Final Standards).

The standard requires that exposure records be kept for at least 30 years ((n)(1)(iii)) and that medical records be kept for duration of employment plus thirty years ((n)(3)(iii)). It is necessary to keep these records for extended periods because of the long latency period commonly associated with carcinogenesis. Cancer often cannot be detected until 20 or more years after first exposure. The extended record retention period is therefore needed because diagnosis of disease in employees is assisted by, and in some cases can only be made by, having present and past exposure data as well as the results of present and past medical examinations.

The employer is also required to maintain records of an employee's cadmium-related training for one year beyond the last date of employment of that employee. Employers are required to certify that employees did participate in such training. Certification of training must contain the name of the employee, date training completed, and signature of employer or provider of the training.

The standard provides for access to exposure and medical records that basically is in accordance with 29 CFR 1910.20, OSHA's standard for "Access to Employee Exposure and Medical Records" under paragraph (n)(5)(i). That standard applies to records required by specific standards, such as this cadmium standard. In addition, it is OSHA's intention that the employee should have

similar access to exposure and medical records that are voluntarily created by an employer. Employees, their designated representatives, and former employees are, in general, allowed unrestricted access to all relevant exposure monitoring records. More limited access is provided for medical records. Access to all the employee's medical records required to be kept under paragraph (n)(3) of this standard is provided to the subject employee, to anyone having the subject employee's specific written consent, and, after the employee's death or incapacitation, to the employee's family members. In addition, OSHA and NIOSH retain access to both kinds of records, but the agencies' access to personally identifiable medical records is subject to agency rules of practice and procedure that have been published at 29 CFR 1913.10 (see 45 FR 35384) and to the limitations to protect confidentiality incorporated in 29 CFR 1910.20.

Upon written request, the employer is required to provide the records within 15 days to those entitled to them. The transfer of employee exposure monitoring and medical records is to be in accordance with the provisions of paragraph (h) of 29 CFR 1910.20. If an employer ceases to do business and there is no successor employer, the employer is to notify NIOSH and transmit the records to the Director of NIOSH for retention, if requested.

The purpose of requiring that certain medical information be made available only to someone with the employee's specific written consent is to assure that confidential medical information not be disseminated without a conscious and specific decision by the employee authorizing it. It is also to assure that persons or organizations appropriately authorized by the employee shall have access to such information. This might include, for example, a union, which, thereby, might be put on notice of potential health hazards in the workplace that might adversely affect the employee and other similarly situated workers.

Observation of Monitoring: Paragraph (o)

This standard contains provisions for employee observation of exposure monitoring. This is in accordance with section 8(c) of the OSH Act, which requires that employers provide employees and their representatives with the opportunity to observe monitoring of employee exposures to toxic substances or harmful physical agents. Observation procedures are set forth that require the observer, whether employee or designated representative, to be provided with the personal protective clothing and equipment that is required to be worn by employees working in the area. The employer is required to assure the use of such clothing, equipment, and respirators, and is responsible for assuring that the observer complies with all other applicable safety and health procedures.

Dates: Paragraph (p)

The standard will become effective on December 14, 1992. All obligations imposed by the standard commence on the effective date unless otherwise noted. All obligations that do not commence on the effective date shall be complied with as soon thereafter as possible and in any event no later than the start-up date, which is a compliance deadline.

Because small businesses frequently have fewer resources for interpreting and implementing complex requirements to protect their workers, and in order to implement an outreach program and to provide technical assistance to employers with small businesses [nineteen (19) or fewer employees], start-up dates for certain provisions are later for these establishments.

The requirements for initial exposure monitoring (paragraph (d)(2)) and for handwashing facilities (paragraph (j)(1)(ii)) must be completed no later than 60 days after the effective date of the standard (120 days for small businesses). The requirements for regulated areas (paragraph (e)) and respiratory protection (paragraph (g)), must be completed no later than 90 days after the effective date of this standard (150 days for small businesses). The requirements for initial medical examinations (paragraph (l)(2)), and employee information and training (paragraph (m)(4)), must be completed no later than 90 days after the effective date of this standard (180 days for small businesses).

In addition, written compliance programs (paragraph (f)(2)) shall be completed and available for inspection and copying no later than one (1) year after the effective date of the standard. Engineering and work practice controls (paragraph (f)(1)) generally are required to be fully implemented no later than two (2) years after the effective date.

Hygiene and lunchroom facilities must be completed as soon as possible and in any event no later than 1 year after the effective date. As stated above, handwashing facilities, permanent or temporary, must be provided in accordance with 29 CFR 1910.141 (d)(1)–(2) as soon as possible and in any event no later than 60 days after the effective date of this section (120 days for small businesses).

With the exception previously stated for small businesses, nearly all of the start-up dates established in this standard are conventional. They have been developed out of OSHA's experience with similar standards and closely parallel start-up dates in other health standards (e.g., Lead Final Standard). The start-up dates in this final standard also closely parallel those in the proposed cadmium standard (55 FR 4128).

Some minor modifications have been made to the proposal. For example, the effective date is 90 days after publication, rather than the proposed 60 days. OSHA decided to give employers slightly more time to comply with the standard. In addition, if employers do not now provide adequate handwashing facilities, they are required to provide adequate temporary or permanent facilities within 60 days after the effective date (120 days for small businesses). The proposal did not include any requirement for prompt provision of handwashing facilities. This omission was pointed out by a commenter, who correctly noted that portable sinks and other hygiene facilities can be readily provided (Ex. 19–7). OSHA agrees. It is important that workers be able to wash off any cadmium from their hands and faces before they eat, smoke and leave work. This will reduce their overall exposure to cadmium and limit the carrying of cadmium dust into their cars and homes. OSHA believes that most employers already provide handwashing facilities and that the cost of providing such facilities, where they are not already provided, is relatively modest.

There is, however, one more substantial change to the proposed start-up dates in this final standard. A provision that would have allowed employers in certain circumstances to delay constructing all hygiene facilities for nearly three years is deleted. During that period, employees would have been deprived of these facilities. The deletion is made for the same reason that the Agency in the final standard is requiring the prompt provision of handwashing facilities. OSHA is convinced that these facilities are needed to protect the health of workers' exposed to cadmium above the PEL.

Several commenters representing management requested, without providing adequate supporting evidence or data, that OSHA defer the start-up dates (compliance deadlines) for various provisions. One, for example, asked that the start-up date for initial monitoring

be 180, not 60, days after the effective date. The only reason provided for this request was the possible shortage of industrial hygienists (Ex. 19–9). OSHA declines to defer this start-up date for several reasons. First, there is no evidence of, or reason to believe there will be a shortage of industrial hygienists. Second, since the standard now sets the effective date at 90, instead of 60, days after promulgation, all employers will have more time to prepare for compliance. In addition, small businesses will have 120 days after the effective date for initial monitoring. This should allow an employer concerned about a possible shortage of industrial hygienists to contact one well in advance of the compliance deadline and arrange for timely initial monitoring.

Another commenter argues that an extended period of time is needed to design, construct and learn how to operate engineering controls, that start-up dates for all other provisions of the standard should be set after the deadline for compliance with the engineering and work practice controls requirement, and that time be provided for phasing in biological and air monitoring sampling and MRP (Ex. 19–40). As stated above, OSHA believes that the compliance times provided in the staggered start-up dates are reasonable and that no additional time is needed to come into compliance with the various requirements. Employers generally will have two years from the effective date of the standard to implement engineering controls to achieve the PEL and to achieve the SECAL. Deferring all other start-up dates until after the deadline for achieving the PEL or SECAL would allow employees who are currently exposed to excessive levels of cadmium and not otherwise adequately protected, for example, by an effective medical surveillance program, to continue to be unnecessarily exposed and unprotected.

The Dry Color Manufacturers Association (DCMA) argues that time also is needed to standardize biological and environmental monitoring methods and to set up a laboratory accreditation program to assure the quality of analysis of monitoring results (Exs. 120, 19–40). OSHA agrees that some time is needed for employers to familiarize themselves with the requirements of medical surveillance, to develop appropriate methods to comply with the requirements, especially with regard to biological monitoring, and to locate laboratories with demonstrated proficiency in the relevant analyses. As a guide to employers and others, OSHA has devoted considerable effort to developing a non-mandatory program concerning standardization of specimen collection and handling and laboratory proficiency which is incorporated in appendix F. The Agency believes employers who follow this protocol, or other comparable criteria that are at least as comprehensive and strict, will be assured that employee monitoring results are accurate and reliable and will generally be in compliance with paragraph (l)(1)(iv) of the standard.

OSHA is aware that a number of laboratories already have demonstrated their proficiency in analyzing CdU and CdB and that the Phaedabas kit is widely accepted as assuring reasonably accurate and reliable measurements of β_2-M. (See Health Effects Section V.) Consequently, OSHA sees no reason why employers will be unable to comply with the provisions relating to biological monitoring by the relevant start-up date, which is 90 days after the effective date of the standard (180 days for small businesses). The Agency is considering establishing mandatory provisions for laboratory proficiency and accreditation.

Appendices: Paragraph (q)

The final cadmium standard contains six appendices that are designed to assist employers and employees in implementing the provisions of this standard. Appendix C is incorporated as part of this standard and imposes additional mandatory obligations on employers covered by this standard. Appendices A, B, D, E and F are non-mandatory, except that appendices A, D, and F must be reviewed by physicians in order for them to be able to medically evaluate employees covered by this standard regarding any cadmium-related illnesses. Also, questions 3–11 and 25–32 of appendix D are required as part of the limited medical examination that is required prior to the use of a respirator. Otherwise, these appendices are not intended to add to, or detract from any obligation that the cadmium standard otherwise imposes.

The Appendices that are included in the standard are:

Appendix A—Substance Safety Data Sheet, Cadmium
Appendix B—Substance Technical Guidelines, Cadmium
Appendix C—Qualitative and Quantitative Fit Testing Procedures
Appendix D—Medical and Occupational History with Reference to Cadmium Exposure (suggested format)
Appendix E—Sampling and Analysis
Appendix F—Protocol for Laboratory Standardization for Biological Monitoring for Cadmium

IX. Summary and Explanation of the Final Standard (Construction Industries)

OSHA believes that, based on currently available information in the cadmium rulemaking record, the requirements set forth in this final rule are necessary and appropriate to provide adequate protection to employees exposed to cadmium.

Based upon the record evidence in this rulemaking (Exs. 8–665; 14–5; 53), OSHA has developed a cadmium standard for the construction industry that is somewhat modified from the standard for general, agriculture, and maritime industries, which is being published separately (29 CFR 1910.1027). However, most of the provisions in this standard are the same as those in the general industry standard, and most of the reasons and supporting evidence for the provisions are also the same. Consequently, this preamble generally relies upon and hereby incorporates by reference the preamble to the general industry standard, where and to the extent relevant. Thus, explanations for particular provisions in this standard generally are not repeated in this preamble for provisions that are the same or essentially the same as those in the general industry standard. The complete discussion of these provisions can be found in the summary and explanation of parallel requirements in the general industry standard in the preamble to that standard.

The language of the standard and the order of the various provisions are consistent with drafting in other recent OSHA health standards, e.g., the Asbestos Construction Standard (29 CFR 1926.58). OSHA believes that a similar style should be followed from standard to standard to facilitate uniformity of interpretation of similar provisions. Modifications made to the cadmium general industry standard were in response to the particular conditions in the construction industry.

(a) Scope

This final cadmium standard for the construction industry applies to all occupational exposure to cadmium and all cadmium compounds, in all forms, including fume and dust, and in all construction work where an employee may potentially be exposed to cadmium. Such work is defined as work involving construction, alteration and/or repair. Such work includes but is not limited to: Wrecking, demolition or salvage of structures where cadmium or materials containing cadmium are present; use of cadmium containing-paints and cutting, brazing, burning, grinding or welding on

surfaces that were painted with cadmium-containing paints; construction, alteration, repair, maintenance, or renovation of structures, substrates, or portions thereof, that contain cadmium, or materials containing cadmium; cadmium welding; cutting and welding cadmium-plated or cadmium alloy steel; brazing or welding with cadmium alloys; installation of products containing cadmium; electrical grounding with cad-welding, or electrical work using cadmium-coated conduit; maintaining or retrofitting cadmium-coated equipment; cadmium contamination/emergency cleanup; and transportation, disposal, storage, or containment of cadmium or materials containing cadmium on the site or location at which construction activities are performed. The standard, as modified herein for the construction industry, covers all occupational exposures to cadmium, because there may be serious health consequences to any person who is occupationally exposed to cadmium. The risk from exposure to cadmium is dependent on the extent of exposure and not on the segment of industry where the employee may be employed. OSHA estimates that approximately 70,000 employees are potentially exposed to cadmium in the construction industry (Table VIII–A1, Office of Regulatory Analysis, Regulatory Impact Assessment Section). This is slightly more than 1% of the 5,000,000 construction workers and about 13% of all 525,000 workers potentially exposed to cadmium in all industry segments.

Under the Construction Safety Act (40 U.S.C. 333), 29 CFR 1911.10 and 29 CFR 1912.3, OSHA consults with the Advisory Committee on Construction Safety and Health (ACCSH) regarding the formulation of regulatory proposals that have significant or unique application to employment in construction. In accordance with that Act, OSHA in mid-1989 consulted with ACCSH. At the time, and with the Advisory Committee's approval, the Agency planned to protect construction workers within the standard for general industry. At its meeting on September 13, 1989, ACCSH recommended that OSHA publish a separate cadmium standard for the construction industry in 29 CFR part 1926, with certain provisions of the general industry standard tailored, as necessary, to the particular conditions in construction. The Advisory Committee established a working group to develop comments on the cadmium proposal and to consider what, if any, modifications to the general industry standard were reasonably necessary and appropriate to protect construction workers from cadmium exposure.

OSHA discussed these matters with the Construction Advisory Committee and agreed to place whatever final cadmium standard was applicable to the construction industry in 29 CFR part 1926. On February 6, 1990 in its notice of proposed rulemaking (55 FR 4052), OSHA proposed to include the construction industry in the cadmium standard for general industry. However, the Agency also gave express notice in that document that the final standard for construction would be published in part 1926. OSHA also gave notice that the Advisory Committee's comments and other record evidence might lead the Agency in the cadmium rulemaking to promulgate a standard for the construction industry that might be different in some respects from the standard to be promulgated for general industry [29 CFR 1910.1027]. OSHA expressly requested the public and interested parties to provide information and comments on how, if at all, the proposed cadmium standard should be modified if a distinctive standard for the construction industry were to be developed out of the unitary proposal (55 FR 4053).

Based upon the record evidence in this rulemaking, including pre-hearing comments submitted by the Advisory Committee concerning special working conditions in the construction industry, testimony at the public hearing by a representative of the Committee, and the draft of recommended modifications to the proposed rule submitted by the Committee (Exs. 8–665; 14–5; 53), OSHA has developed a separate and somewhat modified cadmium standard for the construction industry, 29 CFR 1926.63.

The only important issue raised in the rulemaking concerning the scope of the proposed cadmium standard was whether the standard should apply to the construction industry, as well as general industry. Several commenters favored covering the construction industry in the general industry standard (Exs. 19–8; 19–21; 57; Tr. 7/17/90, pp. 51–217). However, a representative of OSHA's Advisory Committee on Construction Safety and Health testified in opposition to extending the general industry standard to construction and in favor of a construction-specific standard that would address the unique conditions in that industry (Tr. 6/13/90; pp. 4–16).

OSHA agrees with the Advisory Committee that such a standard is needed. Thus, OSHA is publishing this separate standard for the construction industry that is comparable to the general industry standard but adapted to the particular conditions of the construction industry. The primary concern reflected in the comments favoring inclusion of the construction industry within the scope of the general industry standard is that construction workers be assured prompt and adequate protection from excess exposure to cadmium. OSHA believes that this can be accomplished more effectively by promulgation of a comparably protective, construction-specific standard, in conjunction with the promulgation of a general industry standard that excludes the construction industry.

A full discussion of the scope provision is provided in the summary and explanation of the general industry standard.

Definitions

Paragraph (b).

Action level. The final standard retains the same definition of "action level" (AL) incorporated in the proposal for the permissible exposure limit (PEL) of 5 $\mu g/m^3$. The action level is defined as an airborne concentration of cadmium of 2.5 $\mu g/m^3$, calculated as an 8-hour, time-weighted average.

The action level provides the airborne concentration of cadmium at or above which medical surveillance, air monitoring, and the provision of a respirator to any employee who requests one are required. Other requirements of the standard are not triggered until exposures exceed the PEL. Where exposures are determined to be below the action level, no compliance activities are required of the employer, except those required by paragraphs (d)(4), (m)(3) and (m)(4) of this standard for hazard communication. A full discussion of the issues related to the action level is included in the summary and explanation of the general industry standard.

Competent person, in accordance with 29 CFR 1926.32(f), means a person designated by the employer to act on the employer's behalf who is capable of identifying existing and potential cadmium hazards in the workplace and the proper methods to control them in order to protect workers, and who has the authority necessary to take prompt corrective measures to eliminate or control such hazards. The duties of a competent person under this standard shall include at least the following: Determining prior to the performance of work whether cadmium is present in the workplace; establishing, where necessary, regulated areas and assuring

that access to and from those areas is limited to authorized employees; assuring the adequacy of any employee exposure monitoring required by this standard; assuring that all employees exposed to air cadmium levels above the PEL wear the appropriate personal protective equipment and are trained in the use of appropriate methods of exposure control; assuring that proper hygiene facilities are provided and that workers are trained to use those facilities; and assuring that the engineering controls required by this standard are implemented, maintained in proper operating condition, and functioning properly.

In comments made to OSHA (Ex. 57), the Advisory Committee on Construction Occupational Safety and Health (ACCSH) and its Task Force on cadmium requested that OSHA include the definition of a competent person, as defined in 29 CFR 1926.32(f), and that OSHA outline the duties and responsibilities of that competent person in the cadmium standard for the construction industry. OSHA recognizes the need for a competent person in construction. Safety and health problems on a construction site are sufficiently complex and unique to justify requiring the employer to appoint an identifiable "competent person" who is on site to act on the employer's behalf in this regard. For example, multiple employers may be working on different projects at a particular worksite or in adjacent worksites, as part of the same overall construction job. As a result, actions by one employer on the worksite may subject employees of other employers to occupational hazards.

Moreover, hazards on construction jobs may vary according to environmental conditions (e.g., open air exposure, confined spaces), workforce turnover, the processes involved and the frequency and duration of exposures. The ACCSH Task Force identified specific jobs, (e.g., welder, painter, electrical worker) and specific tasks (e.g., brazing/burning/welding surfaces that were painted with cadmium prior to 1970) in which cadmium exposures were expected to be high and therefore needed to be carefully monitored. The Task Force indicated that cadmium exposures in the construction industry typically are short-term and intermittent, although some jobs periodically may involve long-term chronic exposures. However, the Task Force also indicated that no accurate exposure data were available regarding the average length of exposure per week, exposure levels, and worker turnover in various job categories. Consequently, there is an obvious need for site characterization and analysis by a competent person who is able to identify the hazards present and the types of control measures that are effective.

Site characterization is a continuous process because of changing environmental and work conditions as a construction job is being completed. At each phase of site characterization, information must be obtained and evaluated to define the potential hazards on the site. That information must be collected and evaluated by a person designated to represent the employer and who is capable of identifying and controlling hazards. For these reasons, OSHA agrees with the ACCSH Task Force and is including this definition of a competent person (Exs. 14–5; 57).

Employee exposure is defined as the exposure to airborne cadmium that would occur if the employee were not using respiratory equipment. This definition is intended to apply to all variations of the term "employee exposure" that have essentially the same meaning, such as "exposed employee" and "exposure". The definition is consistent with OSHA's previous use of the term in other standards.

Final medical determination is the physicians written medical opinion of the employee's health status. Under paragraphs (l)(3)-(l)(12), the written medical opinion of the examining physician is the "final medical determination." Where either multiple physician review or the alternative physician determination mechanism has been invoked under paragraph (l)(13) or (l)(14), respectively, the final medical determination is the final, written medical finding, determination or recommendation that emerges from that process.

The terms "*Assistant Secretary*", "*authorized person*", "*Director*", "*high-efficiency particulate absolute [HEPA] air filter*", and "*regulated area*" are defined in this final standard essentially as proposed. These definitions are based on OSHA's previous experience and are consistent with OSHA's use of these terms in other health standards. These definitions generally have not been commented upon. The employers' obligations with respect to HEPA filters and regulated areas are discussed later in this preamble. In the discussion of regulated areas a clarification in the final standard is explained.

Permissible Exposure Limit (PEL)

Paragraph (c).

Employers are required to assure that no employee is exposed to an airborne concentration of cadmium in excess of the permissible exposure limit (PEL) of 5 micrograms of cadmium per cubic meter of air ($\mu g/m^3$). A full discussion of this is included in the summary and explanation of the general industry standard.

Exposure Monitoring

Paragraph (d).

This final standard imposes monitoring requirements pursuant to section 6(b)(7) of the OSH Act (29 U.S.C. 655), which mandates that any standard promulgated under section 6(b) shall, where appropriate, "provide for monitoring or measuring of employee exposure at such locations and intervals, and in such manner as may be necessary for the protection of employees." To this end, as discussed below, OSHA has made four significant changes to the monitoring requirements included in the cadmium standard for general industry.

First, prior to the performance of any construction work where employees may be potentially exposed to cadmium, the employer is required by paragraph (d)(1)(i) to establish the applicability of this standard by determining whether cadmium is present in the workplace and whether there is a possibility that an employee may be exposed to cadmium at or above the AL. The employer must designate a competent person to make this determination. Investigation and material testing techniques are to be used, as appropriate, in the determination. Investigation should include a review of relevant plans, past reports, material safety data sheets, and other available records, and consultations with the property owner and discussions with appropriate individuals and agencies. Material testing techniques may include a "spot test analysis" designed for geochemical applications, i.e., for rigorous and sensitive analyses of cadmium content in complex matrices, which was reviewed by ACCSH and may be used for on-site identification of the presence of cadmium (Ex. 14–5).

In comments to OSHA, the Task Force specifically indicated that in the construction of new buildings or structures, any cadmium that is to be used will be specified on the blueprints and contracts used in developing the plans of that construction activity. In these cases, the presence of cadmium at a particular worksite will be known prior to the initiation of any work (Ex. 14–5). However, in the case of wrecking and demolition, or retrofitting and repair

of existing equipment, such information may not be available. In the latter case, prior to the initiation of any work, it must be determined whether cadmium is present at the worksite. For that purpose, the investigation and material testing techniques, discussed above, may provide information about the presence, location, and extent of cadmium (Ex. 14–5).

Under paragraph (d)(1)(i), where cadmium has been determined to be present in the workplace, and the possibility that some employee will be exposed at or above the AL has been established, the competent person is to identify employees potentially exposed to cadmium at or above the action level. This identification may be based upon any information, observations, or calculations that would indicate employee exposure to cadmium, including any previous measurements of airborne cadmium. As indicated in the definition section of this standard, employee exposure is the exposure to airborne cadmium that would occur if the employee were not using a respirator.

Under paragraph (d)(2)(1) (i) and (ii), and except as provided for in paragraph (d)(2)(iii), where an employee has been identified as potentially exposed to cadmium at or above the action level, the employer must conduct initial exposure monitoring as soon as practicable that is representative of the exposure for each employee in the workplace who is or may be exposed to cadmium at or above the action level. In certain circumstances, sampling each employee's exposure to cadmium may be required for initial monitoring. However in many cases, the employer under paragraph (d)(1)(iv) may monitor selected employees to determine "representative employee exposures."

Second, under paragraph (d)(2)(ii), if the employee periodically performs tasks that may expose the employee to a higher concentration of airborne cadmium, the employee must be monitored while performing those tasks. This provision was added to this standard because employees in the construction industry are more likely than in general industry to perform such tasks. The provision only makes express an obligation to monitor that is implicit in the general industry standard. The competent person should assure that any exposure monitoring required by this standard is performed adequately.

Under paragraph (d)(3)(i), if the initial monitoring or periodic monitoring reveals employee exposures to be at or above the action level, the employer shall monitor at a frequency and pattern needed to assure that the monitoring results reflect with reasonable accuracy the employee's typical exposure levels, given the variability in the tasks performed, work practices, and environmental conditions on the job site, and to assure the adequacy of respiratory selection and the effectiveness of engineering and work practice controls.

Third, unlike the general industry standard for cadmium, no minimum frequency for monitoring is required by this standard. That is because the nature of much construction work and the changing nature of the job and work conditions would often limit the value of periodic monitoring on a fixed schedule, e.g., semi-annual monitoring. For example, for the many jobs that run less than six months, it would make no sense to require the employer to monitor at least every six months. Moreover, for tasks that are performed episodically in the course of a job, semi-annual monitoring also would be of questionable value.

Fourth, under paragraph (d)(5)(i), no later than five working days after the receipt of the results of any monitoring performed under this section, the employer shall notify each affected employee individually in writing of the results and shall post the results in an appropriate location that is accessible to affected employees. This is a change from the general industry standard, which allows the employer 15 days to notify the affected employee of his/her monitoring results. OSHA concluded that a shorter notice period would be appropriate for the construction industry in light of the short term nature of many construction jobs.

The changes in the language of the general industry standard basically follows the recommendations of the ACCSH Task Force on cadmium (Ex. 57). A full discussion of the monitoring requirements in this standard can be found in the summary and explanation of the general industry standard.

Regulated Areas

Paragraph (e).

Under paragraph (e)(1) and (e)(2), whenever an employee exposed to cadmium is or can reasonably be expected to be in excess of the permissible exposure limit (PEL), the employer is required to establish a regulated area that is adequately demarcated and alerts employees of its boundaries and that protects employees from airborne exposures in excess of the PEL. OSHA recommends that the employer consider establishing regulated areas wherever the following construction activities are conducted: Electrical grounding with cad-welding; cutting, brazing, burning, grinding or welding on surfaces that were painted with cadmium-containing paints; electrical work using cadmium-coated conduit; use of cadmium containing paints; cutting and welding cadmium-plated steel; brazing or welding with cadmium alloys; fusing of reinforcing steel by cadmium welding; maintaining or retrofitting cadmium-coated equipment; and wrecking and demolition where cadmium is present. A full discussion of regulated areas is provided in the summary and explanation of the general industry standard.

Methods of Compliance

Paragraph (f).

Under paragraph (f)(1)(i), the employer is required to implement engineering and work practice controls to reduce and maintain employee exposure to cadmium at or below the PEL, except to the extent that the employer can demonstrate such controls are not feasible. Under paragraph (f)(1)(ii), the requirement to implement engineering controls to achieve the PEL does not apply where the employer demonstrates that no employee is exposed above the PEL on 30 or more days per year by the employer and that any employee who is exposed above the PEL on 29 or fewer days is only exposed intermittently, by which OSHA means that the employee is effectively not exposed to cadmium on any more than 29 days.

The provisions in paragraph (f)(1) are basically the same as those in the cadmium standard for general industry. However, unlike the general industry standard, there is no provision in this standard for a separate engineering control air limit (SECAL), because there appears to be no need in the construction industry for such a higher engineering-and-work-practice-control limit. No comment was received on the need for a SECAL in any construction sector during the rulemaking. Consequently, employers in the construction industry, like the vast majority of employers covered by the general industry standard (Ex. 13), will have to implement engineering and work practice controls, to the extent feasible, to control air cadmium levels to the PEL. The other provisions in paragraph (f)(2)–(3) also are in general agreement with the general industry standard.

However, under paragraphs (f)(2)–(3), several construction-specific modifications were added to the general industry standard. First under (f)(2)(i), abrasive blasting on cadmium or cadmium-containing materials is to be

conducted in a manner that will provide adequate protection. Second under paragraph (f)(2)(ii), heating cadmium and cadmium-containing materials and welding, cutting, and other forms of heating of cadmium or cadmium-containing materials shall be conducted in accordance with the requirements of 29 CFR 1926.353 and 29 CFR 1926.354, where applicable.

Third, under paragraph (f)(3)(i), in cases where cadmium exposures will be above the TWA PEL, high speed abrasive disc saws or similar abrasive power equipment, such as power grinders, rotary peening machines, needle guns, power brushes, and power sanders, must be equipped with appropriate engineering controls to minimize emissions. In cases in which the exposure level is uncertain, the employer or the designated competent person should determine the exposure level.

Fourth, under paragraph (f)(3)(ii), materials containing cadmium should not be applied by spray methods if the resultant exposures are above the TWA PEL, unless employees are protected with appropriate respirators, i.e., supplied-air respirators with full facepiece, hood, helmet, suit, operated in positive pressure mode, and unless specific measures are instituted to limit overspray and prevent contamination of adjacent areas. In those cases in which exposure levels are uncertain, the employer or designated competent person should determine whether exposures from such operations will be at or below the TWA PEL.

According to comments submitted to OSHA (Ex. 14–5, 10/13/89), cadmium is now considered to be a contaminant in coatings in the construction industry. That is, cadmium is only found in "microscopic" quantities, and for all practical purposes is not applicable in construction activities that involve new coatings. However, cadmium is a component of coatings applied prior to 1970, and OSHA is particularly concerned about the health hazards to workers who handle such coatings. According to industry comments, about twenty years ago, cadmium was used, at times, as a substitute and supplemental filler-pigment, in conjunction with lead in primers and other heavy metal pigmented coatings. However, as a result of the lead regulations and the cost of the use of multi-metal pigments, their use was discontinued.

Therefore, the ACCSH Task Force focused its comments on the relevance of the cadmium standard to activities that involve remodeling or renovation projects. In cases where old coatings are removed, primary concern would be where at least two-three coats of primer on steel had been applied, prior to 1970, to a thickness of 15/1,000th of an inch. If "old" primer is to be burned off, complete burning should be carried out in such a manner so as to control cadmium exposures to levels that are at or below the TWA PEL (Ex. 14–5, 10/13/89).

The employer's obligation in paragraph (f)(5) of this standard concerning a compliance program is similar to the obligation in the general industry standard. It requires the employer, where employee exposure is above the PEL, to establish and implement a written compliance program to reduce employee exposure to or below the PEL. However, there are three ways in which the obligation under this standard differs somewhat from the obligation in the general industry standard. First, since specific elements of the written plan required in the general industry standard might prove burdensome and inappropriate in construction jobs and industries, no specific elements of the plan are required by this standard. Nonetheless, OSHA recommends that such plans include as many of the elements required in the general industry standard as are appropriate. Second, the compliance plan must be established and implemented, to the extent appropriate, prior to beginning the job. Because countless construction jobs will be undertaken after promulgation of this standard, OSHA has made explicit the obligation to establish and implement a compliance plan prior to commencing work. In fact, the same obligation is implicit in the general industry standard for plants that are opened subsequent to the promulgation of that standard.

Under paragraph (f)(5)(ii), written compliance programs must be reviewed and updated as often and as promptly as necessary to reflect significant changes in the employer's compliance status or where it was infeasible to achieve the PEL exclusively by engineering and work practice controls, to reflect significant changes in the lowest air cadmium level that is technologically feasible. However, under paragraph (f)(5)(iii), a competent person is to review the comprehensive compliance program initially and after each change. OSHA believes it is important that the compliance program, which is the overall plan for protecting workers from occupational hazards, be carefully reviewed by a competent person. Under paragraph (f)(5)(iv), written compliance programs are to be submitted upon request for examination and copying to the Assistant Secretary, the Director, affected employees, and designated employee representatives.

To control the hazards associated with cadmium exposure, primary reliance in this standard is still placed upon engineering controls and work practices, which is consistent with good industrial hygiene practice (Tr. 7/17/90; pp. 56, 77; Exs. 19–8; 19–21) and with the Agency's traditional adherence to a hierarchy of controls that prefers engineering and work practice controls over reliance upon respirators. The primary reliance upon engineering and work practice controls is also supported by some employers and company doctors (Exs. 19–31; L–19–57; 118; 19–2). However, OSHA is aware that in the construction industry there are likely to be a considerable number of situations in which engineering controls are not feasible. A complete discussion of methods of compliance can be found in the summary and explanation of the preamble to the cadmium standard for general industry.

Respiratory Protection

Paragraph (g).

This final standard adopts the proposed respiratory protection provisions with little or no substantial modification and is basically the same as the cadmium standard for general industry. The provisions of this standard are in keeping with requirements for respiratory protection in other OSHA health standards (Lead 29 CFR 1910.1025; Benzene 29 CFR 1910.1028), recent developments in the field, and OSHA's revision of the generic standard on respiratory protection (29 CFR 1910.134).

Respirators are necessary as supplementary protection to reduce employee exposure when engineering and work practice controls cannot achieve the necessary reduction to or below the PEL. Respirators may also be necessary at other times, for example: While engineering and work practice controls are being implemented, during emergency situations, during intermittent exposures under the 30-working day exclusion when engineering and work practice controls are not required, and for brief or intermittent exposures that cannot be controlled through engineering and work practice controls. A respirator also must be provided by the employer for all authorized employees in regulated areas.

Because of the risk of serious adverse health effects from cadmium exposures, OSHA accepts the need for requiring respirators in the above mentioned circumstances in order to reduce an

employee's cumulative dose of cadmium.

Table 2 lists the type of respirator to be used at each airborne concentration of cadmium in the workplace. The standard requires fit testing of all respirators to assure at least a minimally acceptable fit. It is also important that all employees who wear respirators be medically screened to determine employee fitness for respirator usage.

Paragraph (l)(6)(ii) of this standard, therefore, generally requires that medical examinations be made available to workers with a job that requires the use of a respirator prior to assignment to that job. A complete discussion of this respirator provision can be found in the summary and explanation of the preamble to the cadmium standard for general industry. That discussion is fully applicable to the requirements in paragraph (g) of this standard because they are the same as the parallel requirements in the general industry standard.

Emergency Situations

Paragraph (h).

To deal with emergency situations, the employer must develop and implement a written plan for emergency situations involving substantial releases of airborne cadmium. This provision basically tracks the proposed cadmium standard and is the same as the cadmium standard for general industry. A fuller discussion of this provision can be found in the summary and explanation of the parallel provision in the preamble to the general industry standard.

Protective Work Clothing and Equipment

Paragraph (i).

This final standard, with few substantial modifications, adopts the requirements of the proposed cadmium standard and is basically the same as the general industry standard regarding protective clothing and equipment. These requirements are typical of other OSHA health standards and are based upon widely accepted principles and conventional practices of industrial hygiene.

Clean protective clothing and equipment shall be provided by the employer at least weekly, and more often as necessary to assure its effectiveness, to each affected employee and at no cost to the employee. OSHA recommends that clean protective clothing be provided at least daily for employees with exposure to cadmium at levels approaching or exceeding 100 $\mu g/m^3$. Removal of cadmium from protective clothing by blowing, shaking, or any other means that disperse cadmium into the air is prohibited.

A complete discussion of this paragraph regarding protective clothing and equipment can be found in the summary and explanation of the preamble to the cadmium standard for general industry. That discussion is fully applicable to the requirements in this standard because they are essentially the same as the parallel requirements in the general industry standard.

Hygiene Areas and Practices

Paragraph (j).

This final standard, like the proposal, requires employers to provide employees exposed to cadmium above the PEL with hygiene and lunchroom facilities and to assure employee compliance with basic hygiene practices to minimize additional potential sources of exposure to cadmium. With the exception of the start-up date, in paragraph (p), below, the requirements in this standard are essentially the same as those in the parallel provision in the cadmium standard for general industry.

OSHA believes it is essential for employees to have separate locker and storage facilities for street and work clothing to prevent cross-contamination of their street clothes. This provision will minimize employee exposure to cadmium after the work shift ends, because it reduces the period during which they may be exposed to cadmium-contaminated work clothes.

A complete discussion of this paragraph regarding hygiene facilities and practices can be found in the summary and explanation of the preamble to the cadmium standard for general industry. That discussion is fully applicable to the requirements in this standard.

Housekeeping

Paragraph (k).

Like other OSHA health standards dealing with toxic dusts or fibers (Asbestos, 29 CFR 1910.1001), this cadmium standard imposes the general housekeeping requirement to maintain all surfaces as free as is practicable of accumulations of cadmium.

These housekeeping provisions are exceptionally important because they minimize additional sources of exposure that engineering controls generally are not designed to control. Good housekeeping is a cost effective way to control employee exposure levels by removing from the worksite cadmium dust that can become reentrained by air currents and carried into employee breathing zones.

A complete discussion of this housekeeping provision can be found in the summary and explanation of the preamble to the cadmium standard for general industry. That discussion is fully applicable to the requirements in paragraph (k) of this standard because they are the same as the parallel requirements in the general industry standard.

Medical Surveillance

Paragraph (l).

(l) *General.* The medical surveillance provisions of paragraph (l) in this standard generally are similar to the general industry standard with the following exceptions:

(1) Under paragraph (l)(1)(i)(A), as requested by the ACCSH Task Force (Ex. 57), all employees who perform the following tasks, operations or jobs are automatically covered by the medical surveillance provisions of this standard, unless the employees are exposed to cadmium on less than 30 days per year: Electrical grounding with cad-welding; cutting, brazing, burning, grinding or welding on surfaces that were painted with cadmium-containing paints; electrical work using cadmium-coated conduit; use of cadmium containing paints; cutting and welding cadmium-plated steel; brazing or welding with cadmium alloys; fusing of reinforcing steel by cadmium welding; maintaining or retrofitting cadmium-coated equipment; and wrecking and demolition where cadmium is present. The ACCSH Task Force recommended that workers performing these tasks or jobs be included in medical surveillance because those workers generally will be exposed to significant levels of airborne cadmium and because ACCSH thought that they therefore should not have to await the results of exposure monitoring to be included in medical surveillance. In addition, all workers exposed at or above the action level are covered unless the employer demonstrates that the employees are exposed above the action level on fewer than 30 days per year (12 consecutive months).

(2) Under paragraph (l)(1)(i)(B), employers must also provide medical surveillance to all employees who might have been exposed to cadmium by the employer prior to the effective date of this standard in tasks specified under paragraph (l)(1)(i)(A), unless the current employer demonstrates that the employee did not in the years prior to the effective date of this standard work in those tasks for the employer for an aggregated total of more than 12 months prior to the effective date of this standard.

This provision, to extend medical surveillance to veteran employees who previously were potentially exposed to relatively high levels of cadmium but no longer are exposed to cadmium in sufficient amounts to make them otherwise eligible for medical surveillance, is similar to the parallel provision in the cadmium standard for general industry.

The only difference is that the minimum aggregate total of previous exposure in this standard is lower than in the general industry standard. The total is lower for two reasons. First, it is believed that many employees who performed in the specified tasks typically were exposed to cadmium at levels considerably above the AL, which is all that is required by the general industry standard. With a higher expected average daily dose, the duration of exposure should be shortened to assure adequate surveillance. Second, in light of employment conditions in the construction industry, such as high turnover and mobility of employees, OSHA believes that requiring that the employee have worked for the employer in the named tasks for much longer than 12 months to be eligible for medical surveillance would make it likely that many veteran construction workers with considerable past exposure to cadmium would not be covered by medical surveillance.

This 12 month minimum requirement in the performance of specific tasks is similar to a parallel provision for inclusion of workers exposed prior to the effective date of the benzene standard (29 CFR 1910.1028, paragraph (i)(1)). In the Benzene standard, the only other OSHA health standard to cover veteran employees who were exposed prior to the effective date of the standard, "veteran" workers who performed a specific task, e.g., tire building, or were exposed above a specific exposure level during one year were included under medical surveillance. The determination of an employee's prior exposure to cadmium must be, where relevant, reasonable, and practical, based on the employee's previous exposure records, first measurements taken of that employee after the effective date of this section, and on comparisons with employee exposure records in the same or similar operations, where the engineering controls, cadmium containing materials, and other relevant working conditions are the same or similar.

(3) In part because of the transient nature of much construction work and employment, deadlines for employer action or earlier deadlines than in the general industry standard are established in this standard. For example, under paragraph (l)(5) of this standard, the employer must reassess employee exposures within 30 days; by contrast, in the general industry standard no deadline is specified. The time period is specified in the construction standard to address the need for prompt action addressed in the testimony of the Construction Advisory Work Committee on Cadmium (Exs. 14–5; 53).

With regard to medical removal protection (MRP) and medical removal protection benefits (MRPB), paragraphs (l) (11) and (12), the provisions in this standard are the same as the parallel provisions in the cadmium standard for general industry. However, because of the different employment conditions in the construction industry, the provisions may impact quite differently in this industry.

In both standards, MRP and MRPB generally assure that an employee who is medically removed from his/her job for cadmium related reasons will be no worse off in terms of wages and employment benefits and rights than if the employee had not been removed. However, under neither standard would MRP and MRPB put the removed employee in a better position than he/she would have been in had the employee not been removed. Thus, if a removed employee's job comes to an end while he/she is on medical removal, the medical removal benefits also come to an end, even if the period for which the employee has been removed is less than the 18-month maximum authorized under this standard. In theory, this is as true under the standard for general industry as under the construction standard. But in practice, this fact is likely to have greater impact in the construction industry, where many jobs and much employment is short-term and the turnover rate among many construction workers is relatively high.

Other provisions in the medical surveillance program remain unchanged from the cadmium standard for general industry. A complete discussion of the medical surveillance provision can be found in the summary and explanation of the preamble to the cadmium standard for general industry. That discussion is fully applicable to the many requirements in paragraph (l) of this standard that are the same or essentially the same as the parallel requirements in the general industry standard.

Communication of Cadmium Hazards to Employees

Paragraph (m).

In this final cadmium standard paragraph (m) incorporates the employer's requirements to communicate to employees about the hazards of occupational exposure to cadmium. These hazard communication provisions are generally the same as those in other OSHA health standards (e.g., paragraph (j), Benzene Final Standard, 29 CFR 1910.1028) and for general industry. However, in a multi-employer workplace, an employer who produces, uses, or stores cadmium in a manner that may expose employees of other employers to cadmium is required by paragraph (m) to notify the other employers of the potential hazard in accordance with paragraph (e) of the hazard communication standard for construction, 29 CFR 1926.59.

This is consistent with OSHA's Hazard Communication Standard (29 CFR 1926.59) for the construction industry which requires all chemical manufacturers and importers to assess the hazards of the chemicals they produce or import and to develop appropriate information about those hazards, which they are required to communicate in various ways to their own exposed employees and to relevant downstream employers, as specified under paragraphs (d)–(h) of the Hazard Communication Standard ((HCS); (29 CFR 1926.59)). Downstream employers, in turn, are required to communicate the information concerning the hazards of such chemicals in various ways to their own employees. The transmittal of hazard information to employees is to be accomplished by means of comprehensive hazard communication programs, which must include container labeling and other forms of warning, material safety data sheets and employee training.

The Cadmium Standard, for example, requires that regulated areas be posted with appropriate warning signs. For some work areas regulated areas are permanent, because air cadmium exposures persist there and cannot be reduced below the PEL by means of engineering controls. Perhaps more important for construction work, the nature of which (and the hazards associated with it) may change dramatically in the course of completing a project, regulated areas may also need to be established on a temporary basis. This might be so during intermittent operations, maintenance and/or emergency situations. The use of warning signs in these types of

situations is especially important since employees who are regularly scheduled to work in or near these areas need to be warned about new or unexpected exposure to cadmium at levels above the PEL.

A complete discussion of the hazard communication provision in this standard can be found in the summary and explanation of the preamble to the cadmium standard for general industry. That discussion is fully applicable to the many requirements in paragraph (m) of this standard that are the same or essentially the same as the parallel requirements in the general industry standard.

Recordkeeping

Paragraph (n).

The recordkeeping provisions of this final standard are essentially the same, except where indicated, as those in the final cadmium standard for general industry and the cadmium proposal, which received little or no public comment. These provisions generally are similar to recordkeeping provisions in other OSHA health standards.

Two provisions in paragraph (n) are different from those in the general industry standard. First, under (n)(iv), the employer must provide a copy of the results of an employee's air monitoring prescribed in paragraph (d) of this standard to an industry trade association and to the employee's union, if any, or, if either of such associations or unions do not exist, to another comparable organization that is competent to maintain such records and is reasonably accessible to employers and employees in the industry. This is to assure that, in an industry with much short-term employment, relatively high rates of worker turnover, and mobile job sites and employees, employers and employees have ready access to a relatively stable back-up source of air monitoring records, if needed.

Second, under paragraph (n)(3)(iv), the employer is required upon request by an employee to provide a copy of the employee's medical record or update, as appropriate, to a medical doctor or union specified by the employee. This requirement also is to assure that, in an industry with much short-term employment, relatively high rates of worker turnover, and mobile job sites and employees, employees have a relatively stable, designated backup source for obtaining their medical records, if needed.

OSHA recognizes that over the years employees may change construction jobs many times, work for many employers, and be exposed to cadmium at various levels and for different durations. OSHA further recognizes that some diseases that may be associated with excess exposure to cadmium, like lung cancer, may take many years to manifest themselves. Over such long periods, employees may misplace or lose records in their possession from earlier times. OSHA is therefore attempting in paragraphs (n)(1)(iv) and (n)(3)(iv) to establish at minimum cost to all concerned some alternative, more stable source of this records.

A complete discussion of the record keeping provision in this standard can be found in the summary and explanation of the preamble to the cadmium standard for general industry. That discussion is fully applicable to the many requirements in paragraph (n) of this standard that are the same or essentially the same as the parallel requirements in the general industry standard.

Observation of Monitoring

Paragraph (o).

This standard contains provisions for employee observation of exposure monitoring. This is in accordance with section 8(c) of the OSH Act, which requires that employers provide employees and their representatives with the opportunity to observe monitoring of employee exposures to toxic substances or harmful physical agents. Observation procedures are set forth that require the observer, whether employee or designated representative, to be provided with the personal protective clothing and equipment that is required to be worn by employees working in the area. The employer is required to assure the use of such clothing, equipment, and respirators, and is responsible for assuring that the observer complies with all other applicable safety and health procedures.

This provision is the same as the parallel provision in the cadmium standard for general industry. A complete discussion of the requirements of paragraph (o) in this standard can be found in the summary and explanation of the preamble to the general industry standard.

Dates

Paragraph (p).

The standard will become effective on December 14, 1992. All obligations imposed by the standard commence on the effective date unless otherwise noted. All obligations that do not commence on the effective date shall be complied with as soon thereafter as possible and in any event no later than the start-up date, which is a compliance deadline.

Because small construction businesses frequently have fewer resources for interpreting and implementing complex requirements to protect their workers, and in order to implement an outreach program and to provide technical assistance to employers with small businesses (nineteen (19) or fewer employees), start-up dates for certain provisions of the standard are later for these establishments.

The requirements for initial exposure monitoring (paragraph (d)(2)) and for hygiene facilities (paragraph (j)) must be completed no later than 60 days after the effective date of the standard (120 days for small construction businesses). The requirements for the permissible exposure limit (paragraph (c)), regulated areas (paragraph (e)) and respiratory protection (paragraph (g)), must be completed no later than 90 days after the effective date of this standard (150 days for small businesses). The requirements for initial medical examinations (paragraph (l)(2)), written compliance programs (paragraph (f)(5)(ii), and employee information and training (paragraph (m)(4)) must be completed no later than 90 days after the effective date of this standard (180 days for small businesses). The start-up dates for hygiene facilities other than handwashing facilities and for lunchroom facilities is considerably shorter in this standard than in the cadmium standard for general industry. This is because OSHA believes that most such facilities in the construction industry will be rented or purchased and will be mobile and will require no substantial amount of time for the employer to design, construct or install them.

In addition, the start-up date for compliance programs also is considerably shorter in this standard than in the cadmium standard for general industry. This is because OSHA believes that compliance with the PEL in the construction industry generally will be achieved by respirators, in conjunction with off-the-shelf, portable engineering controls, which require little or no time for the employer to design, manufacture or install. It also is because so many construction jobs are short term jobs.

Engineering and work practice controls generally are required to be fully implemented no later than 120 days after the effective date (240 days for small businesses). Work practice controls are to implemented as soon as possible. OSHA assumes that most engineering controls in the construction industry are of the off-the-shelf, portable

variety and need not be specially designed, manufactured or elaborately installed.

With the exception previously stated for small construction businesses, nearly all of the start-up dates established in this standard are conventional. They have been developed out of OSHA's experience with similar standards and closely parallel, start-up dates in other health standards (e.g., Lead Final Standard). The start-up dates in this final standard generally also closely parallel those in the proposed cadmium standard. The primary exceptions are discussed in the preamble to the general industry standard. In addition, the effective date of this standard is 90 days after publication of this final standard, rather than the proposed 60 days. OSHA is providing 90 days in order to give employers slightly more time to prepare to comply with all the obligations that take effect on and after that date.

Appendices

Paragraph (q).

The final cadmium standard contains six appendices that are designed to assist employers and employees in implementing the provisions of this standard. Appendix C is incorporated as part of this standard and imposes additional mandatory obligations on employers covered by this standard. Appendices A, B, D, E, and F are non-mandatory, except that appendices A, D, and F must be reviewed by physicians in order for physicians to be licensed to medically evaluate any cadmium-related illnesses. Also, questions 3–11 and 25–32 of appendix D are required as part of the limited medical examination that is required prior to the use of a respirator. Otherwise, these appendices are not intended to add to, or detract from any obligation that the cadmium standard otherwise imposes.

The Appendices that are included in the standard are:

Appendix A—Substance Safety Data Sheet, Cadmium
Appendix B—Substance Technical Guidelines, Cadmium
Appendix C—Qualitative and Quantitative Fit Testing Procedures
Appendix D—Medical and Occupational History with Reference to Cadmium Exposure (suggested format)
Appendix E—Sampling and Analysis
Appendix F—Non-mandatory Protocol for Laboratory Standardization for Biological Monitoring for Cadmium

X. Authority and Signature

This document was prepared under the direction of Dorothy L. Strunk, Acting Assistant Secretary of Labor for Occupational Safety and Health, U.S. Department of Labor, 200 Constitution Ave., NW., Washington, DC 20210.

Accordingly, pursuant to sections 4(b), 6(b), 8(c), and 8(g) of the Occupational Safety and Health Act of 1970 (U.S.C. 655, 657), 29 CFR part 1911 and Secretary of Labor's Order No. 1–90 (55 FR 9033); Construction Work Hours and Safety Standard Act (Construction Safety Act), 40 U.S.C. 333; the Longshore and Harbor Workers' Compensation Act, 33 U.S.C. 941; and 29 CFR part 1911, 29 CFR parts 1910, 1915, 1926 and 1928 are amended as set forth below.

Signed at Washington, DC, this 31st day of August, 1992.

Dorothy L. Strunk,

Acting Assistant Secretary for Occupational Safety and Health.

XI. Final Standard (General, Maritime, and Agriculture Industries)

PART 1910—[AMENDED]

PART 1915—[AMENDED]

Part 1910 and 1915 of title 29 of the Code of Federal Regulation is hereby amended as follows:

1. The authority citation for subpart B of 29 CFR part 1910 is revised to read as follows:

Authority: Secs. 4, 6 and 8 of the Occupational Safety and Health Act, 29 U.S.C. 653, 655, 657; Walsh-Healey Act, 41 U.S.C. 35 et seq.; Service Contract Act of 1965, 41 U.S.C. 352 et seq.; sec. 107, Contract Work Hours and Safety Standards Acts (Construction Safety Act), 40 U.S.C. 333; sec. 42, Longshoremen's and Harbor Workers' Compensation Act, 33 U.S.C. 942; National Foundation of Arts and Humanities Act, 20 U.S.C. 951 et seq.; Secretary of Labor's Order No. 12–71 (36 FR 8754); 8–76 (41 FR 25059), 9–83 (48 FR 35736) or 1–90 (55 FR 9033), as applicable; and 29 CFR part 1911.

Sections 1910.16 and 1910.19 also issued under 29 CFR part 1911.

2. The authority citation for subpart Z of part 1910 continues to read as follows:

Authority: Secs. 6, 8 Occupational Safety and Health Act, 29 U.S.C. 655, 657: Secretary of Labor's Orders 12–71 (36 FR 8754), 8–76 [41 FR 25059), 9–83 (48 FR 35736) or 1–90 (55 FR 9033), as applicable; and 29 CFR part 1911.

All of subpart Z issued under section 6(b) of the Occupational Safety and Health Act, 29 U.S.C. 655(b) except those substances listed in the Final Rule Limits columns of Table Z–1–A, which have identical limits listed in the Transitional Limits columns of Table Z–1–A, Table Z–2 or Table Z–3. The latter were issued under section 6(a) (29 U.S.C. 655(a)).

Section 1910.1000, the Transitional Limits columns of Table Z–1–A, Table Z–2 and Table Z–3 also issued under 5 U.S.C. 553. § 1910.1000, the Transitional limits columns of Table Z–1–A, Table Z–2 and Table Z–3 not issued under 29 CFR part 1911 except for the arsenic, benzene, cotton dust, and formaldehyde listings.

Section 1910.1001 also issued under Sec. 107 of Contract Work Hours and Safety Standards Act, 40 U.S.C. 333.

Section 1910.1002 not issued under 29 U.S.C. 655 or 29 CFR part 1911; also issued under 5 U.S.C. 553.

Sections 1910.1003 through 1910.1018 also issued under 29 U.S.C. 653.

Section 1910.1025 also issued under 29 U.S.C. 653 and 5 U.S.C. 553.

Section 1910.1028 also issued under 29 U.S.C. 653.

Section 1910.1043 also issued under 5 U.S.C. 551 et seq.

Sections 1910.1045 and 1910.1047 also issued under 29 U.S.C. 653.

Section 1910.1048 also issued under 29 U.S.C. 653.

Sections 1910.1200, 1910.1499 and 1910.1500 also issued under 5 U.S.C. 553.

3. The authority citation for part 1915 is revised to read as follows:

Authority: Sec. 41, Longshore and Harbor Workers Compensation Act (33 U.S.C. 941); secs. 4, 6, 8 Occupational Safety and Health Act of 1970 (29 U.S.C. 653, 655, 657); Secretary of Labor's Order No. 12–71 (36 FR 8754), 8–76 (41 FR 25059), 9–83 (48 FR 35736) or 1–90 (55 FR 9033), as applicable; 29 CFR part 1911.

Section 1915.99 also issued under 5 U.S.C. 553.

Part 1910 Subpart B—[Amended]

§ 1910.19 [Amended]

4. A new paragraph (k) is added to § 1910.19 to read as follows:

§ 1910.19 Special provisions for air contaminants.

* * * * *

(k) *Cadmium.* Section 1910.1027 shall apply to the exposure of every employee to cadmium in every employment and place of employment covered by § 1910.16 in lieu of any different standard on exposures to cadmium that would otherwise be applicable by virtue of those sections.

Part 1910 Subpart Z—[Amended]

§ 1910.1000 [Amended]

5. In 1910.1000, Table Z–1–A, the entries "Cadmium fume * * * 0.1 mg/m^3 * * * 0.3 mg/m^3" and "Cadmium dust * * * 0.2 mg/m^2 * * * 0.6 mg/m^3" are removed and replaced with the following entry added in the substance column: "Cadmium; see 1910.1027. See Table Z–2 for the exposure limits for any operations or sectors where the exposure limits in § 1910.1027 are stayed or otherwise not in effect."

6. In § 1910.1000, Table Z–2, a footnote superscript "4" is added after the entries "Cadmium fume (237.5–1970)" and "Cadmium dust (237.5–1970)" and footnote 4 is added after footnote 2 to

read: "4. This standard applies to any operations or sectors for which § 1910.1027 is stayed or otherwise not in effect."

7. In part 1910 a new § 1910.1027 with appendices A, B, C, D, E, and F are added to subpart Z and in part 1915, a new subpart Z is added consisting of § 1915.1027 with appendices A, B, C, D, E, and F to read as set forth below. The text is identical for both parts 1910 and 1915.

§ ____.1027 Cadmium.

(a) *Scope.* This standard applies to all occupational exposures to cadmium and cadmium compounds, in all forms, and in all industries covered by the Occupational Safety and Health Act, except the construction-related industries, which are covered under 29 CFR 1926.63.

(b) *Definitions.*

Action level (AL) is defined as an airborne concentration of cadmium of 2.5 micrograms per cubic meter of air (2.5 $\mu g/m^3$), calculated as an 8-hour time-weighted average (TWA).

Assistant Secretary means the Assistant Secretary of Labor for Occupational Safety and Health, U.S. Department of Labor, or designee.

Authorized person means any person authorized by the employer and required by work duties to be present in regulated areas or any person authorized by the OSH Act or regulations issued under it to be in regulated areas.

Director means the Director of the National Institute for Occupational Safety and Health (NIOSH), U.S. Department of Health and Human Services, or designee.

Employee exposure and similar language referring to the air cadmium level to which an employee is exposed means the exposure to airborne cadmium that would occur if the employee were not using respiratory protective equipment.

Final medical determination is the written medical opinion of the employee's health status by the examining physician under paragraphs (l)(3)-(12) of this section or, if multiple physician review under paragraph (l)(13) of this section or the alternative physician determination under paragraph (l)(14) of this section is invoked, it is the final, written medical finding, recommendation or determination that emerges from that process.

High-efficiency particulate absolute (HEPA) air filter means a filter capable of trapping and retaining at least 99.97 percent of mono-dispersed particles of 0.3 micrometers in diameter.

Regulated area means an area demarcated by the employer where an employee's exposure to airborne concentrations of cadmium exceeds, or can reasonably be expected to exceed the permissible exposure limit (PEL).

This section means this cadmium standard.

(c) *Permissible Exposure Limit (PEL).* The employer shall assure that no employee is exposed to an airborne concentration of cadmium in excess of five micrograms per cubic meter of air (5 $\mu g/m^3$), calculated as an eight-hour time-weighted average exposure (TWA).

(d) *Exposure monitoring*—(1) *General.* (i) Each employer who has a workplace or work operation covered by this section shall determine if any employee may be exposed to cadmium at or above the action level.

(ii) Determinations of employee exposure shall be made from breathing zone air samples that reflect the monitored employee's regular, daily 8-hour TWA exposure to cadmium.

(iii) Eight-hour TWA exposures shall be determined for each employee on the basis of one or more personal breathing zone air samples reflecting full shift exposure on each shift, for each job classification, in each work area. Where several employees perform the same job tasks, in the same job classification, on the same shift, in the same work area, and the length, duration, and level of cadmium exposures are similar, an employer may sample a representative fraction of the employees instead of all employees in order to meet this requirement. In representative sampling, the employer shall sample the employee(s) expected to have the highest cadmium exposures.

(2) *Specific.* (i) Initial monitoring. Except as provided for in paragraphs (d)(2)(ii) and (d)(2)(iii) of this section, the employer shall monitor employee exposures and shall base initial determinations on the monitoring results.

(ii) Where the employer has monitored after September 14, 1991, under conditions that in all important aspects closely resemble those currently prevailing and where that monitoring satisfies all other requirements of this section, including the accuracy and confidence levels of paragraph (d)(6) of this section, the employer may rely on such earlier monitoring results to satisfy the requirements of paragraph (d)(2)(i) of this section.

(iii) Where the employer has objective data, as defined in paragraph (n)(2) of this section, demonstrating that employee exposure to cadmium will not exceed the action level under the expected conditions of processing, use, or handling, the employer may rely upon such data instead of implementing initial monitoring.

(3) *Monitoring Frequency (periodic monitoring).* (i) If the initial monitoring or periodic monitoring reveals employee exposures to be at or above the action level, the employer shall monitor at a frequency and pattern needed to represent the levels of exposure of employees and where exposures are above the PEL to assure the adequacy of respiratory selection and the effectiveness of engineering and work practice controls. However, such exposure monitoring shall be performed at least every six months. The employer, at a minimum, shall continue these semi-annual measurements unless and until the conditions set out in paragraph (d)(3)(ii) of this section are met.

(ii) If the initial monitoring or the periodic monitoring indicates that employee exposures are below the action level and that result is confirmed by the results of another monitoring taken at least seven days later, the employer may discontinue the monitoring for those employees whose exposures are represented by such monitoring.

(4) *Additional Monitoring.* The employer also shall institute the exposure monitoring required under paragraphs (d)(2)(i) and (d)(3) of this section whenever there has been a change in the raw materials, equipment, personnel, work practices, or finished products that may result in additional employees being exposed to cadmium at or above the action level or in employees already exposed to cadmium at or above the action level being exposed above the PEL, or whenever the employer has any reason to suspect that any other change might result in such further exposure.

(5) *Employee Notification of Monitoring Results.* (i) Within 15 working days after the receipt of the results of any monitoring performed under this section, the employer shall notify each affected employee individually in writing of the results. In addition, within the same time period the employer shall post the results of the exposure monitoring in an appropriate location that is accessible to all affected employees.

(ii) Wherever monitoring results indicate that employee exposure exceeds the PEL, the employer shall include in the written notice a statement that the PEL has been exceeded and a description of the corrective action being taken by the employer to reduce employee exposure to or below the PEL.

(6) *Accuracy of measurement.* The employer shall use a method of monitoring and analysis that has an accuracy of not less than plus or minus 25 percent (± 25%), with a confidence level of 95 percent, for airborne concentrations of cadmium at or above the action level, the permissible exposure limit (PEL), and the separate engineering control air limit (SECAL).

(e) *Regulated areas.*—(1) *Establishment.* The employer shall establish a regulated area wherever an employee's exposure to airborne concentrations of cadmium is, or can reasonably be expected to be in excess of the permissible exposure limit (PEL).

(2) *Demarcation.* Regulated areas shall be demarcated from the rest of the workplace in any manner that adequately establishes and alerts employees of the boundaries of the regulated area.

(3) *Access.* Access to regulated areas shall be limited to authorized persons.

(4) *Provision of respirators.* Each person entering a regulated area shall be supplied with and required to use a respirator, selected in accordance with paragraph (g)(2) of this section.

(5) *Prohibited activities.* The employer shall assure that employees do not eat, drink, smoke, chew tobacco or gum, or apply cosmetics in regulated areas, carry the products associated with these activities into regulated areas, or store such products in those areas.

(f) *Methods of compliance.*—(1) *Compliance hierarchy.* (i) Except as specified in paragraphs (f)(1) (ii), (iii) and (iv) of this section the employer shall implement engineering and work practice controls to reduce and maintain employee exposure to cadmium at or below the PEL, except to the extent that the employer can demonstrate that such controls are not feasible.

(ii) Except as specified in paragraphs (f)(1) (iii) and (iv) of this section, in industries where a separate engineering control air limit (SECAL) has been specified for particular processes (See Table 1 in this paragraph (f)(1)(ii)), the employer shall implement engineering and work practice controls to reduce and maintain employee exposure at or below the SECAL, except to the extent that the employer can demonstrate that such controls are not feasible.

TABLE I.—SEPARATE ENGINEERING CONTROL AIRBORNE LIMITS (SECALS) FOR PROCESSES IN SELECTED INDUSTRIES

Industry	Process	SECAL ($\mu g/m^3$)
Nickel cadmium battery	Plate making, plate preparation	50
	All other processes	15
Zinc/Cadmium refining*	Cadmium refining, casting, melting, oxide production, sinter plant	50
Pigment manufacture	Calcine, crushing, milling, blending	50
	All other processes	15
Stabilizers*	Cadmium oxide charging, crushing, drying, blending	50
Lead smelting*	Sinter plant, blast furnace, baghouse, yard area	50
Plating*	Mechanical plating	15

*Processes in these industries that are not specified in this table must achieve the PEL using engineering controls and work practices as required in f(1)(i).

(iii) The requirement to implement engineering and work practice controls to achieve the PEL or, where applicable, the SECAL does not apply where the employer demonstrates the following:

(A) The employee is only intermittently exposed; and

(B) The employee is not exposed above the PEL on 30 or more days per year (12 consecutive months).

(iv) Wherever engineering and work practice controls are required and are not sufficient to reduce employee exposure to or below the PEL or, where applicable, the SECAL, the employer nonetheless shall implement such controls to reduce exposures to the lowest levels achievable. The employer shall supplement such controls with respiratory protection that complies with the requirements of paragraph (g) of this section and the PEL.

(v) The employer shall not use employee rotation as a method of compliance.

(2) *Compliance program.* (i) Where the PEL is exceeded, the employer shall establish and implement a written compliance program to reduce employee exposure to or below the PEL by means of engineering and work practice controls, as required by paragraph (f)(1) of this section. To the extent that engineering and work practice controls cannot reduce exposures to or below the PEL, the employer shall include in the written compliance program the use of appropriate respiratory protection to achieve compliance with the PEL.

(ii) Written compliance programs shall include at least the following:

(A) A description of each operation in which cadmium is emitted; e.g., machinery used, material processed, controls in place, crew size, employee job responsibilities, operating procedures, and maintenance practices;

(B) A description of the specific means that will be employed to achieve compliance, including engineering plans and studies used to determine methods selected for controlling exposure to cadmium, as well as, where necessary, the use of appropriate respiratory protection to achieve the PEL;

(C) A report of the technology considered in meeting the PEL;

(D) Air monitoring data that document the sources of cadmium emissions;

(E) A detailed schedule for implementation of the program, including documentation such as copies of purchase orders for equipment, construction contracts, etc.;

(F) A work practice program that includes items required under paragraphs (h), (i), and (j) of this section;

(G) A written plan for emergency situations, as specified in paragraph (h) of this section; and

(H) Other relevant information.

(iii) The written compliance programs shall be reviewed and updated at least annually, or more often if necessary, to reflect significant changes in the employer's compliance status.

(iv) Written compliance programs shall be provided upon request for examination and copying to affected employees, designated employee representatives as well as to the Assistant Secretary, and the Director.

(3) *Mechanical ventilation.* (i) When ventilation is used to control exposure, measurements that demonstrate the effectiveness of the system in controlling exposure, such as capture velocity, duct velocity, or static pressure shall be made as necessary to maintain its effectiveness.

(ii) Measurements of the system's effectiveness in controlling exposure shall be made as necessary within five working days of any change in production, process, or control that

might result in a significant increase in employee exposure to cadmium.

(iii) Recirculation of air. If air from exhaust ventilation is recirculated into the workplace, the system shall have a high efficiency filter and be monitored to assure effectiveness.

(iv) Procedures shall be developed and implemented to minimize employee exposure to cadmium when maintenance of ventilation systems and changing of filters is being conducted.

(4) *Compliance program.* Where employee exposure to cadmium exceeds the PEL and the employer is required under paragraph (f)(1) of this section to implement controls to comply with the PEL, prior to the commencement of the job, the employer shall establish and implement a written compliance program to reduce employee exposure to or below the PEL.

(g) *Respirator protection.*—(1) *General.* Where respirators are required by this section, the employer shall provide them at no cost to the employee and shall assure that they are used in compliance with the requirements of this section. Respirators shall be used in the following circumstances:

(i) Where exposure levels exceed the PEL, during the time period necessary to install or implement feasible engineering and work practice controls;

(ii) In those maintenance and repair activities and during those brief or intermittent operations where exposures exceed the PEL and engineering and work practice controls are not feasible or are not required;

(iii) In regulated areas, as prescribed in paragraph (e) of this section;

(iv) Where the employer has implemented all feasible engineering and work practice controls and such controls are not sufficient to reduce exposures to or below the PEL;

(v) In emergencies;

(vi) Wherever an employee who is exposed to cadmium at or above the action level requests a respirator;

(vii) Wherever an employee is exposed above the PEL in an industry to which a SECAL is applicable; and

(viii) Wherever an employee is exposed to cadmium above the PEL and engineering controls are not required under paragraph (f)(1)(iii) of this section.

(2) *Respirator selection.* (i) Where respirators are required under this section, the employer shall select and provide the appropriate respirator as specified in Table 2 in this paragraph (g)(2)(i). The employer shall select respirators from among those jointly approved as acceptable protection against cadmium dust, fume, and mist by the Mine Safety and Health Administration (MSHA) and by the National Institute for Occupational Safety and Health (NIOSH) under the provisions of 30 CFR part 11.

TABLE 2.—RESPIRATORY PROTECTION FOR CADMIUM

Airborne concentration or condition of use [a]	Required respirator type [b]
10 × or less	A half mask, air-purifying respirator equipped with a HEPA[c] filter.[d]
25 × or less	A powered air-purifying respirator ("PAPR") with a loose-fitting hood or helmet equipped with a HEPA filter, or a supplied-air respirator with a loose-fitting hood or helmet facepiece operated in the continuous flow mode.
50 × or less	A full facepiece air-purifying respirator equipped with a HEPA filter, or a powered air-purifying respirator with a tight-fitting half mask equipped with a HEPA filter, or a supplied air respirator with a tight-fitting half mask operated in the continuous flow mode.
250 × or less	A powered air-purifying respirator with a tight-fitting full facepiece equipped with a HEPA filter, or a supplied-air respirator with a tight-fitting full facepiece operated in the continuous flow mode.
1000 × or less	A supplied-air respirator with half mask or full facepiece operated in the pressure demand or other positive pressure mode.
>1000 × or unknown concentrations	A self-contained breathing apparatus with unknown concentrations a full facepiece operated in the pressure demand or other positive pressure mode, or a supplied-air respirator with a full facepiece operated in the pressure demand or other positive pressure mode and equipped with an auxiliary escape type self-contained breathing apparatus operated in the pressure demand mode.
Fire fighting	A self-contained breathing apparatus with full facepiece operated in the pressure demand or other positive pressure mode.

[a] Concentrations expressed as multiple of the PEL.
[b] Respirators assigned for higher environmental concentrations may be used at lower exposure levels. Quantitative fit testing is required for all tight-fitting air purifying respirators where airborne concentration of cadmium exceeds 10 times the TWA PEL ($10 \times 5\ \mu g/m^3 = 50\ \mu g/m^3$). A full facepiece respirator is required when eye irritation is experienced.
[c] HEPA means High Efficiency Particulate Absolute.
[d] Fit testing, qualitative or quantitative, is required.
SOURCE: *Respiratory Decision Logic*, NIOSH, 1987.

(ii) The employer shall provide a powered, air-purifying respirator (PAPR) in lieu of a negative pressure respirator wherever:

(A) An employee entitled to a respirator chooses to use this type of respirator; and

(B) This respirator will provide adequate protection to the employee.

(3) *Respirator program.* (i) Where respiratory protection is required, the employer shall institute a respirator protection program in accordance with 29 CFR 1910.134.

(ii) The employer shall permit each employee who is required to use an air purifying respirator to leave the regulated area to change the filter elements or replace the respirator whenever an increase in breathing resistance is detected and shall maintain an adequate supply of filter elements for this purpose.

(iii) The employer shall also permit each employee who is required to wear a respirator to leave the regulated area to wash his or her face and the respirator facepiece whenever necessary to prevent skin irritation associated with respirator use.

(iv) If an employee exhibits difficulty in breathing while wearing a respirator during a fit test or during use, the employer shall make available to the employee a medical examination in accordance with paragraph (l)(6)(ii) of this section to determine if the employee can wear a respirator while performing the required duties.

(v) No employee shall be assigned a task requiring the use of a respirator if, based upon his or her most recent examination, an examining physician determines that the employee will be unable to continue to function normally while wearing a respirator. If the physician determines the employee must be limited in, or removed from his or her current job because of the employee's inability to wear a respirator, the limitation or removal shall be in accordance with paragraphs (l) (11) and (12) of this section.

(4) *Respirator fit testing.* (i) The employer shall assure that the respirator issued to the employee is fitted properly and exhibits the least possible facepiece leakage.

(ii) For each employee wearing a tight-fitting, air purifying respirator (either negative or positive pressure) who is exposed to airborne concentrations of cadmium that do not exceed 10 times the PEL ($10 \times 5\ \mu g/m^3 = 50\ \mu g/m^3$), the employer shall perform either quantitative or qualitative fit testing at the time of initial fitting and at least annually thereafter. If quantitative fit testing is used for a negative pressure respirator, a fit factor that is at least 10 times the protection factor for that class of respirators (Table 2 in paragraph (g)(2)(i) of this section) shall be achieved at testing.

(iii) For each employee wearing a tight-fitting air purifying respirator (either negative or positive pressure) who is exposed to airborne concentrations of cadmium that exceed 10 times the PEL ($10 \times 5\ \mu g/m^3 = 50\ \mu g/m^3$), the employer shall perform quantitative fit testing at the time of initial fitting and at least annually thereafter. For negative-pressure respirators, a fit factor that is at least 10 times the protection factor for that class of respirators (Table 2 in paragraph (g)(2)(i) of this section) shall be achieved during quantitative fit testing.

(iv) For each employee wearing a tight-fitting, supplied-air respirator or self-contained breathing apparatus, the employer shall perform quantitative fit testing at the time of initial fitting and at least annually thereafter. This shall be accomplished by fit testing an air purifying respirator of identical type facepiece, make, model, and size as the supplied air respirator or self-contained breathing apparatus that is equipped with HEPA filters and tested as a surrogate (substitute) in the negative pressure mode. A fit factor that is at least 10 times the protection factor for that class of respirators (Table 2 in paragraph (g)(2)(i) of this section) shall be achieved during quantitative fit testing. A supplied-air respirator or self-contained breathing apparatus with the same type facepiece, make, model, and size as the air purifying respirator with which the employee passed the quantitative fit test may then be used by that employee up to the protection factor listed in Table 2 for that class of respirators.

(v) Fit testing shall be conducted in accordance with appendix C of this section.

(h) *Emergency situations.* The employer shall develop and implement a written plan for dealing with emergency situations involving substantial releases of airborne cadmium. The plan shall include provisions for the use of appropriate respirators and personal protective equipment. In addition, employees not essential to correcting the emergency situation shall be restricted from the area and normal operations halted in that area until the emergency is abated.

(i) *Protective work clothing and equipment*—(1) *Provision and use.* If an employee is exposed to airborne cadmium above the PEL or where skin or eye irritation is associated with cadmium exposure at any level, the employer shall provide at no cost to the employee, and assure that the employee uses, appropriate protective work clothing and equipment that prevents contamination of the employee and the employee's garments. Protective work clothing and equipment includes, but is not limited to:

(i) Coveralls or similar full-body work clothing;

(ii) Gloves, head coverings, and boots or foot coverings; and

(iii) Face shields, vented goggles, or other appropriate protective equipment that complies with 29 CFR 1910.133.

(2) *Removal and storage.* (i) The employer shall assure that employees remove all protective clothing and equipment contaminated with cadmium at the completion of the work shift and do so only in change rooms provided in accordance with paragraph (j)(1) of this section.

(ii) The employer shall assure that no employee takes cadmium-contaminated protective clothing or equipment from the workplace, except for employees authorized to do so for purposes of laundering, cleaning, maintaining, or disposing of cadmium contaminated protective clothing and equipment at an appropriate location or facility away from the workplace.

(iii) The employer shall assure that contaminated protective clothing and equipment, when removed for laundering, cleaning, maintenance, or disposal, is placed and stored in sealed, impermeable bags or other closed, impermeable containers that are designed to prevent dispersion of cadmium dust.

(iv) The employer shall assure that bags or containers of contaminated protective clothing and equipment that are to be taken out of the change rooms or the workplace for laundering, cleaning, maintenance or disposal shall bear labels in accordance with paragraph (m)(2) of this section.

(3) *Cleaning, replacement, and disposal.* (i) The employer shall provide the protective clothing and equipment required by paragraph (i)(1) of this section in a clean and dry condition as often as necessary to maintain its effectiveness, but in any event at least weekly. The employer is responsible for cleaning and laundering the protective clothing and equipment required by this paragraph to maintain its effectiveness and is also responsible for disposing of such clothing and equipment.

(ii) The employer also is responsible for repairing or replacing required protective clothing and equipment as needed to maintain its effectiveness. When rips or tears are detected while an employee is working they shall be immediately mended, or the worksuit shall be immediately replaced.

(iii) The employer shall prohibit the removal of cadmium from protective clothing and equipment by blowing, shaking, or any other means that disperses cadmium into the air.

(iv) The employer shall assure that any laundering of contaminated clothing or cleaning of contaminated equipment in the workplace is done in a manner that prevents the release of airborne cadmium in excess of the permissible exposure limit prescribed in paragraph (c) of this section.

(v) The employer shall inform any person who launders or cleans protective clothing or equipment contaminated with cadmium of the potentially harmful effects of exposure to cadmium and that the clothing and equipment should be laundered or cleaned in a manner to effectively prevent the release of airborne cadmium in excess of the PEL.

(j) *Hygiene areas and practices*—(1) *General.* For employees whose airborne exposure to cadmium is above the PEL, the employer shall provide clean change rooms, handwashing facilities, showers, and lunchroom facilities that comply with 29 CFR 1910.141.

(2) *Change rooms.* The employer shall assure that change rooms are equipped with separate storage facilities for street clothes and for protective clothing and equipment, which are designed to prevent dispersion of cadmium and contamination of the employee's street clothes.

(3) *Showers and handwashing facilities.* (i) The employer shall assure that employees who are exposed to cadmium above the PEL shower during the end of the work shift.

(ii) The employer shall assure that employees whose airborne exposure to cadmium is above the PEL wash their hands and faces prior to eating, drinking, smoking, chewing tobacco or gum, or applying cosmetics.

(4) *Lunchroom facilities.* (i) The employer shall assure that the lunchroom facilities are readily accessible to employees, that tables for eating are maintained free of cadmium, and that no employee in a lunchroom facility is exposed at any time to cadmium at or above a concentration of 2.5 $\mu g/m^3$.

(ii) The employer shall assure that employees do not enter lunchroom facilities with protective work clothing or equipment unless surface cadmium has been removed from the clothing and equipment by HEPA vacuuming or some other method that removes cadmium dust without dispersing it.

(k) *Housekeeping.* (1) All surfaces shall be maintained as free as practicable of accumulations of cadmium.

(2) All spills and sudden releases of material containing cadmium shall be cleaned up as soon as possible.

(3) Surfaces contaminated with cadmium shall, wherever possible, be cleaned by vacuuming or other methods that minimize the likelihood of cadmium becoming airborne.

(4) HEPA-filtered vacuuming equipment or equally effective filtration methods shall be used for vacuuming. The equipment shall be used and emptied in a manner that minimizes the reentry of cadmium into the workplace.

(5) Shoveling, dry or wet sweeping, and brushing may be used only where vacuuming or other methods that minimize the likelihood of cadmium becoming airborne have been tried and found not to be effective.

(6) Compressed air shall not be used to remove cadmium from any surface unless the compressed air is used in conjunction with a ventilation system designed to capture the dust cloud created by the compressed air.

(7) Waste, scrap, debris, bags, containers, personal protective equipment, and clothing contaminated with cadmium and consigned for disposal shall be collected and disposed of in sealed impermeable bags or other closed, impermeable containers. These bags and containers shall be labeled in accordance with paragraph (m)(2) of this section.

(l) *Medical surveillance*—(1) *General*—(i) *Scope.* (A) Currently exposed—The employer shall institute a medical surveillance program for all employees who are or may be exposed to cadmium at or above the action level unless the employer demonstrates that the employee is not, and will not be, exposed at or above the action level on 30 or more days per year (twelve consecutive months); and,

(B) Previously exposed—The employer shall also institute a medical surveillance program for all employees who prior to the effective date of this section might previously have been exposed to cadmium at or above the action level by the employer, unless the employer demonstrates that the employee did not prior to the effective date of this section work for the employer in jobs with exposure to cadmium for an aggregated total of more than 60 months.

(ii) To determine an employee's fitness for using a respirator, the employer shall provide the limited medical examination specified in paragraph (l)(6) of this section.

(iii) The employer shall assure that all medical examinations and procedures required by this standard are performed by or under the supervision of a licensed physician, who has read and is familiar with the health effects section of appendix A to this section, the regulatory text of this section, the protocol for sample handling and laboratory selection in appendix F to this section, and the questionnaire of appendix D to this section. These examinations and procedures shall be provided without cost to the employee and at a time and place that is reasonable and convenient to employees.

(iv) The employer shall assure that the collecting and handling of biological samples of cadmium in urine (CdU), cadmium in blood (CdB), and beta-2 microglobulin in urine (β_2-M) taken from employees under this section is done in a manner that assures their reliability and that analysis of biological samples of cadmium in urine (CdU), cadmium in blood (CdB), and beta-2 microglobulin in urine (β_2-M) taken from employees under this section is performed in laboratories with demonstrated proficiency for that particular analyte. (See appendix F to this section.)

(2) *Initial examination.* (i) The employer shall provide an initial (preplacement) examination to all employees covered by the medical surveillance program required in paragraph (l)(1)(i) of this section. The examination shall be provided to those employees within 30 days after initial assignment to a job with exposure to cadmium or no later than 90 days after the effective date of this section, whichever date is later.

(ii) The initial (preplacement) medical examination shall include:

(A) A detailed medical and work history, with emphasis on: Past, present, and anticipated future exposure to cadmium; any history of renal, cardiovascular, respiratory, hematopoietic, reproductive, and/or musculo-skeletal system dysfunction; current usage of medication with potential nephrotoxic side-effects; and smoking history and current status; and

(B) Biological monitoring that includes the following tests:

(1) Cadmium in urine (CdU), standardized to grams of creatinine (g/Cr);

(2) Beta-2 microglobulin in urine (β_2-M), standardized to grams of creatinine (g/Cr), with pH specified, as described in appendix F to this section; and

(3) Cadmium in blood (CdB), standardized to liters of whole blood (lwb).

(iii) Recent Examination: An initial examination is not required to be provided if adequate records show that the employee has been examined in accordance with the requirements of paragraph (l)(2)(ii) of this section within the past 12 months. In that case, such records shall be maintained as part of the employee's medical record and the prior exam shall be treated as if it were an initial examination for the purposes of paragraphs (l)(3) and (4) of this section.

(3) *Actions triggered by initial biological monitoring:* (i) If the results of the initial biological monitoring tests show the employee's CdU level to be at or below 3 $\mu g/g$ Cr, β_2-M level to be at or below 300 $\mu g/g$ Cr and CdB level to be at or below 5 $\mu g/lwb$, then:

(A) For currently exposed employees, who are subject to medical surveillance under paragraph (l)(1)(i)(A) of this section, the employer shall provide the minimum level of periodic medical surveillance in accordance with the requirements in paragraph (l)(4)(i) of this section; and

(B) For previously exposed employees, who are subject to medical surveillance under paragraph (l)(1)(i)(B) of this section, the employer shall provide biological monitoring for CdU, β_2-M, and CdB within one year after the initial biological monitoring and then the employer shall comply with the requirements of paragraph (l)(4)(v) of this section.

(ii) For all employees who are subject to medical surveillance under paragraph (l)(1)(i) of this section, if the results of the initial biological monitoring tests show the level of CdU to exceed 3 $\mu g/g$ Cr, the level of β_2-M to exceed 300 $\mu g/g$ Cr, or the level of CdB to exceed 5 $\mu g/lwb$, the employer shall:

(A) Within two weeks after receipt of biological monitoring results, reassess the employee's occupational exposure to cadmium as follows:

(1) Reassess the employee's work practices and personal hygiene;

(2) Reevaluate the employee's respirator use, if any, and the respirator program;

(3) Review the hygiene facilities;

(4) Reevaluate the maintenance and effectiveness of the relevant engineering controls;

(5) Assess the employee's smoking history and status;

(B) Within 30 days after the exposure reassessment, specified in paragraph (l)(3)(ii)(A) of this section, take reasonable steps to correct any deficiencies found in the reassessment that may be responsible for the employee's excess exposure to cadmium; and,

(C) Within 90 days after receipt of biological monitoring results, provide a full medical examination to the employee in accordance with the requirements of paragraph (l)(4)(ii) of this section. After completing the medical examination, the examining physician shall determine in a written medical opinion whether to medically remove the employee. If the physician determines that medical removal is not necessary, then until the employee's CdU level falls to or below 3 μg/g Cr, β_2-M level falls to or below 300 μg/g Cr and CdB level falls to or below 5 μg/lwb, the employer shall:

(1) Provide biological monitoring in accordance with paragraph (l)(2)(ii)(B) of this section on a semiannual basis; and

(2) Provide annual medical examinations in accordance with paragraph (l)(4)(ii) of this section.

(iii) For all employees who are subject to medical surveillance under paragraph (l)(1)(i) of this section, if the results of the initial biological monitoring tests show the level of CdU to be in excess of 15 μg/g Cr, or the level of CdB to be in excess of 15 μg/lwb, or the level of β_2-M to be in excess of 1,500 μg/g Cr, the employer shall comply with the requirements of paragraphs (l)(3)(ii)(A)–(B) of this section. Within 90 days after receipt of biological monitoring results, the employer shall provide a full medical examination to the employee in accordance with the requirements of paragraph (l)(4)(ii) of this section. After completing the medical examination, the examining physician shall determine in a written medical opinion whether to medically remove the employee. However, if the initial biological monitoring results and the biological monitoring results obtained during the medical examination both show that: CdU exceeds 15 μg/g Cr; or CdB exceeds 15 μg/lwb; or β_2-M exceeds 1500 μg/g Cr, and in addition CdU exceeds 3 μg/g Cr or CdB exceeds 5 μg/liter of whole blood, then the physician shall medically remove the employee from exposure to cadmium at or above the action level. If the second set of biological monitoring results obtained during the medical examination does not show that a mandatory removal trigger level has been exceeded, then the employee is not required to be removed by the mandatory provisions of this paragraph. If the employee is not required to be removed by the mandatory provisions of this paragraph or by the physician's determination, then until the employee's CdU level falls to or below 3 μg/g Cr, β_2-M level falls to or below 300 μg/g Cr and CdB level falls to or below 5 μg/lwb, the employer shall:

(A) Periodically reassess the employee's occupational exposure to cadmium;

(B) Provide biological monitoring in accordance with paragraph (l)(2)(ii)(B) of this section on a quarterly basis; and

(C) Provide semiannual medical examinations in accordance with paragraph (l)(4)(ii) of this section.

(iv) For all employees to whom medical surveillance is provided, beginning on January 1, 1999, and in lieu of paragraphs (l)(3)(i)–(iii) of this section:

(A) If the results of the initial biological monitoring tests show the employee's CdU level to be at or below 3 μg/g Cr, β_2-M level to be at or below 300 μg/g Cr and CdB level to be at or below 5 μg/lwb, then for currently exposed employees, the employer shall comply with the requirements of paragraph (l)(3)(i)(A) of this section, and for previously exposed employees, the employer shall comply with the requirements of paragraph (l)(3)(i)(B) of this section;

(B) If the results of the initial biological monitoring tests show the level of CdU to exceed 3 μg/g Cr, the level of β_2-M to exceed 300 μg/g Cr, or the level of CdB to exceed 5 μg/lwb, the employer shall comply with the requirements of paragraphs (l)(3)(ii)(A)–(C) of this section; and,

(C) If the results of the initial biological monitoring tests show the level of CdU to be in excess of 7 μg/g Cr, or the level of CdB to be in excess of 10 μg/lwb, or the level of β_2-M to be in excess of 750 μg/g Cr, the employer shall: Comply with the requirements of paragraphs (l)(3)(ii)(A)–(B) of this section; and, within 90 days after receipt of biological monitoring results, provide a full medical examination to the employee in accordance with the requirements of paragraph (l)(4)(ii) of this section. After completing the medical examination, the examining physician shall determine in a written medical opinion whether to medically remove the employee. However, if the initial biological monitoring results and the biological monitoring results obtained during the medical examination both show that: CdU exceeds 7 μg/g Cr; or CdB exceeds 10 μg/lwb; or β_2-M exceeds 750 μg/g Cr, and in addition CdU exceeds 3 μg/g Cr or CdB exceeds 5 μg/liter of whole blood, then the physician shall medically remove the employee from exposure to cadmium at or above the action level. If the second set of biological monitoring results obtained during the medical examination does not show that a mandatory removal trigger level has been exceeded, then the employee is not required to be removed by the mandatory provisions of this paragraph. If the employee is not required to be removed by the mandatory provisions of this paragraph or by the physician's determination, then until the employee's CdU level falls to or below 3 μg/g Cr, β_2-M level falls to or below 300 μg/g Cr and CdB level falls to or below 5 μg/lwb, the employer shall: periodically reassess the employee's occupational exposure to cadmium; provide biological monitoring in accordance with paragraph (l)(2)(ii)(B) of this section on a quarterly basis; and provide semiannual medical examinations in accordance with paragraph (l)(4)(ii) of this section.

(4) *Periodic medical surveillance.* (i) For each employee who is covered under paragraph (l)(1)(i)(A) of this section, the employer shall provide at least the minimum level of periodic medical surveillance, which consists of periodic medical examinations and periodic biological monitoring. A periodic medical examination shall be provided within one year after the initial examination required by paragraph (l)(2) of this section and thereafter at least biennially. Biological sampling shall be provided at least annually, either as part of a periodic medical examination or separately as periodic biological monitoring.

(ii) The periodic medical examination shall include:

(A) A detailed medical and work history, or update thereof, with emphasis on: Past, present and anticipated future exposure to cadmium, smoking history and current status; reproductive history; current use of medications with potential nephrotoxic side-effects; any history of renal, cardiovascular, respiratory, hematopoietic, and/or musculo-skeletal system dysfunction; and as part of the

medical and work history, for employees who wear respirators, questions 3–11 and 25–32 in Appendix D to this section;

(B) A complete physical examination with emphasis on: Blood pressure, the respiratory system, and the urinary system;

(C) A 14 inch by 17 inch, or a reasonably standard sized posterior-anterior chest X-ray (after the initial X-ray, the frequency of chest X-rays is to be determined by the examining physician);

(D) Pulmonary function tests, including forced vital capacity (FVC) and forced expiratory volume at 1 second (FEV1);

(E) Biological monitoring, as required in paragraph (l)(2)(ii)(B) of this section;

(F) Blood analysis, in addition to the analysis required under paragraph (l)(2)(ii)(B) of this section, including blood urea nitrogen, complete blood count, and serum creatinine;

(G) Urinalysis, in addition to the analysis required under paragraph (l)(2)(ii)(B) of this section, including the determination of albumin, glucose, and total and low molecular weight proteins;

(H) For males over 40 years old, prostate palpation, or other at least as effective diagnostic test(s); and

(I) Any additional tests deemed appropriate by the examining physician.

(iii) Periodic biological monitoring shall be provided in accordance with paragraph (l)(2)(ii)(B) of this section.

(iv) If the results of periodic biological monitoring or the results of biological monitoring performed as part of the periodic medical examination show the level of the employee's CdU, β_2-M, or CdB to be in excess of the levels specified in paragraphs (l)(3)(ii)–(iii) of this section; or, beginning on January 1, 1999, in excess of the levels specified in paragraphs (l)(3)(iv) of this section, the employer shall take the appropriate actions specified in paragraphs (l)(3)(ii)–(iv) of this section.

(v) For previously exposed employees under paragraph (l)(1)(i)(B) of this section:

(A) If the employee's levels of CdU did not exceed 3 μg/g Cr, CdB did not exceed 5 μg/lwb, and β_2-M did not exceed 300 μg/g Cr in the initial biological monitoring tests, and if the results of the followup biological monitoring required by paragraph (l)(3)(i)(B) of this section within one year after the initial examination confirm the previous results, the employer may discontinue all periodic medical surveillance for that employee.

(B) If the initial biological monitoring results for CdU, CdB, or β_2-M were in excess of the levels specified in paragraph (l)(3)(i) of this section, but subsequent biological monitoring results required by paragraph (l)(3)(ii)–(iv) of this section show that the employee's CdU levels no longer exceed 3 μg/g Cr, CdB levels no longer exceed 5 μg/lwb, and β_2-M levels no longer exceed 300 μg/g Cr, the employer shall provide biological monitoring for CdU, CdB, and β_2-M within one year after these most recent biological monitoring results. If the results of the followup biological monitoring within one year, specified in this paragraph, confirm the previous results, the employer may discontinue all periodic medical surveillance for that employee.

(C) However, if the results of the follow-up tests specified in paragraph (l)(4)(v)(A) or (B) of this section indicate that the level of the employee's CdU, β_2-M, or CdB exceeds these same levels, the employer is required to provide annual medical examinations in accordance with the provisions of paragraph (l)(4)(ii) of this section until the results of biological monitoring are consistently below these levels or the examining physician determines in a written medical opinion that further medical surveillance is not required to protect the employee's health.

(vi) A routine, biennial medical examination is not required to be provided in accordance with paragraphs (l)(3)(i) and (l)(4) of this section if adequate medical records show that the employee has been examined in accordance with the requirements of paragraph (l)(4)(ii) of this section within the past 12 months. In that case, such records shall be maintained by the employer as part of the employee's medical record, and the next routine, periodic medical examination shall be made available to the employee within two years of the previous examination.

(5) *Actions triggered by medical examinations.* (i) If the results of a medical examination carried out in accordance with this section indicate any laboratory or clinical finding consistent with cadmium toxicity that does not require employer action under paragraph (l)(2), (3) or (4) of this section, the employer, within 30 days, shall reassess the employee's occupational exposure to cadmium and take the following corrective action until the physician determines they are no longer necessary:

(A) Periodically reassess: The employee's work practices and personal hygiene; the employee's respirator use, if any; the employee's smoking history and status; the respiratory protection program; the hygiene facilities; and the maintenance and effectiveness of the relevant engineering controls;

(B) Within 30 days after the reassessment, take all reasonable steps to correct the deficiencies found in the reassessment that may be responsible for the employee's excess exposure to cadmium;

(C) Provide semiannual medical reexaminations to evaluate the abnormal clinical sign(s) of cadmium toxicity until the results are normal or the employee is medically removed; and

(D) Where the results of tests for total proteins in urine are abnormal, provide a more detailed medical evaluation of the toxic effects of cadmium on the employee's renal system.

(6) *Examination for respirator use.* (i) To determine an employee's fitness for respirator use, the employer shall provide a medical examination that includes the elements specified in paragraph (l)(6)(i)(A)–(D) of this section. This examination shall be provided prior to the employee's being assigned to a job that requires the use of a respirator or no later than 90 days after this section goes into effect, whichever date is later, to any employee without a medical examination within the preceding 12 months that satisfies the requirements of this paragraph.

(A) A detailed medical and work history, or update thereof, with emphasis on: Past exposure to cadmium; smoking history and current status; any history of renal, cardiovascular, respiratory, hematopoietic, and/or musculoskeletal system dysfunction; a description of the job for which the respirator is required; and questions 3–11 and 25–32 in appendix D to this section;

(B) A blood pressure test;

(C) Biological monitoring of the employee's levels of CdU, CdB and β_2-M in accordance with the requirements of paragraph (l)(2)(ii)(B) of this section, unless such results already have been obtained within the previous 12 months; and

(D) Any other test or procedure that the examining physician deems appropriate.

(ii) After reviewing all the information obtained from the medical examination required in paragraph (l)(6)(i) of this section, the physician shall determine whether the employee is fit to wear a respirator.

(iii) Whenever an employee has exhibited difficulty in breathing during a respirator fit test or during use of a respirator, the employer, as soon as possible, shall provide the employee with a periodic medical examination in accordance with paragraph (l)(4)(ii) of this section to determine the employee's fitness to wear a respirator.

(iv) Where the results of the examination required under paragraph (l)(6)(i) or (ii) of this section are abnormal, medical limitation or prohibition of respirator use shall be considered. If the employee is allowed to wear a respirator, the employee's ability to continue to do so shall be periodically evaluated by a physician.

(7) *Emergency examinations.* (i) In addition to the medical surveillance required in paragraphs (l)(2)–(6) of this section, the employer shall provide a medical examination as soon as possible to any employee who may have been acutely exposed to cadmium because of an emergency.

(ii) The examination shall include the requirements of paragraph (l)(4)(ii) of this section, with emphasis on the respiratory system, other organ systems considered appropriate by the examining physician, and symptoms of acute overexposure, as identified in paragraphs II (B)(1)–(2) and IV of appendix A to this section.

(8) *Termination of employment examination.* (i) At termination of employment, the employer shall provide a medical examination in accordance with paragraph (l)(4)(ii) of this section, including a chest X-ray, to any employee to whom at any prior time the employer was required to provide medical surveillance under paragraphs (l)(1)(i) or (l)(7) of this section. However, if the last examination satisfied the requirements of paragraph (l)(4)(ii) of this section and was less than six months prior to the date of termination, no further examination is required unless otherwise specified in paragraphs (l)(3) or (l)(5) of this section;

(ii) However, for employees covered by paragraph (l)(1)(i)(B) of this section, if the employer has discontinued all periodic medical surveillance under paragraph (l)(4)(v) of this section, no termination of employment medical examination is required.

(9) *Information provided to the physician.* The employer shall provide the following information to the examining physician:

(i) A copy of this standard and appendices;

(ii) A description of the affected employee's former, current, and anticipated duties as they relate to the employee's occupational exposure to cadmium;

(iii) The employee's former, current, and anticipated future levels of occupational exposure to cadmium;

(iv) A description of any personal protective equipment, including respirators, used or to be used by the employee, including when and for how long the employee has used that equipment; and

(v) relevant results of previous biological monitoring and medical examinations.

(10) *Physician's written medical opinion.* (i) The employer shall promptly obtain a written, signed medical opinion from the examining physician for each medical examination performed on each employee. This written opinion shall contain:

(A) The physician's diagnosis for the employee;

(B) The physician's opinion as to whether the employee has any detected medical condition(s) that would place the employee at increased risk of material impairment to health from further exposure to cadmium, including any indications of potential cadmium toxicity;

(C) The results of any biological or other testing or related evaluations that directly assess the employee's absorption of cadmium;

(D) Any recommended removal from, or limitation on the activities or duties of the employee or on the employee's use of personal protective equipment, such as respirators;

(E) A statement that the physician has clearly and carefully explained to the employee the results of the medical examination, including all biological monitoring results and any medical conditions related to cadmium exposure that require further evaluation or treatment, and any limitation on the employee's diet or use of medications.

(ii) The employer promptly shall obtain a copy of the results of any biological monitoring provided by an employer to an employee independently of a medical examination under paragraphs (l)(2) and (l)(4) of this section, and, in lieu of a written medical opinion, an explanation sheet explaining those results.

(iii) The employer shall instruct the physician not to reveal orally or in the written medical opinion given to the employer specific findings or diagnoses unrelated to occupational exposure to cadmium.

(11) *Medical Removal Protection (MRP)*—(i) *General.* (A) The employer shall temporarily remove an employee from work where there is excess exposure to cadmium on each occasion that medical removal is required under paragraph (l)(3), (l)(4), or (l)(6) of this section and on each occasion that a physician determines in a written medical opinion that the employee should be removed from such exposure. The physician's determination may be based on biological monitoring results, inability to wear a respirator, evidence of illness, other signs or symptoms of cadmium-related dysfunction or disease, or any other reason deemed medically sufficient by the physician.

(B) The employer shall medically remove an employee in accordance with paragraph (l)(11) of this section regardless of whether at the time of removal a job is available into which the removed employee may be transferred.

(C) Whenever an employee is medically removed under paragraph (l)(11) of this section, the employer shall transfer the removed employee to a job where the exposure to cadmium is within the permissible levels specified in that paragraph as soon as one becomes available.

(D) For any employee who is medically removed under the provisions of paragraph (l)(11)(i) of this section, the employer shall provide follow-up biological monitoring in accordance with (l)(2)(ii)(B) of this section at least every three months and follow-up medical examinations semi-annually at least every six months until in a written medical opinion the examining physician determines that either the employee may be returned to his/her former job status as specified under paragraph (l)(11)(iv)–(v) of this section or the employee must be permanently removed from excess cadmium exposure.

(E) The employer may not return an employee who has been medically removed for any reason to his/her former job status until a physician determines in a written medical opinion that continued medical removal is no longer necessary to protect the employee's health.

(ii) Where an employee is found unfit to wear a respirator under paragraph (l)(6)(ii) of this section, the employer shall remove the employee from work where exposure to cadmium is above the PEL.

(iii) Where removal is based on any reason other than the employee's inability to wear a respirator, the employer shall remove the employee from work where exposure to cadmium is at or above the action level.

(iv) Except as specified in paragraph (l)(11)(v) of this section, no employee who was removed because his/her level of CdU, CdB and/or β_2-M exceeded the mandatory medical removal trigger levels in paragraph (l)(3) or (l)(4) of this section may be returned to work with exposure to cadmium at or above the action level until the employee's levels of CdU fall to or below 3 μg/g Cr, CdB falls to or below 5 μg/lwb, and β_2-M falls to or below 300 μg/g Cr.

(v) However, when in the examining physician's opinion continued exposure to cadmium will not pose an increased risk to the employee's health and there are special circumstances that make continued medical removal an inappropriate remedy, the physician shall fully discuss these matters with the employee, and then in a written determination may return a worker to his/her former job status despite what would otherwise be unacceptably high biological monitoring results. Thereafter, the returned employee shall continue to be provided with medical surveillance as if he/she were still on medical removal until the employee's levels of CdU fall to or below 3 μg/g Cr, CdB falls to or below 5 μg/lwb, and β_2-M falls to or below 300 μg/g Cr.

(vi) Where an employer, although not required by paragraph (l)(11)(i)–(iii) of this section to do so, removes an employee from exposure to cadmium or otherwise places limitations on an employee due to the effects of cadmium exposure on the employee's medical condition, the employer shall provide the same medical removal protection benefits to that employee under paragraph (l)(12) of this section as would have been provided had the removal been required under paragraph (l)(11)(i)–(iii) of this section.

(12) *Medical Removal Protection Benefits (MRPB).* (i) The employer shall provide MRPB for up to a maximum of 18 months to an employee each time and while the employee is temporarily medically removed under paragraph (l)(11) of this section.

(ii) For purposes of this section, the requirement that the employer provide MRPB means that the employer shall maintain the total normal earnings, seniority, and all other employee rights and benefits of the removed employee, including the employee's right to his/her former job status, as if the employee had not been removed from the employee's job or otherwise medically limited.

(iii) Where, after 18 months on medical removal because of elevated biological monitoring results, the employee's monitoring results have not declined to a low enough level to permit the employee to be returned to his/her former job status:

(A) The employer shall make available to the employee a medical examination pursuant to this section in order to obtain a final medical determination as to whether the employee may be returned to his/her former job status or must be permanently removed from excess cadmium exposure; and

(B) The employer shall assure that the final medical determination indicates whether the employee may be returned to his/her former job status and what steps, if any, should be taken to protect the employee's health.

(iv) The employer may condition the provision of MRPB upon the employee's participation in medical surveillance provided in accordance with this section.

(13) *Multiple physician review.* (i) If the employer selects the initial physician to conduct any medical examination or consultation provided to an employee under this section, the employee may designate a second physician to:

(A) Review any findings, determinations, or recommendations of the initial physician; and

(B) Conduct such examinations, consultations, and laboratory tests as the second physician deems necessary to facilitate this review.

(ii) The employer shall promptly notify an employee of the right to seek a second medical opinion after each occasion that an initial physician provided by the employer conducts a medical examination or consultation pursuant to this section. The employer may condition its participation in, and payment for, multiple physician review upon the employee doing the following within fifteen (15) days after receipt of this notice, or receipt of the initial physician's written opinion, whichever is later:

(A) Informing the employer that he or she intends to seek a medical opinion; and

(B) Initiating steps to make an appointment with a second physician.

(iii) If the findings, determinations, or recommendations of the second physician differ from those of the initial physician, then the employer and the employee shall assure that efforts are made for the two physicians to resolve any disagreement.

(iv) If the two physicians have been unable to quickly resolve their disagreement, then the employer and the employee, through their respective physicians, shall designate a third physician to:

(A) Review any findings, determinations, or recommendations of the other two physicians; and

(B) Conduct such examinations, consultations, laboratory tests, and discussions with the other two physicians as the third physician deems necessary to resolve the disagreement among them.

(v) The employer shall act consistently with the findings, determinations, and recommendations of the third physician, unless the employer and the employee reach an agreement that is consistent with the recommendations of at least one of the other two physicians.

(14) *Alternate physician determination.* The employer and an employee or designated employee representative may agree upon the use of any alternate form of physician determination in lieu of the multiple physician review provided by paragraph (l)(13) of this section, so long as the alternative is expeditious and at least as protective of the employee.

(15) *Information the employer must provide the employee.* (i) The employer shall provide a copy of the physician's written medical opinion to the examined employee within two weeks after receipt thereof.

(ii) The employer shall provide the employee with a copy of the employee's biological monitoring results and an explanation sheet explaining the results within two weeks after receipt thereof.

(iii) Within 30 days after a request by an employee, the employer shall provide the employee with the information the employer is required to provide the examining physician under paragraph (l)(9) of this section.

(16) *Reporting.* In addition to other medical events that are required to be reported on the OSHA Form No. 200, the employer shall report any abnormal condition or disorder caused by exposure to occupational factors associated with employment as specified in Chapter (V)(E) of the Reporting Guidelines for Occupational Injuries and Illnesses.

(m) *Communication of cadmium hazards to employees*—(1) *General.* In communications concerning cadmium hazards, employers shall comply with the requirements of OSHA's Hazard Communication Standard, 29 CFR 1910.1200, including but not limited to the requirements concerning warning signs and labels, material safety data sheets (MSDS), and employee information and training. In addition, employers shall comply with the following requirements:

(2) *Warning signs.* (i) Warning signs shall be provided and displayed in regulated areas. In addition, warning signs shall be posted at all approaches to regulated areas so that an employee may read the signs and take necessary protective steps before entering the area.

(ii) Warning signs required by paragraph (m)(2)(i) of this section shall bear the following information:

DANGER
CADMIUM
CANCER HAZARD
CAN CAUSE LUNG AND KIDNEY DISEASE

AUTHORIZED PERSONNEL ONLY
RESPIRATORS REQUIRED IN THIS AREA

(iii) The employer shall assure that signs required by this paragraph are illuminated, cleaned, and maintained as necessary so that the legend is readily visible.

(3) *Warning labels.* (i) Shipping and storage containers containing cadmium, cadmium compounds, or cadmium contaminated clothing, equipment, waste, scrap, or debris shall bear appropriate warning labels, as specified in paragraph (m)(3)(ii) of this section.

(ii) The warning labels shall include at least the following information:

DANGER
CONTAINS CADMIUM
CANCER HAZARD
AVOID CREATING DUST
CAN CAUSE LUNG AND KIDNEY DISEASE

(iii) Where feasible, installed cadmium products shall have a visible label or other indication that cadmium is present.

(4) *Employee information and training.* (i) The employer shall institute a training program for all employees who are potentially exposed to cadmium, assure employee participation in the program, and maintain a record of the contents of such program.

(ii) Training shall be provided prior to or at the time of initial assignment to a job involving potential exposure to cadmium and at least annually thereafter.

(iii) The employer shall make the training program understandable to the employee and shall assure that each employee is informed of the following:

(A) The health hazards associated with cadmium exposure, with special attention to the information incorporated in appendix A to the section;

(B) The quantity, location, manner of use, release, and storage of cadmium in the workplace and the specific nature of operations that could result in exposure to cadmium, especially exposures above the PEL;

(C) The engineering controls and work practices associated with the employee's job assignment;

(D) The measures employees can take to protect themselves from exposure to cadmium, including modification of such habits as smoking and personal hygiene, and specific procedures the employer has implemented to protect employees from exposure to cadmium such as appropriate work practices, emergency procedures, and the provision of personal protective equipment;

(E) The purpose, proper selection, fitting, proper use, and limitations of respirators and protective clothing;

(F) The purpose and a description of the medical surveillance program required by paragraph (l) of this section;

(G) The contents of this section and its appendices; and

(H) The employee's rights of access to records under § 1910.20(g)(1) and (2).

(iv) Additional access to information and training program and materials.

(A) The employer shall make a copy of this section and its appendices readily available without cost to all affected employees and shall provide a copy if requested.

(B) The employer shall provide to the Assistant Secretary or the Director, upon request, all materials relating to the employee information and the training program.

(n) *Recordkeeping*—(1) *Exposure monitoring.* (i) The employer shall establish and keep an accurate record of all air monitoring for cadmium in the workplace.

(ii) This record shall include at least the following information:

(A) The monitoring date, duration, and results in terms of an 8-hour TWA of each sample taken;

(B) The name, social security number, and job classification of the employees monitored and of all other employees whose exposures the monitoring is intended to represent;

(C) A description of the sampling and analytical methods used and evidence of their accuracy;

(D) The type of respiratory protective device, if any, worn by the monitored employee;

(E) A notation of any other conditions that might have affected the monitoring results.

(iii) The employer shall maintain this record for at least thirty (30) years, in accordance with 29 CFR 1910.20.

(2) *Objective data for exemption from requirement for initial monitoring.* (i) For purposes of this section, objective data are information demonstrating that a particular product or material containing cadmium or a specific process, operation, or activity involving cadmium cannot release dust or fumes in concentrations at or above the action level even under the worst-case release conditions. Objective data can be obtained from an industry-wide study or from laboratory product test results from manufacturers of cadmium-containing products or materials. The data the employer uses from an industry-wide survey must be obtained under workplace conditions closely resembling the processes, types of material, control methods, work practices and environmental conditions in the employer's current operations.

(ii) The employer shall establish and maintain a record of the objective data for at least 30 years.

(3) *Medical surveillance.* (i) The employer shall establish and maintain an accurate record for each employee covered by medical surveillance under paragraph (l)(1)(i) of this section.

(ii) The record shall include at least the following information about the employee:

(A) Name, social security number, and description of the duties;

(B) A copy of the physician's written opinions and an explanation sheet for biological monitoring results;

(C) A copy of the medical history, and the results of any physical examination and all test results that are required to be provided by this section, including biological tests, X-rays, pulmonary function tests, etc., or that have been obtained to further evaluate any condition that might be related to cadmium exposure;

(D) The employee's medical symptoms that might be related to exposure to cadmium; and

(E) A copy of the information provided to the physician as required by paragraph (l)(9)(ii)–(v) of this section.

(iii) The employer shall assure that this record is maintained for the duration of employment plus thirty (30) years, in accordance with 29 CFR 1910.20.

(4) *Training.* The employer shall certify that employees have been trained by preparing a certification record which includes the identity of the person trained, the signature of the employer or the person who conducted the training, and the date the training was completed. The certification records shall be prepared at the completion of training and shall be maintained on file for one (1) year beyond the date of training of that employee.

(5) *Availability.* (i) Except as otherwise provided for in this section, access to all records required to be maintained by paragraphs (n)(1)–(4) of this section shall be in accordance with the provisions of 29 CFR 1910.20.

(ii) Within 15 days after a request, the employer shall make an employee's medical records required to be kept by paragraph (n)(3) of this section available for examination and copying to the subject employee, to designated representatives, to anyone having the specific written consent of the subject employee, and after the employee's death or incapacitation, to the employee's family members.

(6) *Transfer of records.* Whenever an employer ceases to do business and there is no successor employer to

receive and retain records for the prescribed period or the employer intends to dispose of any records required to be preserved for at least 30 years, the employer shall comply with the requirements concerning transfer of records set forth in 29 CFR 1910.20 (h).

(o) *Observation of monitoring*—(1) *Employee observation.* The employer shall provide affected employees or their designated representatives an opportunity to observe any monitoring of employee exposure to cadmium.

(2) *Observation procedures.* When observation of monitoring requires entry into an area where the use of protective clothing or equipment is required, the employer shall provide the observer with that clothing and equipment and shall assure that the observer uses such clothing and equipment and complies with all other applicable safety and health procedures.

(p) *Dates*—(1) *Effective date.* This section shall become effective December 14, 1992.

(2) *Start-up dates.* All obligations of this section commence on the effective date except as follows:

(i) *Exposure monitoring.* Except for small businesses (nineteen (19) or fewer employees), initial monitoring required by paragraph (d)(2) of this section shall be completed as soon as possible and in any event no later than 60 days after the effective date of this standard. For small businesses, initial monitoring required by paragraph (d)(2) of this section shall be completed as soon as possible and in any event no later than 120 days after the effective date of this standard.

(ii) *Regulated areas.* Except for small business, defined under paragraph (p)(2)(i) of this section, regulated areas required to be established by paragraph (e) of this section shall be set up as soon as possible after the results of exposure monitoring are known and in any event no later than 90 days after the effective date of this section. For small businesses, regulated areas required to be established by paragraph (e) of this section shall be set up as soon as possible after the results of exposure monitoring are known and in any event no later than 150 days after the effective date of this section.

(iii) *Respiratory protection.* Except for small businesses, defined under paragraph (p)(2)(i) of this section, respiratory protection required by paragraph (g) of this section shall be provided as soon as possible and in any event no later than 90 days after the effective date of this section. For small businesses, respiratory protection required by paragraph (g) of this section shall be provided as soon as possible and in any event no later than 150 days after the effective date of this section.

(iv) *Compliance program.* Written compliance programs required by paragraph (f)(2) of this section shall be completed and available for inspection and copying as soon as possible and in any event no later than 1 year after the effective date of this section.

(v) *Methods of compliance.* The engineering controls required by paragraph (f)(1) of this section shall be implemented as soon as possible and in any event no later than two (2) years after the effective date of this section. Work practice controls shall be implemented as soon as possible. Work practice controls that are directly related to engineering controls to be implemented in accordance with the compliance plan shall be implemented as soon as possible after such engineering controls are implemented.

(vi) *Hygiene and lunchroom facilities.* (A) Handwashing facilities, permanent or temporary, shall be provided in accordance with 29 CFR 1910.141 (d)(1) and (2) as soon as possible and in any event no later than 60 days after the effective date of this section.

(B) Change rooms, showers, and lunchroom facilities shall be completed as soon as possible and in any event no later than 1 year after the effective date of this section.

(vii) *Employee information and training.* Except for small businesses, defined under paragraph (p)(2)(i) of this section, employee information and training required by paragraph (m)(4) of this section shall be provided as soon as possible and in any event no later than 90 days after the effective date of this standard. For small businesses, employee information and training required by paragraph (m)(4) of this standard shall be provided as soon as possible and in any event no later than 180 days after the effective date of this standard.

(viii) *Medical surveillance.* Except for small businesses, defined under paragraph (p)(2)(i) of this section, initial medical examinations required by paragraph (l) of this section shall be provided as soon as possible and in any event no later than 90 days after the effective date of this standard. For small businesses, initial medical examinations required by paragraph (l) of this section shall be provided as soon as possible and in any event no later than 180 days after the effective date of this standard.

(q) *Appendices.* (1) Appendix C to this section is incorporated as part of this section, and compliance with its contents is mandatory.

(2) Except where portions of appendices A, B, D, E, and F to this section are expressly incorporated in requirements of this section, these appendices are purely informational and are not intended to create any additional obligations not otherwise imposed or to detract from any existing obligations.

Appendix A to § _____—Substance Safety Data Sheet

Cadmium

I. Substance Identification

A. Substance: Cadmium.

B. 8-Hour, Time-weighted-average, Permissible Exposure Limit (TWA PEL):

1. TWA PEL: Five micrograms of cadmium per cubic meter of air 5 $\mu g/m^3$, time-weighted average (TWA) for an 8-hour workday.

C. Appearance: Cadmium metal—soft, blue-white, malleable, lustrous metal or grayish-white powder. Some cadmium compounds may also appear as a brown, yellow, or red powdery substance.

II. Health Hazard Data

A. Routes of Exposure. Cadmium can cause local skin or eye irritation. Cadmium can affect your health if you inhale it or if you swallow it.

B. Effects of Overexposure.

1. Short-term (acute) exposure: Cadmium is much more dangerous by inhalation than by ingestion. High exposures to cadmium that may be immediately dangerous to life or health occur in jobs where workers handle large quantities of cadmium dust or fume; heat cadmium-containing compounds or cadmium-coated surfaces; weld with cadmium solders or cut cadmium-containing materials such as bolts.

2. Severe exposure may occur before symptoms appear. Early symptoms may include mild irritation of the upper respiratory tract, a sensation of constriction of the throat, a metallic taste and/or a cough. A period of 1–10 hours may precede the onset of rapidly progressing shortness of breath, chest pain, and flu-like symptoms with weakness, fever, headache, chills, sweating and muscular pain. Acute pulmonary edema usually develops within 24 hours and reaches a maximum by three days. If death from asphyxia does not occur, symptoms may resolve within a week.

3. Long-term (chronic) exposure. Repeated or long-term exposure to cadmium, even at relatively low concentrations, may result in kidney damage and an increased risk of cancer of the lung and of the prostate.

C. Emergency First Aid Procedures.

1. Eye exposure: Direct contact may cause redness or pain. Wash eyes immediately with large amounts of water, lifting the upper and lower eyelids. Get medical attention immediately.

2. Skin exposure: Direct contact may result in irritation. Remove contaminated clothing and shoes immediately. Wash affected area with soap or mild detergent and large amounts of water. Get medical attention immediately.

3. Ingestion: Ingestion may result in vomiting, abdominal pain, nausea, diarrhea, headache and sore throat. Treatment for

symptoms must be administered by medical personnel. Under no circumstances should the employer allow any person whom he retains, employs, supervises or controls to engage in therapeutic chelation. Such treatment is likely to translocate cadmium from pulmonary or other tissue to renal tissue. Get medical attention immediately.

4. Inhalation: If large amounts of cadmium are inhaled, the exposed person must be moved to fresh air at once. If breathing has stopped, perform cardiopulmonary resuscitation. Administer oxygen if available. Keep the affected person warm and at rest. Get medical attention immediately.

5. Rescue: Move the affected person from the hazardous exposure. If the exposed person has been overcome, attempt rescue only after notifying at least one other person of the emergency and putting into effect established emergency procedures. Do not become a casualty yourself. Understand your emergency rescue procedures and know the location of the emergency equipment before the need arises.

III. Employee Information

A. Protective Clothing and Equipment.

1. Respirators: You may be required to wear a respirator for non-routine activities; in emergencies; while your employer is in the process of reducing cadmium exposures through engineering controls; and where engineering controls are not feasible. If respirators are worn in the future, they must have a joint Mine Safety and Health Administration (MSHA) and National Institute for Occupational Safety and Health (NIOSH) label of approval. Cadmium does not have a detectable odor except at levels well above the permissible exposure limits. If you can smell cadmium while wearing a respirator, proceed immediately to fresh air. If you experience difficulty breathing while wearing a respirator, tell your employer.

2. Protective Clothing: You may be required to wear impermeable clothing, gloves, foot gear, a face shield, or other appropriate protective clothing to prevent skin contact with cadmium. Where protective clothing is required, your employer must provide clean garments to you as necessary to assure that the clothing protects you adequately. The employer must replace or repair protective clothing that has become torn or otherwise damaged.

3. Eye Protection: You may be required to wear splash-proof or dust resistant goggles to prevent eye contact with cadmium.

B. Employer Requirements.

1. Medical: If you are exposed to cadmium at or above the action level, your employer is required to provide a medical examination, laboratory tests and a medical history according to the medical surveillance provisions under paragraph (1) of this standard. (See summary chart and tables in this appendix A.) These tests shall be provided without cost to you. In addition, if you are accidentally exposed to cadmium under conditions known or suspected to constitute toxic exposure to cadmium, your employer is required to make special tests available to you.

2. Access to Records: All medical records are kept strictly confidential. You or your representative are entitled to see the records of measurements of your exposure to cadmium. Your medical examination records can be furnished to your personal physician or designated representative upon request by you to your employer.

3. Observation of Monitoring: Your employer is required to perform measurements that are representative of your exposure to cadmium and you or your designated representative are entitled to observe the monitoring procedure. You are entitled to observe the steps taken in the measurement procedure, and to record the results obtained. When the monitoring procedure is taking place in an area where respirators or personal protective clothing and equipment are required to be worn, you or your representative must also be provided with, and must wear the protective clothing and equipment.

C. Employee Requirements.—You will not be able to smoke, eat, drink, chew gum or tobacco, or apply cosmetics while working with cadmium in regulated areas. You will also not be able to carry or store tobacco products, gum, food, drinks or cosmetics in regulated areas because these products easily become contaminated with cadmium from the workplace and can therefore create another source unnecessary of cadmium exposure.

Some workers will have to change out of work clothes and shower at the end of the day, as part of their workday, in order to wash cadmium from skin and hair. Handwashing and cadmium-free eating facilities shall be provided by the employer and proper hygiene should always be performed before eating. It is also recommended that you do not smoke or use tobacco products, because among other things, they naturally contain cadmium. For further information, read the labeling on such products.

IV. Physician Information

A. Introduction.—The medical surveillance provisions of paragraph (1) generally are aimed at accomplishing three main interrelated purposes: First, identifying employees at higher risk of adverse health effects from excess, chronic exposure to cadmium; second, preventing cadmium-induced disease; and third, detecting and minimizing existing cadmium-induced disease. The core of medical surveillance in this standard is the early and periodic monitoring of the employee's biological indicators of: (a) Recent exposure to cadmium; (b) cadmium body burden; and (c) potential and actual kidney damage associated with exposure to cadmium.

The main adverse health effects associated with cadmium overexposure are lung cancer and kidney dysfunction. It is not yet known how to adequately biologically monitor human beings to specifically prevent cadmium-induced lung cancer. By contrast, the kidney can be monitored to provide prevention and early detection of cadmium-induced kidney damage. Since, for non-carcinogenic effects, the kidney is considered the primary target organ of chronic exposure to cadmium, the medical surveillance provisions of this standard effectively focus on cadmium-induced kidney disease. Within that focus, the aim, where possible, is to prevent the onset of such disease and, where necessary, to minimize such disease as may already exist. The by-products of successful prevention of kidney disease are anticipated to be the reduction and prevention of other cadmium-induced diseases.

B. Health Effects.—The major health effects associated with cadmium overexposure are described below.

1. Kidney: The most prevalent non-malignant disease observed among workers chronically exposed to cadmium is kidney dysfunction. Initially, such dysfunction is manifested as proteinuria. The proteinuria associated with cadmium exposure is most commonly characterized by excretion of low-molecular weight proteins (15,000 to 40,000 MW) accompanied by loss of electrolytes, uric acid, calcium, amino acids, and phosphate. The compounds commonly excreted include: beta-2-microglobulin (β_2-M), retinol binding protein (RBP), immunoglobulin light chains, and lysozyme. Excretion of low molecular weight proteins are characteristic of damage to the proximal tubules of the kidney (Iwao *et al.*, 1980).

It has also been observed that exposure to cadmium may lead to urinary excretion of high-molecular weight proteins such as albumin, immunoglobulin G, and glycoproteins (Ex. 29). Excretion of high-molecular weight proteins is typically indicative of damage to the glomeruli of the kidney. Bernard *et al.*, (1979) suggest that damage to the glomeruli and damage to the proximal tubules of the kidney may both be linked to cadmium exposure but they may occur independently of each other.

Several studies indicate that the onset of low-molecular weight proteinuria is a sign of irreversible kidney damage (Friberg *et al.*, 1974; Roels *et al.*, 1982; Piscator 1984; Elinder *et al.*, 1985; Smith *et al.*, 1986). Above specific levels of β_2-M associated with cadmium exposure it is unlikely that β_2-M levels return to normal even when cadmium exposure is eliminated by removal of the individual from the cadmium work environment (Friberg, Ex. 29, 1990).

Some studies indicate that such proteinuria may be progressive; levels of β_2-M observed in the urine increase with time even after cadmium exposure has ceased. See, for example, Elinder *et al.*, 1985. Such observations, however, are not universal, and it has been suggested that studies in which proteinuria has not been observed to progress may not have tracked patients for a sufficiently long time interval (Jarup, Ex. 8-661).

When cadmium exposure continues after the onset of proteinuria, chronic nephrotoxicity may occur (Friberg, Ex. 29). Uremia results from the inability of the glomerulus to adequately filter blood. This leads to severe disturbance of electrolyte concentrations and may lead to various clinical complications including kidney stones (L-140-50).

After prolonged exposure to cadmium, glomerular proteinuria, glucosuria, aminoaciduria, phosphaturia, and hypercalciuria may develop (Exs. 8-86, 4-28, 14-16). Phosphate, calcium, glucose, and amino acids are essential to life, and under normal conditions, their excretion should be

regulated by the kidney. Once low molecular weight proteinuria has developed, these elements dissipate from the human body. Loss of glomerular function may also occur, manifested by decreased glomerular filtration rate and increased serum creatinine. Severe cadmium-induced renal damage may eventually develop into chronic renal failure and uremia (Ex. 55).

Studies in which animals are chronically exposed to cadmium confirm the renal effects observed in humans (Friberg *et al.*, 1986). Animal studies also confirm problems with calcium metabolism and related skeletal effects which have been observed among humans exposed to cadmium in addition to the renal effects. Other effects commonly reported in chronic animal studies include anemia, changes in liver morphology, immunosuppression and hypertension. Some of these effects may be associated with co-factors. Hypertension, for example, appears to be associated with diet as well as cadmium exposure. Animals injected with cadmium have also shown testicular necrosis (Ex. 8–86B).

2. Biological Markers

It is universally recognized that the best measures of cadmium exposures and its effects are measurements of cadmium in biological fluids, especially urine and blood. Of the two, CdU is conventionally used to determine body burden of cadmium in workers without kidney disease. CdB is conventionally used to monitor for recent exposure to cadmium. In addition, levels of CdU and CdB historically have been used to predict the percent of the population likely to develop kidney disease (Thun *et al.*, Ex. L–140–50; WHO, Ex. 8–674; ACGIH, Exs. 8–667, 140–50).

The third biological parameter upon which OSHA relies for medical surveillance is Beta-2-microglobulin in urine (β_2-M), a low molecular weight protein. Excess β_2-M has been widely accepted by physicians and scientists as a reliable indicator of functional damage to the proximal tubule of the kidney (Exs. 8–447, 144–3–C, 4–47, L–140–45, 19–43–A).

Excess β_2-M is found when the proximal tubules can no longer reabsorb this protein in a normal manner. This failure of the proximal tubules is an early stage of a kind of kidney disease that commonly occurs among workers with excessive cadmium exposure. Used in conjunction with biological test results indicating abnormal levels of CdU and CdB, the finding of excess β_2-M can establish for an examining physician that any existing kidney disease is probably cadmium-related (Trs. 6/6/90, pp. 82–86, 122, 134). The upper limits of normal levels for cadmium in urine and cadmium in blood are 3 μg Cd/gram creatinine in urine and 5 μgCd/liter whole blood, respectively. These levels were derived from broad-based population studies.

Three issues confront the physicians in the use of β_2-M as a marker of kidney dysfunction and material impairment. First, there are a few other causes of elevated levels of β_2-M not related to cadmium exposures, some of which may be rather common diseases and some of which are serious diseases (e.g., myeloma or transient flu, Exs. 29 and 8–086). These can be medically evaluated as alternative causes (Friberg, Ex. 29). Also, there are other factors that can cause β_2-M to degrade so that low levels would result in workers with tubular dysfunction. For example, regarding the degradation of β_2-M, workers with acidic urine (pH<6) might have β_2-M levels that are within the "normal" range when in fact kidney dysfunction has occurred (Ex. L–140–1) and the low molecular weight proteins are degraded in acid urine. Thus, it is very important that the pH of urine be measured, that urine samples be buffered as necessary (See appendix F.), and that urine samples be handled correctly, i.e., measure the pH of freshly voided urine samples, then if necessary, buffer to pH>6 (or above for shipping purposes), measure pH again and then, perhaps, freeze the sample for storage and shipping. (See also appendix F.) Second, there is debate over the pathological significance of proteinuria, however, most world experts believe that β_2-M levels greater than 300 μg/g Cr are abnormal (Elinder, Ex. 55, Friberg, Ex. 29). Such levels signify kidney dysfunction that constitutes material impairment of health. Finally, detection of β_2-M at low levels has often been considered difficult, however, many laboratories have the capability of detecting excess β_2-M using simple kits, such as the Phadebas Delphia test, that are accurate to levels of 100 μg β_2-M/g Cr U (Ex. L–140–1).

Specific recommendations for ways to measure β_2-M and proper handling of urine samples to prevent degradation of β_2-M have been addressed by OSHA in appendix F, in the section on laboratory standardization. All biological samples must be analyzed in a laboratory that is proficient in the analysis of that particular analyte, under paragraph (l)(1)(iv). (See appendix F). Specifically, under paragraph (l)(1)(iv), the employer is to assure that the collecting and handling of biological samples of cadmium in urine (CdU), cadmium in blood (CdB), and beta-2 microglobulin in urine (β_2-M) taken from employees is collected in a manner that assures reliability. The employer must also assure that analysis of biological samples of cadmium in urine (CdU), cadmium in blood (CdB), and beta-2 microglobulin in urine (β_2-M) taken from employees is performed in laboratories with demonstrated proficiency for that particular analyte. (See appendix F.)

3. Lung and Prostate Cancer

The primary sites for cadmium-associated cancer appear to be the lung and the prostate (L–140–50). Evidence for an association between cancer and cadmium exposure derives from both epidemiological studies and animal experiments. Mortality from prostate cancer associated with cadmium is slightly elevated in several industrial cohorts, but the number of cases is small and there is not clear dose-response relationship. More substantive evidence exists for lung cancer.

The major epidemiological study of lung cancer was conducted by Thun *et al.*, (Ex. 4–68). Adequate data on cadmium exposures were available to allow evaluation of dose-response relationships between cadmium exposure and lung cancer. A statistically significant excess of lung cancer attributed to cadmium exposure was observed in this study even when confounding variables such as co-exposure to arsenic and smoking habits were taken into consideration (Ex. L–140–50).

The primary evidence for quantifying a link between lung cancer and cadmium exposure from animal studies derives from two rat bioassay studies; one by Takenaka *et al.*, (1983), which is a study of cadmium chloride and a second study by Oldiges and Glaser (1990) of four cadmium compounds.

Based on the above cited studies, the U.S. Environmental Protection Agency (EPA) classified cadmium as "B1", a probable human carcinogen, in 1985 (Ex. 4–4). The International Agency for Research on Cancer (IARC) in 1987 also recommended that cadmium be listed as "2A", a probable human carcinogen (Ex. 4–15). The American Conference of Governmental Industrial Hygienists (ACGIH) has recently recommended that cadmium be labeled as a carcinogen. Since 1984, NIOSH has concluded that cadmium is possibly a human carcinogen and has recommended that exposures be controlled to the lowest level feasible.

4. Non-carcinogenic Effects

Acute pneumonitis occurs 10 to 24 hours after initial acute inhalation of high levels of cadmium fumes with symptoms such as fever and chest pain (Exs. 30, 8–86B). In extreme exposure cases pulmonary edema may develop and cause death several days after exposure. Little actual exposure measurement data is available on the level of airborne cadmium exposure that causes such immediate adverse lung effects, nonetheless, it is reasonable to believe a cadmium concentration of approximately 1 mg/m^3 over an eight hour period is "immediately dangerous" (55 FR 4052, ANSI; Ex. 8–86B).

In addition to acute lung effects and chronic renal effects, long term exposure to cadmium may cause other severe effects on the respiratory system. Reduced pulmonary function and chronic lung disease indicative of emphysema have been observed in workers who have had prolonged exposure to cadmium dust or fumes (Exs. 4–29, 4–22, 4–42, 4–50, 4–63). In a study of workers conducted by Kazantzis *et al.*, a statistically significant excess of worker deaths due to chronic bronchitis was found, which in his opinion was directly related to high cadmium exposures of 1 mg/m^3 or more (Tr. 6/8/90, pp. 156–157).

Cadmium need not be respirable to constitute a hazard. Inspirable cadmium particles that are too large to be respirable but small enough to enter the tracheobronchial region of the lung can lead to bronchoconstriction, chronic pulmonary disease, and cancer of that portion of the lung. All of these diseases have been associated with occupational exposure to cadmium (Ex. 8–86B). Particles that are constrained by their size to the extra-thoracic regions of the respiratory system such as the nose and maxillary sinuses can be swallowed through mucocillary clearance and be absorbed into the body (ACGIH, Ex. 8–692). The impaction of these particles in the upper airways can lead to anosmia, or loss of sense of smell, which is an early indication of overexposure among workers exposed to heavy metals. This condition is commonly

reported among cadmium-exposed workers (Ex. 8–86–B).

C. Medical Surveillance

In general, the main provisions of the medical surveillance section of the standard, under paragraphs (l)(1)–(17) of the regulatory text, are as follows:

1. Workers exposed above the action level are covered;

2. Workers with intermittent exposures are not covered;

3. Past workers who are covered receive biological monitoring for at least one year;

4. Initial examinations include a medical questionnaire and biological monitoring of cadmium in blood (CdB), cadmium in urine (CdU), and Beta-2-microglobulin in urine (β_2-M);

5. Biological monitoring of these three analytes is performed at least annually; full medical examinations are performed biennially;

6. Until five years from the effective date of the standard, medical removal is required when CdU is greater than 15 μg/gram creatinine (g Cr), or CdB is greater than 15 μg/liter whole blood (lwb), or β_2-M is greater than 1500 μg/g Cr, and CdB is greater than 5 μg/lwb or CdU is greater than 3 μg/g Cr;

7. Beginning five years after the standard is in effect, medical removal triggers will be reduced;

8. Medical removal protection benefits are to be provided for up to 18 months;

9. Limited initial medical examinations are required for respirator usage;

10. Major provisions are fully described under section (l) of the regulatory text; they are outlined here as follows:

A. Eligibility
B. Biological monitoring
C. Actions triggered by levels of CdU, CdB, and β_2-M (See Summary Charts and Tables in Attachment-1.)
D. Periodic medical surveillance
E. Actions triggered by periodic medical surveillance (See appendix A Summary Chart and Tables in Attachment-1.)
F. Respirator usage
G. Emergency medical examinations
H. Termination examination
I. Information to physician
J. Physician's medical opinion
K. Medical removal protection
L. Medical removal protection benefits
M. Multiple physician review
N. Alternate physician review
O. Information employer gives to employee
P. Recordkeeping
Q. Reporting on OSHA form 200

11. The above mentioned summary of the medical surveillance provisions, the summary chart, and tables for the actions triggered at different levels of CdU, CdB and β_2-M (in appendix A Attachment-1) are included only for the purpose of facilitating understanding of the provisions of paragraphs (l)(3) of the final cadmium standard. The summary of the provisions, the summary chart, and the tables do not add to or reduce the requirements in paragraph (l)(3).

D. Recommendations to Physicians

1. It is strongly recommended that patients with tubular proteinuria are counseled on: The hazards of smoking; avoidance of nephrotoxins and certain prescriptions and over-the-counter medications that may exacerbate kidney symptoms; how to control diabetes and/or blood pressure; proper hydration, diet, and exercise (Ex. 19–2). A list of prominent or common nephrotoxins is attached. (See appendix A Attachment-2.)

2. DO NOT CHELATE: KNOW WHICH DRUGS ARE NEPHROTOXINS OR ARE ASSOCIATED WITH NEPHRITIS.

3. The gravity of cadmium-induced renal damage is compounded by the fact there is no medical treatment to prevent or reduce the accumulation of cadmium in the kidney (Ex. 8–619). Dr. Friberg, a leading world expert on cadmium toxicity, indicated in 1992, that there is no form of chelating agent that could be used without substantial risk. He stated that tubular proteinuria has to be treated in the same way as other kidney disorders (Ex. 29).

4. After the results of a workers' biological monitoring or medical examination are received the employer is required to provide an information sheet to the patient, briefly explaining the significance of the results. (See Attachment 3 of this appendix A.)

5. For additional information the physician is referred to the following additional resources:

a. The physician can always obtain a copy of the preamble, with its full discussion of the health effects, from OSHA's Computerized Information System (OCIS).

b. The Docket Officer maintains a record of the rulemaking. The Cadmium Docket (H–057A), is located at 200 Constitution Ave. NW., room N–2625, Washington, DC 20210; telephone: 202–523–7894.

c. The following articles and exhibits in particular from that docket (H–057A):

Exhibit number	Author and paper title
8–447	Lauwerys *et. al.*, Guide for physicians, "Health Maintenance of Workers Exposed to Cadmium," published by the Cadmium Council.
4–67	Takenaka, S., H. Oldigos, H. Konig, D. Hochrainer, G. Oberdorster. "Carcinogenicity of Cadmium Chloride Aerosols in Wistar Rats". *JNCI* 70:367–373, 1983. (32)
4–68	Thun, M.J., T.M. Schnoor, A.B. Smith, W.E. Halperin, R.A. Lemen. "Mortality Among a Cohort of U.S. Cadmium Production Workers—An Update." *JNCI* 74(2):325–33, 1985. (8)
4–25	Elinder, C.G., Kjellstrom, T., Hogstedt, C., *et al.*, "Cancer Mortality of Cadmium Workers." *Brit. J. Ind. Med.* 42:651–655, 1985. (14)
4–26	Ellis, K.J. *et al.*, "Critical Concentrations of Cadmium in Human Renal Cortex: Dose Effect Studies to Cadmium Smelter Workers." *J. Toxicol. Environ. Health* 7:691–703, 1981. (76)
4–27	Ellis, K.J., S.H. Cohn and T.J. Smith. "Cadmium Inhalation Exposure Estimates: Their Significance with Respect to Kidney and Liver Cadmium Burden." *J. Toxicol. Environ. Health* 15:173–187, 1985.
4–28	Falck, F.Y., Jr., Fine, L.J., Smith, R.G., McClatchey, K.D., Annesley, T., England, B., and Schork, A.M. "Occupational Cadmium Exposure and Renal Status." *Am. J. Ind. Med.* 4:541, 1983. (64)
8–86A	Friberg, L., C.G. Elinder, *et al.*, "Cadmium and Health a Toxicological and Epidemiological Appraisal, Volume I, Exposure, Dose, and Metabolism." CRC Press, Inc., Boca Raton, FL, 1986. (Available from the OSHA Technical Data Center)
8–86B	Friberg, L., C.G. Elinder, *et al.*, "Cadmium and Health: A Toxicological and Epidemiological Appraisal, Volume II, Effects and Response." CRC Press, Inc., Boca Raton, FL, 1986. (Available from the OSHA Technical Data Center)
L–140–45	Elinder, C.G., "Cancer Mortality of Cadmium Workers", *Brit. J. Ind. Med.*, 42, 651–655, 1985.
L–140–50	Thun, M., Elinder, C.G., Friberg, L, "Scientific Basis for an Occupational Standard for Cadmium, *Am. J. Ind. Med.*, 20; 629–642, 1991.

V. Information Sheet

The information sheet (appendix A Attachment-3.) or an equally explanatory one should be provided to you after any biological monitoring results are reviewed by the physician, or where applicable, after any medical examination.

APPENDIX A

Attachment 1—Appendix A Summary Chart and Tables A and B of Actions Triggered by Biological Monitoring

Appendix A Summary Chart: Section (1)(3) Medical Surveillance

Categorizing Biological Monitoring Results

(A) Biological monitoring results categories are set forth in Appendix A Table A for the periods ending December 31, 1998 and for the period beginning January 1, 1999.

(B) The results of the biological monitoring for the initial medical exam and the subsequent exams shall determine an employee's biological monitoring result category.

Actions Triggered by Biological Monitoring

(A)

(i) The actions triggered by biological monitoring for an employee are set forth in Appendix A Table B.

(ii) The biological monitoring results for each employee under section (1)(3) shall

determine the actions required for that employee. That is, for any employee in biological monitoring category C, the employer will perform all of the actions for which there is an X in column C of Appendix A Table B.

(iii) An employee is assigned the alphabetical category ("A" being the lowest) depending upon the test results of the three biological markers.

(iv) An employee is assigned category A if monitoring results for all three biological markers fall at or below the levels indicated in the table listed for category A.

(v) An employee is assigned category B if any monitoring result for any of the three biological markers fall within the range of levels indicated in the table listed for category B, providing no result exceeds the levels listed for category B.

(vi) An employee is assigned category C if any monitoring result for any of the three biological markers are above the levels listed for category C.

(B) The user of Appendix A Tables A and B should know that these tables are provided only to facilitate understanding of the relevant provisions of paragraph (l)(3) of this section. Appendix A Tables A and B are not meant to add to or subtract from the requirements of those provisions.

Appendix A Table A

Categorization of Biological Monitoring Results

APPLICABLE THROUGH 1998 ONLY

Biological marker	Monitoring result categories		
	A	B	C
Cadmium in urine (CdU) (μg/g creatinine)	≤3	>3 and ≤16	>15
β_2-microglobulin (β_2-M) (μg/g creatinine)	≤300	>300 and ≤1500	>1500*
Cadmium in blood (CdB) (μg/liter whole blood)	≤5	>5 and ≤15	>15

* If an employee's β_2-M levels are above 1,500 μg/g creatinine, in order for mandatory medical removal to be required (See Appendix A Table B.), either the employee's CdU level must also be >3 μg/g creatinine or CdB level must also be >5 μg/liter whole blood.

APPLICABLE BEGINNING JANUARY 1, 1999

Biological marker	Monitoring result categories		
	A	B	C
Cadmium in urine (CdU) (μg/g creatinine)	≤3	>3 and ≤7	>7
β_2-microglobulin (β_2-M) (μg/g creatinine)	≤300	>300 and ≤750	>750*
Cadmium in blood (CdB) (μg/liter whole blood)	≤5	>5 and ≤10	>10

* If an employee's β_2-M levels are above 750 μg/g creatinine, in order for mandatory medical removal to be required (See Appendix A Table B.), either the employee's CdU level must also be >3 μg/g creatinine or CdB level must also be >5 μg/liter whole blood.

Appendix A Table B—Actions Determined by Biological Monitoring

This table presents the actions required based on the monitoring result in Appendix A Table A. Each item is a separate requirement in citing non-compliance. For example, a medical examination within 90 days for an employee in category B is separate from the requirement to administer a periodic medical examination for category B employees on an annual basis.

Required actions	Monitoring result category		
	A [1]	B [1]	C [1]
(1) Biological monitoring:			
(a) Annual	X		
(b) Semiannual		X	
(c) Quarterly			X
(2) Medical examination:			
(a) Biennial	X		
(b) Annual		X	
(c) Semiannual			X
(d) Within 90 days		X	X
(3) Assess within two weeks:			
(a) Excess cadmium exposure		X	X
(b) Work practices		X	X
(c) Personal hygiene		X	X
(d) Respirator usage		X	X
(e) Smoking history		X	X
(f) Hygiene facilities		X	X
(g) Engineering controls		X	X
(h) Correct within 30 days		X	X
(i) Periodically assess exposures			X
(4) Discretionary medical removal		X	X
(5) Mandatory medical removal			X [2]

[1] For all employees covered by medical surveillance exclusively because of exposures prior to the effective date of this standard, if they are in Category A, the employer shall follow the requirements of paragraphs (l)(3)(i)(B) and (l)(4)(v)(A). If they are in Category B or C, the employer shall follow the requirements of paragraphs (l)(4)(v)(B)–(C).

[2] See footnote Appendix A Table A.

Appendix A—Attachment-2: List of Medications

A list of the more common medications that a physician, and the employee, may wish to review is likely to include some of the following: (1) Anticonvulsants: Paramethadione, phenytoin, trimethadone; (2) antihypertensive drugs: Captopril, methyldopa; (3) antimicrobials: Aminoglycosides, amphotericin B, cephalosporins, ethambutol; (4) antineoplastic agents: Cisplatin, methotrexate, mitomycin-C, nitrosoureas, radiation; (4) sulfonamide diuretics: Acetazolamide, chlorthalidone, furosemide, thiazides; (5) halogenated alkanes, hydrocarbons, and solvents that may occur in some settings: Carbon tetrachloride, ethylene glycol, toluene; iodinated radiographic contrast media; nonsteroidal anti-inflammatory drugs; and, (7) other miscellaneous compounds: Acetominophen, allopurinol, amphetamines, azathioprine, cimetidine, cyclosporine, lithium, methoxyflurane, methysergide, D-penicillamine, phenacetin, phenendione. A list of drugs associated with acute interstitial nephritis includes: (1) Antimicrobial drugs: Cephalosporins, chloramphenicol, colistin, erythromycin, ethambutol, isoniazid, para-aminosalicylic acid, penicillins, polymyxin B, rifampin, sulfonamides, tetracyclines, and vancomycin; (2) other miscellaneous drugs: Allopurinol, antipyrene, azathioprine, captopril, cimetidine, clofibrate, methyldopa, phenindione, phenylpropanolamine, phenytoin, probenecid, sulfinpyrazone, sulfonamid diuretics, triamterene: and, (3) metals: Bismuth, gold.

This list have been derived from commonly available medical textbooks (e.g., Ex. 14–18). The list has been included merely to facilitate the physician's, employer's, and employee's understanding. The list does not represent an official OSHA opinion or policy regarding the use of these medications for particular employees. The use of such medications should be under physician discretion.

Attachment 3—Biological Monitoring and Medical Examination Results

Employee _____
Testing Date _____
Cadmium in Urine _____ μg/g Cr—Normal Levels: ≤3 μg/g Cr.
Cadmium in Blood _____ μg/lwb—Normal Levels: ≤5 μg/lwb.
Beta-2-microglobulin in Urine _____ μg/g Cr—Normal Levels: ≤300 μg/g Cr.
Physical Examination Results: N/A _____ Satisfactory _____ Unsatisfactory _____ (see physician again).
Physician's Review of Pulmonary Function Test: N/A _____ Normal _____ Abnormal _____
Next biological monitoring or medical examination scheduled for _____

The biological monitoring program has been designed for three main purposes: 1) to identify employees at risk of adverse health effects from excess, chronic exposure to cadmium; 2) to prevent cadmium-induced disease(s); and 3) to detect and minimize existing cadmium-induced disease(s).

The levels of cadmium in the urine and blood provide an estimate of the total amount of cadmium in the body. The amount of a specific protein in the urine (beta-2-microglobulin) indicates changes in kidney function. All three tests must be evaluated together. A single mildly elevated result may not be important if testing at a later time indicates that the results are normal and the workplace has been evaluated to decrease possible sources of cadmium exposure. The levels of cadmium or beta-2-microglobulin may change over a period of days to months and the time needed for those changes to occur is different for each worker.

If the results for biological monitoring are above specific "high levels" [cadmium urine greater than 10 micrograms per gram of creatinine (μg/g Cr), cadmium blood greater than 10 micrograms per liter of whole blood (μg/lwb), or beta-2-microglobulin greater than 1000 micrograms per gram of creatinine (μg/g Cr)], the worker has a much greater chance of developing other kidney diseases.

One way to measure for kidney function is by measuring beta-2-microglobulin in the urine. Beta-2-microglobulin is a protein which is normally found in the blood as it is being filtered in the kidney, and the kidney reabsorbs or returns almost all of the beta-2-microglobulin to the blood. A very small amount (less than 300 μg/g Cr in the urine) of beta-2-microglobulin is not reabsorbed into the blood, but is released in the urine. If cadmium damages the kidney, the amount of beta-2-microglobulin in the urine increases because the kidney cells are unable to reabsorb the beta-2-microglobulin normally. An increase in the amount of beta-2-microglobulin in the urine is a very early sign of kidney dysfunction. A small increase in beta-2-microglobulin in the urine will serve as an early warning sign that the worker may be absorbing cadmium from the air, cigarettes contaminated in the workplace, or eating in areas that are cadmium contaminated.

Even if cadmium causes permanent changes in the kidney's ability to reabsorb beta-2-microglobulin, and the beta-2-microglobulin is above the "high levels", the loss of kidney function may not lead to any serious health problems. Also, renal function naturally declines as people age. The risk for changes in kidney function for workers who have biological monitoring results between the "normal values" and the "high levels" is not well known. Some people are more cadmium-tolerant, while others are more cadmium-susceptible.

For anyone with even a slight increase of beta-2-microglobulin, cadmium in the urine, or cadmium in the blood, it is very important to protect the kidney from further damage. Kidney damage can come from other sources than excess cadmium-exposure so it is also recommended that if a worker's levels are "high" he/she should receive counseling about drinking more water; avoiding cadmium-tainted tobacco and certain medications (nephrotoxins, acetaminophen); controlling diet, vitamin intake, blood pressure and diabetes; etc.

Appendix B to § _____—Substance Technical Guidelines for Cadmium

I. Cadmium Metal

A. *Physical and Chemical Data.*

1. *Substance Identification.*

Chemical name: Cadmium.
Formula: Cd.
Molecular Weight: 112.4.
Chemical Abstracts Service (CAS) Registry No.: 7740–43–9.
Other Identifiers: RETCS EU9800000; EPA D006; DOT 2570 53.
Synonyms: Colloidal Cadmium: Kadmium (German): CI 77180.

2. *Physical data.*

Boiling point: (760 mm Hg): 765 degrees C.
Melting point: 321 degrees C.
Specific Gravity: (H_2O=@ 20 °C): 8.64.
Solubility: Insoluble in water; soluble in dilute nitric acid and in sulfuric acid.
Appearance: Soft, blue-white, malleable, lustrous metal or grayish-white powder.

B. *Fire, Explosion and Reactivity Data.*

1. *Fire.*

Fire and Explosion Hazards: The finely divided metal is pyrophoric, that is the dust is a severe fire hazard and moderate explosion hazard when exposed to heat or flame. Burning material reacts violently with extinguishing agents such as water, foam, carbon dioxide, and halons.
Flash point: Flammable (dust).
Extinguishing media: Dry sand, dry dolomite, dry graphite, or sodimum chloride.

2. *Reactivity.*

Conditions contributing to instability: Stable when kept in sealed containers under normal temperatures and pressure, but dust may ignite upon contact with air. Metal tarnishes in moist air.
Incompatibilities: Ammonium nitrate, fused: Reacts violently or explosively with cadmium dust below 20 °C. Hydrozoic acid: Violent explosion occurs after 30 minutes. Acids: Reacts violently, forms hydrogen gas. Oxidizing agents or metals: Strong reaction with cadmium dust. Nitryl fluoride at slightly elevated temperature: Glowing or white incandescence occurs. Selenium: Reacts exothermically. Ammonia: Corrosive reaction. Sulfur dioxide: Corrosive reaction. Fire extinguishing agents (water, foam, carbon dioxide, and halons): Reacts violently. Tellurium: Incandescent reaction in hydrogen atmosphere.
Hazardous decomposition products: The heated metal rapidly forms highly toxic, brownish fumes of oxides of cadmium.

C. *Spill, Leak and Disposal Procedures.*

1. *Steps to be taken if the materials is released or spilled.* Do not touch spilled material. Stop leak if you can do it without risk. Do not get water inside container. For large spills, dike spill for later disposal. Keep unnecessary people away. Isolate hazard area and deny entry. The Superfund Amendments and Reauthorization Act of 1986 Section 304 requires that a release equal to or greater than the reportable quantity for this substance (1 pound) must be immediately reported to the local emergency planning committee, the state emergency response commission, and the National Response Center (800) 424–8802; in Washington, DC metropolitan area (202) 426–2675.

II. Cadmium Oxide

A. *Physical and Chemical Date.*

1. *Substance identification.*

Chemical name: Cadmium Oxide.
Formula: CdO.

Molecular Weight: 128.4.
CAS No.: 1306–19–0.
Other Identifiers: RTECS EV1929500.
Synonyms: Kadmu tlenek (Polish).
2. *Physical data.*
Boiling point (760 mm Hg): 950 degrees C decomposes.
Melting point: 1500 °C.
Specific Gravity: (H_2O=1@20 °C): 7.0.
Solubility: Insoluble in water; soluble in acids and alkalines.
Appearance: Red or brown crystals.
B. *Fire, Explosion and Reactivity Data.*
1. *Fire.*
Fire and Explosion Hazards: Negligible fire hazard when exposed to heat or flame.
Flash point: Nonflammable.
Extinguishing media: Dry chemical, carbon dioxide, water spray or foam.
2. *Reactivity.*
Conditions contributing to instability: Stable under normal temperatures and pressures.
Incompatibilities: Magnesium may reduce CdO_2 explosively on heating.
Hazardous decomposition products: Toxic fumes of cadmium.
C. *Spill Leak and Disposal Procedures.*
1. *Steps to be taken if the material is released or spilled.* Do not touch spilled material. Stop leak if you can do it without risk. For small spills, take up with sand or other absorbent material and place into containers for later disposal. For small dry spills, use a clean shovel to place material into clean, dry container and then cover. Move containers from spill area. For larger spills, dike far ahead of spill for later disposal. Keep unnecessary people away. Isolate hazard area and deny entry. The Superfund Amendments and Reauthorization Act of 1986 Section 304 requires that a release equal to or greater than the reportable quantity for this substance (1 pound) must be immediately reported to the local emergency planning committee, the state emergency response commission, and the National Response Center (800) 424–8802; in Washington, DC metropolitan area (202) 426–2675.

III. Cadmium Sulfide.
A. *Physical and Chemical Data.*
1. *Substance Identification.*
Chemical name: Cadmium sulfide.
Formula: CdS.
Molecular weight: 144.5.
CAS No. 1306–23–6.
Other Identifiers: RTECS EV3150000.
Synonyms: Aurora yellow; Cadmium Golden 366; Cadmium Lemon Yellow 527; Cadmium Orange; Cadmium Primrose 819; Cadmium Sulphide; Cadmium Yellow; Cadmium Yellow 000; Cadmium Yellow Conc. Deep; Cadmium Yellow Conc. Golden; Cadmium Yellow Conc. Lemon; Cadmium Yellow Conc. Primrose; Cadmium Yellow Oz. Dark; Cadmium Yellow Primrose 47–1400; Cadmium Yellow 10G Conc.; Cadmium Yellow 892; Cadmopur Golden Yellow N; Cadmopur Yellow; Capsebon; C.I. 77199; C.I. Pigment Orange 20; CI Pigment Yellow 37; Ferro Lemon Yellow; Ferro Orange Yellow; Ferro Yellow; Greenockite; NCI–C02711.
2. *Physical data.*
Boiling point (760 mm. Hg): sublines in N_2 at 980 °C.
Melting point: 1750 degrees C (100 atm).
Specific Gravity: (H_2O=1@ 20 °C): 4.82.
Solubility: Slightly soluble in water; soluble in acid.
Appearance: Light yellow or yellow-orange crystals.
B. *Fire, Explosion and Reactivity Data.*
1. *Fire.*
Fire and Explosion Hazards: Neglible fire hazard when exposed to heat or flame.
Flash point: Nonflammable.
Extinguishing media: Dry chemical, carbon dioxide, water spray or foam.
2. *Reactivity.*
Conditions contributing to instability: Generally non-reactive under normal conditions. Reacts with acids to form toxic hydrogen sulfide gas.
Incompatibilities: Reacts vigorously with iodinemonochloride.
Hazardous decomposition products: Toxic fumes of cadmium and sulfur oxides.
C. *Spill Leak and Disposal Procedures.*
1. *Steps to be taken if the material is released or spilled.* Do not touch spilled material. Stop leak if you can do it without risk. For small, dry spills, with a clean shovel place material into clean, dry container and cover. Move containers from spill area. For larger spills, dike far ahead of spill for later disposal. Keep unnecessary people away. Isolate hazard and deny entry.

IV. Cadmium Chloride
A. *Physical and Chemical Data.*
1. *Substance Identification.*
Chemcail name: Cadmium chloride.
Formula: $CdC1_2$.
Molecular weight: 183.3.
CAS No. 10108–64–2.
Other Identifiers: RTECS EY0175000.
Synonyms: Caddy; Cadmium dichloride; NA 2570 (DOT); UI-CAD; dichlorocadmium.
2. *Physical data.*
Boiling point (760 mm Hg): 960 degrees C.
Melting point: 568 degrees C.
Specific Gravity: (H_2O=1 @ 20 °C): 4.05.
Solubility: Soluble in water (140 g/100 cc); soluble in acetone.
Appearance: Small, white crystals.
B. *Fire, Explosion and Reactivity Data.*
1. *Fire.*
Fire and Explosion Hazards: Negligible fire and negligible explosion hazard in dust form when exposed to heat or flame.
Flash point: Nonflamable.
Extinguishing media: Dry chemical, carbon dioxide, water spray or foam.
2. *Reactivity.*
Conditions contributing to instability: Generally stable under normal temperatures and pressures.
Incompatibilities: Bromine triflouride rapidly attacks cadmium chloride. A mixture of potassium and cadmium chloride may produce a strong explosion on impact.
Hazardous decomposition products: Thermal ecompostion may release toxic fumes of hydrogen chloride, chloride, chlorine or oxides of cadmium.
C. *Spill Leak and Disposal Procedures.*
1. *Steps to be taken if the materials is released or spilled.* Do not touch spilled material. Stop leak if you can do it without risk. For small, dry spills, with a clean shovel place material into clean, dry container and cover. Move containers from spill area. For larger spills, dike far ahead of spill for later disposal. Keep unnecessary people away. Isolate hazard and deny entry. The Superfund Amendments and Reauthorization Act of 1986 Section 304 requires that a release equal to or greater than the reportable quantity for this substance (100 pounds) must be immediately reported to the local emergency planning committee, the state emergency response commission, and the National Response Center (800) 424–8802; in Washington, DC Metropolitan area (202) 426–2675.

Appendix C to § _____—Qualitative and Quantitative Fit Testing Procedures

I. Fit Test Protocols

A. General: The employer shall include the following provisions in the fit test procedures. These provisions apply to both qualitative fit testing (QLFT) and quantitative fit testing (QNFT). All testing is to be conducted annually.

1. The test subject shall be allowed to pick the most comfortable respirator from a selection including respirators of various sizes from different manufacturers. The selection shall include at least three sizes of elastomeric facepieces of the type of respirator that is to be tested, i.e., three sizes of half mask; or three sizes of full facepiece. Respirators of each size must be provided from at least two manufacturers.

2. Prior to the selection process, the test subject shall be shown how to put on a respirator, how it should be positioned on the face, how to set strap tension and how to determine a comfortable fit. A mirror shall be available to assist the subject in evaluating the fit and positioning the respirator. This instruction may not constitute the subject's formal training on respirator use; it is only a review.

3. The test subject shall be informed that he/she is being asked to select the respirator which provides the most comfortable fit. Each respirator represents a different size and shape, and if fitted, maintained and used properly, will provide substantial protection.

4. The test subject shall be instructed to hold each facepiece up to the face and eliminate those which obviously do not give a comfortable fit.

5. The more comfortable facepieces are noted; the most comfortable mask is donned and worn at least five minutes to assess comfort. Assistance in assessing comfort can be given by discussing the points in item 6 below. If the test subject is not familiar with using a particular respirator, the test subject shall be directed to don the mask several times and to adjust the straps each time to become adept at setting proper tension on the straps.

6. Assessment of comfort shall include reviewing the following points with the test subject and allowing the test subject adequate time to determine the comfort of the respirator:

(a) Position of the mask on the nose;
(b) Room for eye protection;
(c) Room to talk; and
(d) Position of mask on face and cheeks.

7. The following criteria shall be used to help determine the adequacy of the respirator fit:

(a) Chin properly placed;

(b) Adequate strap tension, not overly tightened;

(c) Fit across nose bridge;

(d) Respirator of proper size to span distance from nose to chin;

(e) Tendency of respirator to slip; and

(f) Self-observation in mirror to evaluate fit and respirator position.

8. The test subject shall conduct the negative and positive pressure fit checks as described below or in ANSI Z88.2–1980. Before conducting the negative or positive pressure test, the subject shall be told to seat the mask on the face by moving the head from side-to-side and up and down slowly while taking in a few slow deep breaths. Another facepiece shall be selected and retested if the test subject fails the fit check tests.

(a). *Positive pressure test.* Close off the exhalation valve and exhale gently onto the facepiece. The face fit is considered satisfactory if a slight positive pressure can be built up inside the facepiece without any evidence of outward leakage of air at the seal. For most respirators this method of leak testing requires the wearer to first remove the exhalation valve cover before closing off the exhalation valve and then carefully replacing it after the test.

(b). *Negative pressure test.* Close off the inlet opening of the canister or cartridge(s) by covering with the palm of the hand(s) or by replacing the filter seal(s). Inhale gently so that the facepiece collapses slightly, and hold the breath for ten seconds. If the facepiece remains in its slightly collapsed condition and no inward leakage of air is detected, the tightness of the respirator is considered satisfactory.

9. The test shall not be conducted if there is any hair growth between the skin and the facepiece sealing surface, such as stubble beard growth, beard, or long sideburns which cross the respirator sealing surface. Any type of apparel which interferes with a satisfactory fit shall be altered or removed.

10. If a test subject exhibits difficulty in breathing during the tests, she or he shall be referred to a physician trained in respiratory disease or pulmonary medicine to determine, in accordance with paragraph (l)(2) and (3) of this standard, whether the test subject can wear a respirator while performing her or his duties.

11. The test subject shall be given the opportunity to wear the successfully fitted respirator for a period of two weeks. If at any time during this period the respirator becomes uncomfortable, the test subject shall be given the opportunity to select a different facepiece and to be retested.

12. The employer shall maintain a record of the fit test administered to an employee. The record shall contain at least the following information:

(a) Name of employee;

(b) Type of respirator;

(c) Brand, size of respirator;

(d) Date of test; and

(e) Where QNFT is used, the fit factor and strip chart recording or other recording of the results of the test. The record shall be maintained until the next fit test is administered.

13. Exercise regimen. Prior to the commencement of the fit test, the test subject shall be given a description of the fit test and the test subject's responsibilities during the test procedure. The description of the process shall include a description of the test exercises that the subject will be performing. The respirator to be tested shall be worn for at least 5 minutes before the start of the fit test.

14. Test Exercises. The test subject shall perform exercises, in the test environment, in the manner described below:

(a) Normal breathing. In a normal standing position, without talking, the subject shall breathe normally.

(b) Deep breathing. In a normal standing position, without talking, the subject shall breathe slowly and deeply, taking care so as to not hyperventilate.

(c) Turning head side to side. Standing in place, the subject shall slowly turn his/her head from side to side between the extreme positions on each side. The head shall be held at each extreme momentarily so the subject can inhale at each side.

(d) Moving head up and down. Standing in place, the subject shall slowly move his/her head up and down. The subject shall be instructed to inhale in the up position (i.e., when looking toward the ceiling).

(e) Talking. The subject shall talk out loud slowly and loud enough so as to be heard clearly by the test conductor. The subject can read from a prepared text such as the Rainbow Passage, count backward from 100, or recite a memorized poem or song.

(f) Grimace. The test subject shall grimace by smiling or frowning.

(g) Bending over. The test subject shall bend at the waist as if he/she were to touch his/her toes. Jogging in place shall be substituted for this exercise in those test environments such as shroud type QNFT units which prohibit bending at the waist.

(h) Normal breathing. Same as exercise 1.

Each test exercise shall be performed for one minute except for the grimace exercise which shall be performed for 15 seconds. The test subject shall be questioned by the test conductor regarding the comfort of the respirator upon completion of the protocol. If it has become uncomfortable, another model of respirator shall be tried.

B. Qualitative Fit Test (QLFT) Protocols

1. General

(a) The employer shall assign specific individuals who shall assume full responsibility for implementing the respirator qualitative fit test program.

(b) The employer shall assure that persons administering QLFTs are able to prepare test solutions, calibrate equipment and perform tests properly, recognize invalid tests, and assure that test equipment is in proper working order.

(c) The employer shall assure that QLFT equipment is kept clean and well maintained so as to operate within the parameters for which it was designed.

2. Isoamyl Acetate Protocol

(a) Odor threshold screening. The odor threshold screening test, performed without wearing a respirator, is intended to determine if the individual tested can detect the odor of isoamyl acetate.

(1) Three 1-liter glass jars with metal lids are required.

(2) Odor free water (e.g. distilled or spring water) at approximately 25 degrees C shall be used for the solutions.

(3) The isoamyl acetate (IAA) (also known as isopentyl acetate) stock solution is prepared by adding 1 cc of pure IAA to 800 cc of odor free water in a 1 liter jar and shaking for 30 seconds. A new solution shall be prepared at least weekly.

(4) The screening test shall be conducted in a room separate from the room used for actual fit testing. The two rooms shall be well ventilated and shall not be connected to the same recirculating ventilation system.

(5) The odor test solution is prepared in a second jar by placing 0.4 cc of the stock solution into 500 cc of odor free water using a clean dropper or pipette. The solution shall be shaken for 30 seconds and allowed to stand for two to three minutes so that the IAA concentration above the liquid may reach equilibrium. This solution shall be used for only one day.

(6) A test blank shall be prepared in a third jar by adding 500 cc of odor free water.

(7) The odor test and test blank jars shall be labeled 1 and 2 for jar identification. Labels shall be placed on the lids so they can be periodically peeled, dried off and switched to maintain the integrity of the test.

(8) The following instruction shall be typed on a card and placed on the table in front of the two test jars (i.e., 1 and 2): "The purpose of this test is to determine if you can smell banana oil at a low concentration. The two bottles in front of you contain water. One of these bottles also contains a small amount of banana oil. Be sure the covers are on tight, then shake each bottle for two seconds. Unscrew the lid of each bottle, one at a time, and sniff at the mouth of the bottle. Indicate to the test conductor which bottle contains banana oil."

(9) The mixtures used in the IAA odor detection test shall be prepared in an area separate from where the test is performed, in order to prevent olfactory fatigue in the subject.

(10) If the test subject is unable to correctly identify the jar containing the odor test solution, the IAA qualitative fit test shall not be performed.

(11) If the test subject correctly identifies the jar containing the odor test solution, the test subject may proceed to respirator selection and fit testing.

(b) Isoamyl acetate fit test—

(1) The fit test chamber shall be similar to a clear 55-gallon drum liner suspended inverted over a 2-foot diameter frame so that the top of the chamber is about 6 inches above the test subject's head. The inside top center of the chamber shall have a small hook attached.

(2) Each respirator used for the fitting and fit testing shall be equipped with organic vapor cartridges or offer protection against

organic vapors. The cartridges or masks shall be changed at least weekly.

(3) After selecting, donning, and properly adjusting a respirator, the test subject shall wear it to the fit testing room. This room shall be separate from the room used for odor threshold screening and respirator selection, and shall be well ventilated, as by an exhaust fan or lab hood, to prevent general room contamination.

(4) A copy of the test exercises and any prepared text from which the subject is to read shall be taped to the inside of the test chamber.

(5) Upon entering the test chamber, the test subject shall be given a 6-inch by 5-inch piece of paper towel, or other porous, absorbent, single-ply material, folded in half and wetted with 0.75 cc of pure IAA. The test subject shall hang the wet towel on the hook at the top of the chamber.

(6) Allow two minutes for the IAA test concentration to stabilize before starting the fit test exercises. This would be an appropriate time to talk with the test subject; to explain the fit test, the importance of his/her cooperation, and the purpose for the head exercises; and to demonstrate some of the exercises.

(7) If at any time during the test, the subject detects the banana like odor of IAA, the respirator fit is inadequate. The subject shall quickly exit from the test chamber and leave the test area to avoid olfactory fatigue.

(8) If the respirator fit was inadequate, the subject shall return to the selection room and remove the respirator, repeat the odor sensitivity test, select and put on another respirator, return to the test chamber and again begin the procedure described in paragraph (I)(B)(2)(b) (1) through (7) of this appendix. The process continues until a respirator that fits well has been found. Should the odor sensitivity test be failed, the subject shall wait about 5 minutes before retesting. Odor sensitivity will usually have returned by this time.

(9) When a respirator is found that passes the test, its efficiency shall be demonstrated for the subject by having the subject break the face seal and take a breath before exiting the chamber.

(10) When the test subject leaves the chamber, the subject shall remove the saturated towel and return it to the person conducting the test. To keep the test area from becoming contaminated, the used towels shall be kept in a self sealing bag so there is no significant IAA concentration build-up in the test chamber during subsequent tests.

3. Irritant Fume Protocol

(a) The respirator to be tested shall be equipped with high-efficiency particulate air (HEPA) filters.

(b) The test subject shall be allowed to smell a weak concentration of the irritant smoke before the respirator is donned to become familiar with its characteristic odor.

(c) Break both ends of a ventilation smoke tube containing stannic oxychloride, such as the MSA part No. 5645, or equivalent. Attach one end of the smoke tube to a low flow air pump set to deliver 200 milliliters per minute.

(d) Advise the test subject that the smoke can be irritating to the eyes and instruct the subject to keep his/her eyes closed while the test is performed.

(e) The test conductor shall direct the stream of irritant smoke from the smoke tube towards the face seal area of the test subject. He/she shall begin at least 12 inches from the facepiece and gradually move to within one inch, moving around the whole perimeter of the mask.

(f) The exercises identified in section I. A. 14 above shall be performed by the test subject while the respirator seal is being challenged by the smoke.

(g) Each test subject passing the smoke test without evidence of a response shall be given a sensitivity check of the smoke from the same tube once the respirator has been removed to determine whether he/she reacts to the smoke. Failure to evoke a response shall void the fit test.

(h) The fit test shall be performed in a location with exhaust ventilation sufficient to prevent general contamination of the testing area by the test agent.

C. Quantitative Fit Test (QNFT) Protocol

1. General

(a) The employer shall assign specific individuals who shall assume full responsibility for implementing the respirator quantitative fit test program.

(b) The employer shall ensure that persons administering QNFT are able to calibrate equipment and perform tests properly, recognize invalid tests, calculate fit factors properly and assure that test equipment is in proper working order.

(c) The employer shall assure that QNFT equipment is kept clean and well maintained so as to operate at the parameters for which it was designed.

2. Definitions

(a) Quantitative fit test. The test is performed in a test chamber. The normal air-purifying element of the respirator is replaced by a high-efficiency particulate air (HEPA) filter in the case of particulate QNFT aerosols or a sorbent offering contaminant penetration protection equivalent to high-efficiency filters where the QNFT test agent is a gas or vapor.

(b) Challenge agent means the aerosol, gas or vapor introduced into a test chamber so that its concentration inside and outside the respirator may be measured.

(c) Test subject means the person wearing the respirator for quantitative fit testing.

(d) Normal standing position means standing erect and straight with arms down along the sides and looking straight ahead.

(e) Maximum peak penetration method means the method of determining test agent penetration in the respirator as determined by strip chart recordings of the test. The highest peak penetration for a given exercise is taken to be representative of average penetration into the respirator for that exercise.

(f) Average peak penetration method means the method of determining test agent penetration into the respirator utilizing a strip chart recorder, integrator, or computer. The agent penetration is determined by an average of the peak heights on the graph or by computer integration, for each exercise except the grimace exercise. Integrators or computers which calculate the actual test agent penetration into the respirator for each exercise will also be considered to meet the requirements of the average peak penetration method.

(g) "Fit Factor" means the ration of challenge agent concentration outside with respect to the inside of a respirator inlet covering (facepiece or enclosure).

3. Apparatus

(a) Instrumentation. Aerosol generation, dilution, and measurement systems using corn oil or sodium chloride as test aerosols shall be used for quantitative fit testing.

(b) Test chamber. The test chamber shall be large enough to permit all test subjects to perform freely all required exercises without disturbing the challenge agent concentration or the measurement apparatus. The test chamber shall be equipped and constructed so that the challenge agent is effectively isolated from the ambient air, yet uniform in concentration throughout the chamber.

(c) When testing air-purifying respirators, the normal filter or cartridge element shall be replaced with a high-efficiency particulate filter supplied by the same manufacturer.

(d) The sampling instrument shall be selected so that a strip chart record may be made of the test showing the rise and fall of the challenge agent concentration with each inspiration and expiration at fit factors of at least 2,000. Integrators or computers which integrate the amount of test agent penetration leakage into the respirator for each exercise may be used provided a record of the readings is made.

(e) The combination of substitute air-purifying elements, challenge agent and challenge agent concentration in the test chamber shall be such that the test subject is not exposed in excess of an established exposure limit for the challenge agent at any time during the testing process.

(f) The sampling port on the test specimen respirator shall be placed and constructed so that no leakage occurs around the port (e.g. where the respirator is probed), a free air flow is allowed into the sampling line at all times and so that there is no interference with the fit or performance of the respirator.

(g) The test chamber and test set up shall permit the person administering the test to observe the test subject inside the chamber during the test.

(h) The equipment generating the challenge atmosphere shall maintain the concentration of challenge agent inside the test chamber constant to within a 10-percent variation for the duration of the test.

(i) The time lag (interval between an event and the recording of the event on the strip chart or computer or integrator) shall be kept to a minimum. There shall be a clear association between the occurrence of an event inside the test chamber and its being recorded.

(j) The sampling line tubing for the test chamber atmosphere and for the respirator sampling port shall be of equal diameter and of the same material. The length of the two lines shall be equal.

(k) The exhaust flow from the test chamber shall pass through a high-efficiency filter before release.

(l) When sodium chloride aerosol is used, the relative humidity inside the test chamber shall not exceed 50 percent.

(m) The limitations of instrument detection shall be taken into account when determining the fit factor.

(n) Test respirators shall be maintained in proper working order and inspected for deficiencies such as cracks, missing valves and gaskets, etc.

4. Procedural Requirements

(a) When performing the initial positive or negative pressure test the sampling line shall be crimped closed in order to avoid air pressure leakage during either of these tests.

(b) An abbreviated screening isoamyl acetate test or irritant fume test may be utilized in order to quickly identify poor fitting respirators which passed the positive and/or negative pressure test and thus reduce the amount of QNFT time. When performing a screening isoamyl acetate test, combination high-efficiency organic vapor cartridges/canisters shall be used.

(c) A reasonably stable challenge agent concentration shall be measured in the test chamber prior to testing. For canopy or shower curtain type of test units the determination of the challenge agent stability may be established after the test subject has entered the test environment.

(d) Immediately after the subject enters the test chamber, the challenge agent concentration inside the respirator shall be measured to ensure that the peak penetration does not exceed 5 percent for a half mask or 1 percent for a full facepiece respirator.

(e) A stable challenge concentration shall be obtained prior to the actual start of testing.

(f) Respirator restraining straps shall not be overtightened for testing. The straps shall be adjusted by the wearer without assistance from other persons to give a reasonable comfortable fit typical of normal use.

(g) The test shall be terminated whenever any single peak penetration exceeds 5 percent for half masks and 1 percent for full facepiece respirators. The test subject shall be refitted and retested. If two of the three required tests are terminated, the fit shall be deemed inadequate.

(h) In order to successfully complete a QNFT, three successful fit tests are required. The results of each of the three independent fit tests must exceed the minimum fit factor needed for the class of respirator (e.g. half mask respirator, full facepiece respirator).

(i) Calculation of fit factors.

(1) The fit factor shall be determined for the quantitative fit test by taking the ratio of the average chamber concentration to the concentration inside the respirator.

(2) The average test chamber concentration is the arithmetic average of the test chamber concentration at the beginning and at the end of the test.

(3) The concentration of the challenge agent inside the respirator shall be determined by one of the following methods:

(i) Average peak concentration;

(ii) Maximum peak concentration;

(iii) Integration by calculation of the area under the individual peak for each exercise. This includes computerized integration.

(j) Interpretation of test results. The fit factor established by the quantitative fit testing shall be the lowest of the three fit factor values calculated from the three required fit tests.

(k) The test subject shall not be permitted to wear a half mask, or full facepiece respirator unless a minimum fit factor equivalent to at least 10 times the hazardous exposure level is obtained.

(l) Filters used for quantitative fit testing shall be replaced at least weekly, or whenever increased breathing resistance is encountered, or when the test agent has altered the integrity of the filter media. Organic vapor cartridges/canisters shall be replaced daily (when used) or sooner if there is any indication of breakthrough by a test agent.

Appendix D to § _____—Occupational Health History Interview With Reference to Cadmium Exposure

Directions

(To be read by employee and signed prior to the interview)

Please answer the questions you will be asked as completely and carefully as you can. These questions are asked of everyone who works with cadmium. You will also be asked to give blood and urine samples. The doctor will give your employer a written opinion on whether you are physically capable of working with cadmium. Legally, the doctor cannot share personal information you may tell him/her with your employer. The following information is considered strictly confidential. The results of the tests will go to you, your doctor and your employer. You will also receive an information sheet explaining the results of any biological monitoring or physical examinations performed.

If you are just being hired, the results of this interview and examination will be used to:

(1) Establish your health status and see if working with cadmium might be expected to cause unusual problems,

(2) Determine your health status today and see if there are changes over time,

(3) See if you can wear a respirator safely.

If you are not a new hire:

OSHA says that everyone who works with cadmium can have periodic medical examinations performed by a doctor. The reasons for this are:

(a) If there are changes in your health, either because of cadmium or some other reason, to find them early,

(b) to prevent kidney damage.

Please sign below.

I have read these directions and understand them:

_____

Employee signature

_____

Date

Thank you for answering these questions.

(Suggested Format)

Name _____

Age _____

Social Security # _____

Company _____

Job _____

Type of Preplacement Exam:

[ ] Periodic
[ ] Termination
[ ] Initial
[ ] Other

Blood Pressure _____

Pulse Rate _____

1. How long have you worked at the job listed above?
   [ ] Not yet hired
   [ ] Number of months
   [ ] Number of years
2. Job Duties etc.

_____

_____

_____

3. Have you *ever* been told by a doctor that you had bronchitis?
   [ ] Yes
   [ ] No
   If yes, how long ago?
   [ ] Number of months
   [ ] Number of years
4. Have you *ever* been told by a doctor that you had emphysema?
   [ ] Yes
   [ ] No
   If yes, how long ago?
   [ ] Number of years
   [ ] Number of months
5. Have you ever been told by a doctor that you had other lung problems?
   [ ] Yes
   [ ] No
   If yes, please describe type of lung problems and when you had these problems

_____

_____

_____

6. In the past year, have you had a cough?
   [ ] Yes
   [ ] No
   If yes, did you cough up sputum?
   [ ] Yes
   [ ] No
   If yes, how long did the cough with sputum production last?
   [ ] Less than 3 months
   [ ] 3 months or longer
   If yes, for how many years have you had episodes of cough with sputum production lasting this long?
   [ ] Less than one
   [ ] 1
   [ ] 2
   [ ] Longer than 2
7. Have you ever smoked cigarettes?
   [ ] Yes
   [ ] No
8. Do you now smoke cigarettes?
   [ ] Yes
   [ ] No

9. If you smoke or have smoked cigarettes, for how many years have you smoked, or did you smoke?
[ ] Less than 1 year
[ ] Number of years
What is or was the greatest number of packs per day that you have smoked?
[ ] Number of packs
If you quit smoking cigarettes, how many years ago did you quit?
[ ] Less than 1 year
[ ] Number of years
How many packs a day do you now smoke?
[ ] Number of packs per day

10. Have you ever been told by a doctor that you had a kidney or urinary tract disease or disorder?
[ ] Yes
[ ] No

11. Have you ever had any of these disorders?

Kidney stones	[ ] Yes	[ ] No
Protein in urine	[ ] Yes	[ ] No
Blood in urine	[ ] Yes	[ ] No
Difficulty urinating	[ ] Yes	[ ] No
Other kidney/Urinary disorders.	[ ] Yes	[ ] No

Please describe problems, age, treatment, and follow up for any kidney or urinary problems you have had:

_____

_____

_____

12. Have you ever been told by a doctor or other health care provider who took your blood pressure that your blood pressure was high?
[ ] Yes
[ ] No

13. Have you ever been advised to take any blood pressure medication?
[ ] Yes
[ ] No

14. Are you presently taking any blood pressure medication?
[ ] Yes
[ ] No

15. Are you presently taking any other medication?
[ ] Yes
[ ] No

16. Please list any blood pressure or other medications and describe how long you have been taking each one:

Medicine:

_____

_____

_____

How Long Taken

_____

_____

_____

17. Have you ever been told by a doctor that you have diabetes? (sugar in your blood or urine)
[ ] Yes
[ ] No
If yes, do you presently see a doctor about your diabetes?
[ ] Yes
[ ] No
If yes, how do you control your blood sugar?
[ ] Diet alone
[ ] Diet plus oral medicine
[ ] Diet plus insulin (injection)

18. Have you ever been told by a doctor that you had:

Anemia	[ ] Yes	[ ] No
A low blood count?	[ ] Yes	[ ] No

19. Do you presently feel that you tire or run out of energy sooner than normal or sooner than other people your age?
[ ] Yes
[ ] No
If yes, for how long have you felt that you tire easily?
[ ] Less than 1 year
[ ] Number of years

20. Have you given blood within the last year?
[ ] Yes
[ ] No
If yes, how many times?
[ ] Number of times
How long ago was the last time you gave blood?
[ ] Less than 1 month
[ ] Number of months

21. Within the last year have you had any injuries with heavy bleeding?
[ ] Yes
[ ] No
If yes, how long ago?
[ ] Less than 1 month
[ ] Number of months
Describe: _____

_____

_____

_____

22. Have you recently had any surgery?
[ ] Yes
[ ] No
If yes, please describe: _____

_____

_____

_____

23. Have you seen any blood lately in your stool or after a bowel movement?
[ ] Yes
[ ] No

24. Have you ever had a test for blood in your stool?
[ ] Yes
[ ] No
If yes, did the test show any blood in the stool?
[ ] Yes
[ ] No
What further evaluation and treatment were done? _____

_____

_____

The following questions pertain to the ability to wear a respirator. Additional information for the physician can be found in The Respiratory Protective Devices Manual.

25. Have you ever been told by a doctor that you have asthma?
[ ] Yes
[ ] No
If yes, are you presently taking any medication for asthma? Mark all that apply.
[ ] Shots
[ ] Pills
[ ] Inhaler

26. Have you ever had a heart attack?
[ ] Yes
[ ] No
If yes, how long ago?
[ ] Number of years
[ ] Number of months

27. Have you ever had pains in your chest?
[ ] Yes
[ ] No
If yes, when did it usually happen?
[ ] While resting
[ ] While working
[ ] While exercising
[ ] Activity didn't matter

28. Have you ever had a thyroid problem?
[ ] Yes
[ ] No

29. Have you ever had a seizure or fits?
[ ] Yes
[ ] No

30. Have you ever had a stroke (cerebrovascular accident)?
[ ] Yes
[ ] No

31. Have you ever had a ruptured eardrum or a serious hearing problem?
[ ] Yes
[ ] No

32. Do you now have a claustrophobia, meaning fear of crowded or closed in spaces or any psychological problems that would make it hard for you to wear a respirator?
[ ] Yes
[ ] No

The following questions pertain to reproductive history.

33. Have you or your partner had a problem conceiving a child?
[ ] Yes
[ ] No
If yes, specify:
[ ] Self
[ ] Present mate
[ ] Previous mate

34. Have you or your partner consulted a physician for a fertility or other reproductive problem?
[ ] Yes
[ ] No
If yes, specify who consulted the physician:
[ ] Self
[ ] Spouse/partner
[ ] Self and partner
If yes, specify diagnosis made: _____

recovery study of the AAS–HGA analytical technique.

3. Multiple analyses of the reagent blank and a series of standard solutions to determine the working standard range and the qualitative and quantitative detection limits for both atomic absorption analytical techniques.

4.1.2. The analytical method recovery results at all test levels were calculated from concentration-response curves and statistically examined for outliers at the 99% confidence level. Possible outliers were determined using the Treatment of Outliers test (5.10.). In addition, the sample results of the two analytical techniques, at 0.5, 1.0 and 2.0 times their target concentrations, were tested for homogeneity of variances also at the 99% confidence level. Homogeneity of the coefficients of variation was determined using the Bartlett's test (5.11.). The overall analytical error (OAE) at the 95% confidence level was calculated using the equation (5.12.):

$$OAE = \pm[|Bias| + (1.96)(CV_t(pooled))(100\%)]$$

4.1.3. A derivation of the International Union of Pure and Applied Chemistry (IUPAC) detection limit equation (5.13.) was used to determine the qualitative and quantitative detection limits for both atomic absorption analytical techniques:

$$C_{ld} = k(sd)/m \qquad \text{(Equation 1)}$$

Where:

C_{ld} = the smallest reliable detectable concentration an analytical instrument can determine at a given confidence level.

k = 3 for the Qualitative Detection Limit at the 99.86% Confidence Level

= 10 for the Quantitative Detection Limit at the 99.99% Confidence Level.

sd = standard deviation of the reagent blank (Rbl) readings.

m = analytical sensitivity or slope as calculated by linear regression.

4.1.4. Collection efficiencies of metallic fume and dust atmospheres on 0.8-μm mixed cellulose ester membrane filters are well documented and have been shown to be excellent (5.11.). Since elemental cadmium and the cadmium component of cadmium compounds are nonvolatile, stability studies of cadmium spiked MCEF samples were not performed.

4.2. Equipment

4.2.1. A Perkin-Elmer (PE) Model 603 spectrophotometer equipped with a manual gas control system, a stainless steel nebulizer, a burner mixing chamber, a flow spoiler and a 10 cm. (one-slot) burner head was used in the experimental validation of the flame AAS analytical technique. A PE cadmium hollow cathode lamp, operated at the manufacturer's recommended current setting for continuous operation (4 mA), was used as the source lamp. Instrument parameters are listed in Appendix A.

4.2.2. A PE Model 5100 spectrophotometer, Zeeman HGA–600 graphite furnace atomizer and AS–60 HGA autosampler were used in the experimental validation of the AAS–HGA analytical technique. The spectrophotometer was equipped with a PE Series 7700 professional computer and Model PR–310 printer. A PE System 2 cadmium electrodeless discharge lamp, operated at the manufacturer's recommended current setting for modulated operation (170 mA), was used as the source lamp. Instrument parameters are listed in Appendix B.

4.3. Reagents

4.3.1. J.T. Baker Chem. Co. (Analyzed grade) concentrated nitric acid, 69.0–71.0%, and concentrated hydrochloric acid, 36.5–38.0%, were used to prepare the samples and standards.

4.3.2. Ammonium phosphate, monobasic, $NH_4H_2PO_4$ and magnesium nitrate, $Mg(NO_3)_2$, both manufactured by the Mallinckrodt Chem. Co., were used to prepare the matrix modifier for AAS–HGA analysis.

4.4. Standard Preparation for Flame AAS Analysis

4.4.1. Dilute stock solutions: Prepared 0.01, 0.1, 1, 10 and 100 μg/mL cadmium standard stock solutions by making appropriate serial dilutions of a commercially available 1,000 μg/mL cadmium standard stock solution (RICCA Chemical Co., Lot# A102) with the diluting solution (4% HNO_3, 0.4% HCl).

4.4.2. Analyzed Standards: Prepared cadmium standards in the range of 0.001 to 2.0 μg/mL by pipetting 2 to 10 mL of the appropriate dilute cadmium stock solution into a 100-mL volumetric flask and diluting to volume with the diluting solution. (See Section 3.7.2.)

4.5. Standard Preparation for AAS–HGA Analysis

4.5.1. Dilute stock solutions: Prepared 1, 10, 100 and 1,000 ng/mL cadmium standard stock solutions by making appropriate serial dilutions of a commercially available 1,000 μg/mL cadmium standard stock solution (J.T. Baker Chemical Co., Instra-analyzed, Lot# D22642) with the diluting solution (4% HNO_3, 0.4% HCl).

4.5.2. Analyzed Standards: Prepared cadmium standards in the range of 0.1 to 40 ng/mL by pipetting 2 to 10 mL of the appropriate dilute cadmium stock solution into a 100-mL volumetric flask and diluting to volume with the diluting solution. (See Section 3.8.2.)

4.6. Detection Limits and Standard Working Range for Flame AAS Analysis

4.6.1. Analyzed the reagent blank solution and the entire series of cadmium standards in the range of 0.001 to 2.0 μg/mL three to six times according to the instructions given in Section 3.10. The diluting solution (4% HNO_3, 0.4% HCl) was used as the reagent blank. The integration time on the PE 603 spectrophotometer was set to 3.0 seconds and a four-fold expansion of the absorbance reading of the 2.0 μg/mL cadmium standard was made prior to analysis. The 2.0 μg/mL standard gave a net absorbance reading of 0.350 abs. units prior to expansion in agreement with the manufacturer's specifications (5.6.).

4.6.2. The net absorbance readings of the reagent blank and the low concentration Cd standards from 0.001 to 0.1 μg/mL and the statistical analysis of the results are shown in Table I. The standard deviation, sd, of the six net absorbance readings of the reagent blank is 1.05 abs. units. The slope, m, as calculated by a linear regression plot of the net absorbance readings (shown in Table II) of the 0.02 to 1.0 μg/mL cadmium standards versus their concentration is 772.7 abs. units/(μg/mL).

4.6.3. If these values for sd and the slope, m, are used in Eqn. 1 (Sect. 4.1.3.), the qualitative and quantitative detection limits as determined by the IUPAC Method are:

C_{ld} = (3)(1.05 abs. units)/(772.7 abs. units/(μg/mL))

= 0.0041 μg/mL for the qualitative detection limit.

C_{ld} = (10)(1.05 abs. units)/(772.7 abs. units/μg/mL))

= 0.014 μg/mL for the quantitative detection limit.

The qualitative and quantitative detection limits for the flame AAS analytical technique are 0.041 μg and 0.14 μg cadmium, respectively, for a 10 mL solution volume. These correspond, respectively, to 0.2 μg/m³ and 0.70 μg/m³ for a 200 L air volume.

4.6.4. The recommended Cd standard working range for flame AAS analysis is 0.02 to 2.0 μg/mL. The net absorbance readings of the reagent blank and the recommended working range standards and the statistical analysis of the results are shown in Table II. The standard of lowest concentration in the working range, 0.02 μg/mL, is slightly greater than the calculated quantitative detection limit, 0.014 μg/mL. The standard of highest concentration in the working range, 2.0 μg/mL, is at the upper end of the linear working range suggested by the manufacturer (5.6.). Although the standard net absorbance readings are not strictly linear at concentrations above 0.5 μg/mL, the deviation from linearity is only about 10% at the upper end of the recommended standard working range. The deviation from linearity is probably caused by the four-fold expansion of the signal suggested in the method. As shown in Table II, the precision of the standard net absorbance readings are excellent throughout the recommended working range; the relative standard deviations of the readings range from 0.009 to 0.064.

4.7. Detection Limits and Standard Working Range for AAS–HGA Analysis

4.7.1. Analyzed the reagent blank solution and the entire series of cadmium standards in the range of 0.1 to 40 ng/mL according to the instructions given in Section 3.11. The diluting solution (4% HNO_3, 0.4% HCl) was used as the reagent blank. A fresh aliquot of the reagent blank and of each standard was used for every analysis. The experimental characteristic mass value was 0.41 pg, calculated from the average peak area (abs-sec) reading of the 5 ng/mL standard which is approximately midway in the linear portion of the working standard range. This agreed within 20% with the characteristic mass value, 0.35 pg, listed by the manufacturer of the instrument (5.2.).

4.7.2. The peak area (abs-sec) readings of the reagent blank and the low concentration Cd standards from 0.1 to 2.0 ng/mL and statistical analysis of the results are shown in Table III. Five of the reagent blank peak area readings were zero and the sixth reading was

1 and was an outlier. The near lack of a blank signal does not satisfy a strict interpretation of the IUPAC method for determining the detection limits. Therefore, the standard deviation of the six peak area readings of the 0.2 ng/mL cadmium standard, 0.75 abs-sec, was used to calculate the detection limits by the IUPAC method. The slope, m, as calculated by a linear regression plot of the peak area (abs-sec) readings (shown in Table IV) of the 0.2 to 10 ng/mL cadmium standards versus their concentration is 51.5 abs-sec/(ng/mL).

4.7.3. If 0.75 abs-sec (sd) and 51.5 abs-sec/(ng/mL) (m) are used in Eqn. 1 (Sect. 4.1.3.), the qualitative and quantitative detection limits as determined by the IUPAC method are:

C_{ld} = (3)(0.75 abs-sec)/(51.5 abs-sec/(ng/mL) = 0.044 ng/mL for the qualitative detection limit.

C_{ld} = (10)(0.75 abs-sec)/(51.5 abs-sec/(ng/mL) = 0.15 ng/mL for the quantitative detection limit.

The qualitative and quantitative detection limits for the AAS-HGA analytical technique are 0.44 ng and 1.5 ng cadmium, respectively, for a 10 mL solution volume. These correspond, respectively, to 0.007 $\mu g/m^3$ and 0.025 $\mu g/m^3$ for a 60 L air volume.

4.7.4. The peak area (abs-sec) readings of the Cd standards from 0.2 to 40 ng/mL and the statistical analysis of the results are given in Table IV. The recommended standard working range for AAS-HGA analysis is 0.2 to 20 ng/mL. The standard of lowest concentration in the recommended working range is slightly greater than the calculated quantitative detection limit, 0.15 ng/mL. The deviation from linearity of the peak area readings of the 20 ng/mL standard, the highest concentration standard in the recommended working range, is approximately 10%. The deviations from linearity of the peak area readings of the 30 and 40 ng/mL standards are significantly greater than 10%. As shown in Table IV, the precision of the peak area readings are satisfactory throughout the recommended working range; the relative standard deviations of the readings range from 0.025 to 0.083.

4.8. Analytical Method Recovery for Flame AAS Analysis

4.8.1. Four sets of spiked MCEF samples were prepared by injecting 20 μL of 10, 50, 100 and 200 $\mu g/mL$ dilute cadmium stock solutions on 37 mm diameter filters (part no. AAWP 037 00, Millipore Corp., Bedford, MA) with a calibrated micropipet. The dilute stock solutions were prepared by making appropriate serial dilutions of a commercially available 1,000 $\mu g/mL$ cadmium standard stock solution (RICCA Chemical Co., Lot# A102) with the diluting solution (4% HNO_3, 0.4% HCl). Each set contained six samples and a sample blank. The amount of cadmium in the prepared sets were equivalent to 0.1, 0.5, 1.0 and 2.0 times the TWA PEL target concentration of 5 $\mu g/m^3$ for a 400 L air volume.

4.8.2. The air-dried spiked filters were digested and analyzed for their cadmium content by flame atomic absorption spectroscopy (AAS) following the procedure described in Section 3. The 0.02 to 2.0μ g/mL cadmium standards (the suggested working range) were used in the analysis of the spiked filters.

4.8.3. The results of the analysis are given in Table V. One result at 0.5 times the TWA PEL target concentration was an outlier and was excluded from statistical analysis. Experimental justification for rejecting it is that the outlier value was probably due to a spiking error. The coefficients of variation for the three test levels at 0.5 to 2.0 times the TWA PEL target concentration passed the Bartlett's test and were pooled.

4.8.4. The average recovery of the six spiked filter samples at 0.1 times the TWA PEL target concentration was 118.2% with a coefficient of variation (CV_1) of 0.128. The average recovery of the spiked filter samples in the range of 0.5 to 2.0 times the TWA target concentration was 104.0% with a pooled coefficient of variation (CV_1) of 0.010. Consequently, the analytical bias found in these spiked sample results over the tested concentration range was +4.0% and the OAE was ±6.0%.

4.9. Analytical Method Recovery for AAS-HGA Analysis

4.9.1. Three sets of spiked MCEF samples were prepared by injecting 15μ L of 5, 10 and 20 $\mu g/mL$ dilute cadmium stock solutions on 37 mm diameter filters (part no. AAWP 037 00, Millipore Corp., Bedford, MA) with a calibrated micropipet. The dilute stock solutions were prepared by making appropriate serial dilutions of a commercially available certified 1,000 $\mu g/mL$ cadmium standard stock solution (Fisher Chemical Co., Lot# 913438-24) with the diluting solution (4% HNO_3, 0.4% HCl). Each set contained six samples and a sample blank. The amount of cadmium in the prepared sets were equivalent to 0.5, 1 and 2 times the Action Level TWA target concentration of 2.5 $\mu g/m^3$ for a 60 L air volume.

4.9.2. The air-dried spiked filters were digested and analyzed for their cadmium content by flameless atomic absorption spectroscopy using a heated graphite furnace atomizer following the procedure described in Section 3. A five-fold dilution of the spiked filter samples at 2 times the Action Level TWA was made prior to their analysis. The 0.05 to 20 ng/mL cadmium standards were used in the analysis of the spiked filters.

4.9.3. The results of the analysis are given in Table VI. There were no outliers. The coefficients of variation for the three test levels at 0.5 to 2.0 times the Action Level TWA PEL passed the Bartlett's test and were pooled. The average recovery of the spiked filter samples was 94.2% with a pooled coefficient of variation (CV_1) of 0.043. Consequently, the analytical bias was −5.8% and the OAE was ±14.2%.

4.10. Conclusions

The experiments performed in this evaluation show the two atomic absorption analytical techniques included in this method to be precise and accurate and have sufficient sensitivity to measure airborne cadmium over a broad range of exposure levels and sampling periods.

5. References

5.1. Slavin, W. Graphite Furnace AAS—A Source Book; Perkin-Elmer Corp., Spectroscopy Div.: Ridgefield, CT , 1984: p. 18 and pp. 83–90.

5.2. Grosser, Z., Ed.; Techniques in Graphite Furnace Atomic Absorption Spectrophotometry; Perkin-Elmer Corp., Spectroscopy Div.: Ridgefield, CT, 1985.

5.3. Occupational Safety and Health Administration Salt Lake Technical Center: Metal and Metalloid Particulate in Workplace Atmospheres (Atomic Absorption) (USDOL/OSHA Method No. ID–121). In OSHA Analytical Methods Manual 2nd ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, 1991.

5.4. Occupational Safety and Health Administration Salt Lake Technical Center: Metal and Metalloid Particulate in Workplace Atmospheres (ICP) (USDOL/OSHA Method No. ID–125C). In OSHA Analytical Methods Manual 2nd ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, 1991.

5.5. Windholz, M., Ed.: The Merck Index, 10th ed.; Merck & Co.: Rahway, NJ, 1983.

5.6. Analytical Methods for Atomic Absorption Spectrophotometry, The Perkin-Elmer Corporation: Norwalk, CT, 1982.

5.7. Slavin, W., D.C. Manning, G. Carnrick, and E. Pruszkowska: Properties of the Cadmium Determination with the Platform Furnace and Zeeman Background Correction. Spectrochim. Acta 38B:1157–1170 (1983).

5.8. Occupational Safety and Health Administration Salt Lake Technical Center: Standard Operating Procedure for Atomic Absorption. Salt Lake City, UT: USDOL/OSHA-SLTC, In progress.

5.9. Occupational Safety and Health Administration Salt Lake Technical Center: AAS-HGA Standard Operating Procedure. Salt Lake City, UT: USDOL/OSHA-SLTC, In progress.

5.10. Mandel, J.: Accuracy and Precision, Evaluation and Interpretation of Analytical Results, The Treatment of Outliers. In Treatise On Analytical Chemistry, 2nd ed., Vol.1, edited by I. M. Kolthoff and P. J. Elving. New York: John Wiley and Sons, 1978. pp. 282–285.

5.11. National Institute for Occupational Safety and Health: Documentation of the NIOSH Validation Tests by D. Taylor, R. Kupel, and J. Bryant (DHEW/NIOSH Pub. No. 77–185). Cincinnati, OH: National Institute for Occupational Safety and Health, 1977.

5.12. Occupational Safety and Health Administration Analytical Laboratory: Precision and Accuracy Data Protocol for Laboratory Validations. In OSHA Analytical Methods Manual 1st ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists (Pub. No. ISBN: 0–936712–66–X), 1985.

5.13. Long, G.L. and J.D. Winefordner: Limit of Detection—A Closer Look at the IUPAC Definition. Anal.Chem. 55:712A–724A (1983).

5.14. American Conference of Governmental Industrial Hygienists: Documentation of Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, 1986.

TABLE I.—CD DETECTION LIMIT STUDY

[Flame AAS Analysis]

STD (µg/mL)	Absorbance reading at 228.8 nm		Statistical analysis
Reagent blank	5	2	n=6.
	4	3	mean=3.50.
	4	3	std dev=1.05.
			CV=0.30.
0.001	6	6	n=6.
	2	4	mean=5.00.
	6	6	std dev=1.67.
			CV=0.335.
0.002	5	7	n=6.
	7	3	mean=5.50.
	7	4	std dev=1.76.
			CV=0.320.
0.005	7	7	n=6.
	8	8	mean=7.33.
	8	6	std dev=0.817.
			CV=0.111.
0.010	10	9	n=6.
	10	13	mean=10.3.
	10	10	std dev=1.37.
			CV=0.133.
0.020	20	23	n=6.
	20	22	mean=20.8.
	20	20	std dev=1.33.
			CV=0.064.
0.050	42	42	n=6.
	42	42	mean=42.5.
	42	45	std dev=1.22.
			CV=0.029.
0.10		84	n=3.
		80	mean=82.3.
		83	std dev=2.08.
			CV=0.025.

TABLE II.—CD STANDARD WORKING RANGE STUDY

[Flame AAS Analysis]

STD (µg/mL)	Absorbance reading at 228.8 nm		Statistical analysis
Reagent blank	5	2	n=6.
	4	3	mean=3.50.
	4	3	std dev=1.05.
			CV=0.30.
0.020	20	23	n=6.
	20	22	mean=20.8.
	20	20	std dev=1.33.
			CV=0.064.
0.050	42	42	n=6.
	42	42	mean=42.5.
	42	45	std dev=1.22.
			CV=0.029.
0.10		84	n=3.
		80	mean=82.3.
		83	std dev=2.08.
			CV=0.025.
0.20		161	n=3.
		161	mean=160.0.
		158	std dev=1.73.
			CV=0.011.
0.50		391	n=3.
		389	mean=391.0.
		393	std dev=2.00.
			CV=0.005.
1.00		760	n=3.
		748	mean=753.3.
		752	std dev=6.11.
			CV=0.008.
2.00		1416	n=3.
		1426	mean=1414.3.
		1401	std dev=12.6.
			CV=0.009.

35. Have you or your partner ever conceived a child resulting in a miscarriage, still birth or deformed offspring?
[ ] Yes
[ ] No
If yes, specify:
[ ] Miscarriage
[ ] Still birth
[ ] Deformed offspring
If outcome was a deformed offspring, please specify type:

36. Was this outcome a result of a pregnancy of:
[ ] Yours with present partner
[ ] Yours with a previous partner
37. Did the timing of any abnormal pregnancy outcome coincide with present employment?
[ ] Yes
[ ] No
List dates of occurrences:

38. What is the occupation of your spouse or partner?

For Women Only

39. Do you have menstrual periods?
[ ] Yes
[ ] No
Have you had menstrual irregularities?
[ ] Yes
[ ] No
If yes, specify type:

If yes, what was the approximated date this problem began?

Approximate date problem stopped?

For Men Only

40. Have you ever been diagnosed by a physician as having prostate gland problem(s)?
[ ] Yes
[ ] No
If yes, please describe type of problem(s) and what was done to evaluate and treat the problem(s):

Appendix E to § ____—Cadmium in Workplace Atmospheres

Method Number: ID-189
Matrix: Air
OSHA Permissible Exposure Limits: 5 $\mu g/m^3$ (TWA), 2.5 $\mu g/m^3$ (Action Level TWA)
Collection Procedure: A known volume of air is drawn through a 37-mm diameter filter cassette containing a 0.8-μm mixed cellulose ester membrane filter (MCEF).
Recommended Air Volume: 960 L
Recommended Sampling Rate: 2.0 L/min
Analytical Procedure: Air filter samples are digested with nitric acid. After digestion, a small amount of hydrochloric acid is added. The samples are then diluted to volume with deionized water and analyzed by either flame atomic absorption spectroscopy (AAS) or flameless atomic absorption spectroscopy using a heated graphite furnace atomizer (AAS-HGA).
Detection Limits:
Qualitative: 0.2 $\mu g/m^3$ for a 200 L sample by Flame AAS, 0.007 $\mu g/m^3$ for a 60 L sample by AAS-HGA
Quantitative: 0.70 $\mu g/m^3$ for a 200 L sample by Flame AAS, 0.025 $\mu g/m^3$ for a 60 L sample by AAS-HGA
Precision and Accuracy: (Flame AAS Analysis and AAS-HGA Analysis):
Validation Level: 2.5 to 10 $\mu g/m^3$ for a 400 L air vol, 1.25 to 5.0 $\mu g/m^3$ for a 60 L air vol
CV_1 (pooled): 0.010, 0.043
Analytical Bias: +4.0%, −5.8%
Overall Analytical Error: ±0.0%, ±14.2%
Method Classification: Validated
Date: June, 1992

Inorganic Service Branch II, OSHA Salt Lake Technical Center, Salt Lake City, Utah

Commercial manufacturers and products mentioned in this method are for descriptive use only and do not constitute endorsements by USDOL-OSHA. Similar products from other sources can be substituted.

1. Introduction

1.1. Scope

This method describes the collection of airborne elemental cadmium and cadmium compounds on 0.8-μm mixed cellulose ester membrane filters and their subsequent analysis by either flame atomic absorption spectroscopy (AAS) or flameless atomic absorption spectroscopy using a heated graphite furnace atomizer (AAS-HGA). It is applicable for both TWA and Action Level TWA Permissible Exposure Level (PEL) measurements. The two atomic absorption analytical techniques included in the method do not differentiate between cadmium fume and cadmium dust samples. They also do not differentiate between elemental cadmium and its compounds.

1.2. Principle

Airborne elemental cadmium and cadmium compounds are collected on a 0.8-μm mixed cellulose ester membrane filter (MCEF). The air filter samples are digested with concentrated nitric acid to destroy the organic matrix and dissolve the cadmium analytes. After digestion, a small amount of concentrated hydrochloric acid is added to help dissolve other metals which may be present. The samples are diluted to volume with deionized water and then aspirated into the oxidizing air/acetylene flame of an atomic absorption spectrophotometer for analysis of elemental cadmium.

If the concentration of cadmium in a sample solution is too low for quantitation by this flame AAS analytical technique, and the sample is to be averaged with other samples for TWA calculations, aliquots of the sample and a matrix modifier are later injected onto a L'vov platform in a pyrolytically-coated graphite tube of a Zeeman atomic absorption spectrophotometer/graphite furnace assembly for analysis of elemental cadmium. The matrix modifier is added to stabilize the cadmium metal and minimize sodium chloride as an interference during the high temperature charring step of the analysis (5.1., 5.2.).

1.3. History

Previously, two OSHA sampling and analytical methods for cadmium were used concurrently (5.3., 5.4.). Both of these methods also required 0.8-μm mixed cellulose ester membrane filters for the collection of air samples. These cadmium air filter samples were analyzed by either flame atomic absorption spectroscopy (5.3.) or inductively coupled plasma/atomic emission spectroscopy (ICP-AES) (5.4.). Neither of these two analytical methods have adequate sensitivity for measuring workplace exposure to airborne cadmium at the new lower TWA and Action Level TWA PEL levels when consecutive samples are taken on one employee and the sample results need to be averaged with other samples to determine a single TWA.

The inclusion of two atomic absorption analytical techniques in the new sampling and analysis method for airborne cadmium permits quantitation of sample results over a broad range of exposure levels and sampling periods. The flame AAS analytical technique included in this method is similar to the previous procedure given in the General Metals Method ID-121 (5.3.) with some modifications. The sensitivity of the AAS-HGA analytical technique included in this method is adequate to measure exposure levels at 1/10 the Action Level TWA, or lower, when less than full-shift samples need to be averaged together.

1.4. Properties (5.5.)

Elemental cadmium is a silver-white, blue-tinged, lustrous metal which is easily cut with a knife. It is slowly oxidized by moist air to form cadmium oxide. It is insoluble in water, but reacts readily with dilute nitric acid. Some of the physical properties and other descriptive information of elemental cadmium are given below:

CAS No.	7440-43-9
Atomic Number	48
Atomic Symbol	Cd
Atomic Weight	112.41
Melting Point	321 °C
Boiling Point	765 °C
Density	8.65 g/mL (25 °C)

The properties of specific cadmium compounds are described in reference 5.5.

1.5. Method Performance

A synopsis of method performance is presented below. Further information can be found in Section 4.

1.5.1. The qualitative and quantitative detection limits for the flame AAS analytical technique are 0.04 μg (0.004 μg/mL) and 0.14 μg (0.014 μg/mL) cadmium, respectively, for a 10 mL solution volume. These correspond, respectively, to 0.2 $\mu g/m^3$ and 0.70 $\mu g/m^3$ for a 200 L air volume.

1.5.2. The qualitative and quantitative detection limits for the AAS-HGA analytical technique are 0.44 ng (0.044 ng/mL) and 1.5 ng (0.15 ng/mL) cadmium, respectively, for a 10 mL solution volume. These correspond, respectively, to 0.007 $\mu g/m^3$ and 0.025 $\mu g/m^3$ for a 60 L air volume.

1.5.3. The average recovery by the flame AAS analytical technique of 17 spiked MCEF samples containing cadmium in the range of 0.5 to 2.0 times the TWA target concentration of 5 $\mu g/m^3$ (assuming a 400 L air volume) was 104.0% with a pooled coefficient of variation (CV_1) of 0.010. The flame analytical technique exhibited a positive bias of +4.0% for the validated concentration range. The overall analytical error (OAE) for the flame AAS analytical technique was ±6.0%.

1.5.4. The average recovery by the AAS-HGA analytical technique of 18 spiked MCEF samples containing cadmium in the range of 0.5 to 2.0 times the Action Level TWA target concentration of 2.5 $\mu g/m^3$ (assuming a 60 L air volume) was 94.2% with a pooled coefficient of variation (CV_1) of 0.043. The AAS-HGA analytical technique exhibited a negative bias of −5.8% for the validated concentration range. The overall analytical error (OAE) for the AAS-HGA analytical technique was ±14.2%.

1.5.5. Sensitivity in flame atomic absorption is defined as the characteristic concentration of an element required to produce a signal of 1% absorbance (0.0044 absorbance units). Sensitivity values are listed for each element by the atomic absorption spectrophotometer manufacturer and have proved to be a very valuable diagnostic tool to determine if instrumental parameters are optimized and if the instrument is performing up to specification. The sensitivity of the spectrophotometer used in the validation of the flame AAS analytical technique agreed with the manufacturer specifications (5.6.); the 2 μg/mL cadmium standard gave an absorbance reading of 0.350 abs. units.

1.5.6. Sensitivity in graphite furnace atomic absorption is defined in terms of the characteristic mass, the number of picograms required to give an integrated absorbance value of 0.0044 absorbance-second (5.7.). Data suggests that under Stabilized Temperature Platform Furnace (STPF) conditions (see Section 1.6.2.), characteristic mass values are transferable between properly functioning instruments to an accuracy of about 20% (5.2.). The characteristic mass for STPF analysis of cadmium with Zeeman background correction listed by the manufacturer of the instrument used in the validation of the AAS-HGA analytical technique was 0.35 pg. The experimental characteristic mass value observed during the determination of the working range and detection limits of the AAS-HGA analytical technique was 0.41 pg.

1.6.Interferences

1.6.1. High concentrations of silicate interfere in determining cadmium by flame AAS (5.6.). However, silicates are not significantly soluble in the acid matrix used to prepare the samples.

1.6.2. Interferences, such as background absorption, are reduced to a minimum in the AAS-HGA analytical technique by taking full advantage of the Stabilized Temperature Platform Furnace (STPF) concept. STPF includes all of the following parameters (5.2.):

a. Integrated Absorbance,
b. Fast Instrument Electronics and Sampling Frequency,
c. Background Correction,
d. Maximum Power Heating,
e. Atomization off the L'vov platform in a pyrolytically coated graphite tube,
f. Gas Stop during Atomization,
g. Use of Matrix Modifiers.

1.7. Toxicology (5.14.)

Information listed within this section is synopsis of current knowledge of the physiological effects of cadmium and is not intended to be used as the basis for OSHA policy. IARC classifies cadmium and certain of its compounds as Group 2A carcinogens (probably carcinogenic to humans). Cadmium fume is intensely irritating to the respiratory tract. Workplace exposure to cadmium can cause both chronic and acute effects. Acute effects include tracheobronchitis, pneumonitis, and pulmonary edema. Chronic effects include anemia, rhinitis/anosmia, pulmonary emphysema, proteinuria and lung cancer. The primary target organs for chronic disease are the kidneys (non-carcinogenic) and the lungs (carcinogenic).

2. Sampling

2.1. Apparatus

2.1.1. Filter cassette unit for air sampling: A 37-mm diameter mixed cellulose ester membrane filter with a pore size of 0.8-μm contained in a 37-mm polystyrene two- or three-piece cassette filter holder (part no. MAWP 037 A0, Millipore Corp., Bedford, MA). The filter is supported with a cellulose backup pad. The cassette is sealed prior to use with a shrinkable gel band.

2.1.2. A calibrated personal sampling pump whose flow is determined to an accuracy of ±5% at the recommended flow rate with the filter cassette unit in line.

2.2. Procedure

2.2.1. Attach the prepared cassette to the calibrated sampling pump (the backup pad should face the pump) using flexible tubing. Place the sampling device on the employee such that air is sampled from the breathing zone.

2.2.2. Collect air samples at a flow rate of 2.0 L/min. If the filter does not become overloaded, a full-shift (at least seven hours) sample is strongly recommended for TWA and Action Level TWA measurements with a maximum air volume of 960 L. If overloading occurs, collect consecutive air samples for shorter sampling periods to cover the full workshift.

2.2.3. Replace the end plugs into the filter cassettes immediately after sampling. Record the sampling conditions.

2.2.4. Securely wrap each sample filter cassette end-to-end with an OSHA Form 21 sample seal.

2.2.5. Submit at least one blank sample with each set of air samples. The blank sample should be handled the same as the other samples except that no air is drawn through it.

2.2.6. Ship the samples to the laboratory for analysis as soon as possible in a suitable container designed to prevent damage in transit.

3. Analysis

3.1. Safety Precautions

3.1.1. Wear safety glasses, protective clothing and gloves at all times.

3.1.2. Handle acid solutions with care. Handle all cadmium samples and solutions with extra care (see Sect. 1.7.). Avoid their direct contact with work area surfaces, eyes, skin and clothes. Flush acid solutions which contact the skin or eyes with copious amounts of water.

3.1.3. Perform all acid digestions and acid dilutions in an exhaust hood while wearing a face shield. To avoid exposure to acid vapors, do not remove beakers containing concentrated acid solutions from the exhaust hood until they have returned to room temperature and have been diluted or emptied.

3.1.4. Exercise care when using laboratory glassware. Do not use chipped pipets, volumetric flasks, beakers or any glassware with sharp edges exposed in order to avoid the possibility of cuts or abrasions.

3.1.5. Never pipet by mouth.

3.1.6. Refer to the instrument instruction manuals and SOPs (5.8., 5.9.) for proper and safe operation of the atomic absorption spectrophotometer, graphite furnace atomizer and associated equipment.

3.1.7. Because metallic elements and other toxic substances are vaporized during AAS flame or graphite furnace atomizer operation, it is imperative that an exhaust vent be used. Always ensure that the exhaust system is operating properly during instrument use.

3.2. Apparatus for Sample and Standard Preparation

3.2.1. Hot plate, capable of reaching 150 °C, installed in an exhaust hood.

3.2.2. Phillips beakers, 125 mL.

3.2.3. Bottles, narrow-mouth, polyethylene or glass with leakproof caps: used for storage of standards and matrix modifier.

3.2.4. Volumetric flasks, volumetric pipets, beakers and other associated general laboratory glassware.

3.2.5. Forceps and other associated general laboratory equipment.

3.3. Apparatus for Flame AAS Analysis

3.3.1. Atomic absorption spectrophotometer consisting of a(an):

Nebulizer and burner head
Pressure regulating devices capable of maintaining constant oxidant and fuel pressures
Optical system capable of isolating the desired wavelength of radiation (228.8 nm)
Adjustable slit
Light measuring and amplifying device
Display, strip chart, or computer interface for indicating the amount of absorbed radiation

Cadmium hollow cathode lamp or electrodeless discharge lamp (EDL) and power supply

3.3.2. Oxidant: compressed air, filtered to remove water, oil and other foreign substances.

3.3.3. Fuel: standard commercially available tanks of acetylene dissolved in acetone; tanks should be equipped with flash arresters.

Caution: Do not use grades of acetylene containing solvents other than acetone because they may damage the PVC tubing used in some instruments.

3.3.4. Pressure-reducing valves: two gauge, two-stage pressure regulators to maintain fuel and oxidant pressures somewhat higher than the controlled operating pressures of the instrument.

3.3.5. Exhaust vent installed directly above the spectrophotometer burner head.

3.4. Apparatus for AAS–HGA Analysis

3.4.1. Atomic absorption spectrophotometer consisting of a(an):

Heated graphite furnace atomizer (HGA) with argon purge system
Pressure-regulating devices capable of maintaining constant argon purge pressure
Optical system capable of isolating the desired wavelength of radiation (228.8 nm)
Adjustable slit
Light measuring and amplifying device
Display, strip chart, or computer interface for indicating the amount of absorbed radiation (as integrated absorbance, peak area)
Background corrector: Zeeman or deuterium arc. The Zeeman background corrector is recommended
Cadmium hollow cathode lamp or electrodeless discharge lamp (EDL) and power supply
Autosampler capable of accurately injecting 5 to 20 µL sample aliquots onto the L'vov Platform in a graphite tube

3.4.2. Pyrolytically coated graphite tubes containing solid, pyrolytic L'vov platforms.

3.4.3. Polyethylene sample cups, 2.0 to 2.5 mL, for use with the autosampler.

3.4.4. Inert purge gas for graphite furnace atomizer: compressed gas cylinder of purified argon.

3.4.5. Two gauge, two-stage pressure regulator for the argon gas cylinder.

3.4.6. Cooling water supply for graphite furnace atomizer.

3.4.7. Exhaust vent installed directly above the graphite furnace atomizer.

3.5. Reagents

All reagents should be ACS analytical reagent grade or better.

3.5.1. Deionized water with a specific conductance of less than 10 µS

3.5.2. Concentrated nitric acid, HNO_3.

3.5.3. Concentrated hydrochloric acid, HCl.

3.5.4. Ammonium phosphate, monobasic, $NH_4H_2PO_4$.

3.5.5. Magnesium nitrate, $Mg(NO_3)_2$.

3.5.6. Diluting solution (4% HNO_3, 0.4% HCl): Add 40 mL HNO_3 and 4 mL HCl carefully to approximately 500 mL deionized water and dilute to 1 L with deionized water.

3.5.7. Cadmium standard stock solution, 1,000 µg/mL: Use a commercially available certified 1,000 µg/mL cadmium standard or, alternatively, dissolve 1.0000 g of cadmium metal in a minimum volume of 1:1 HCl and dilute to 1 L with 4% HNO_3. Observe expiration dates of commercial standards. Properly dispose of commercial standards with no expiration dates or prepared standards one year after their receipt or preparation date.

3.5.8. Matrix modifier for AAS–HGA analysis: Dissolve 1.0 g $NH_4H_2PO_4$ and 0.15 g $Mg(NO_3)_2$ in approximately 200 mL deionized water. Add 1 mL HNO_3 and dilute to 500 mL with deionized water.

3.5.9 Nitric Acid, 1:1 HNO_3/DI H_2O mixture: Carefully add a measured volume of concentrated HNO_3 to an equal volume of DI H_2O.

3.5.10. Nitric acid, 10% v/v: Carefully add 100 mL of concentrated HNO_3 to 500 mL of DI H_2O and dilute to 1 L.

3.6. Glassware Preparation

3.6.1. Clean Phillips beakers by refluxing with 1:1 nitric acid on a hot plate in a fume hood. Thoroughly rinse with deionized water and invert the beakers to allow them to drain dry.

3.6.2. Rinse volumetric flasks and all other glassware with 10% nitric acid and deionized water prior to use.

3.7. Standard Preparation for Flame AAS Analysis

3.7.1. Dilute stock solutions: Prepare 1, 5, 10 and 100 µg/mL cadmium standard stock solutions by making appropriate serial dilutions of 1,000 µg/mL cadmium standard stock solution with the diluting solution described in Section 3.5.6.

3.7.2. Working standards: Prepare cadmium working standards in the range of 0.02 to 2.0 µg/mL by making appropriate serial dilutions of the dilute stock solutions with the same diluting solution. A suggested method of preparation of the working standards is given below.

Working standard (µg/mL)	Std solution (µg/mL)	Aliquot (mL)	Final vol. (mL)
0.02	1	10	500
0.05	5	5	500
0.1	10	5	500
0.2	10	10	500
0.5	10	25	500
1	100	5	500
2	100	10	500

Store the working standards in 500-mL, narrow-mouth polyethylene or glass bottles with leak proof caps. Prepare every twelve months.

3.8. Standard Preparation for AAS–HGA Analysis

3.8.1. Dilute stock solutions: Prepare 10, 100 and 1,000 ng/mL cadmium standard stock solutions by making appropriate ten-fold serial dilutions of the 1,000 µg/mL cadmium standard stock solution with the diluting solution described in Section 3.5.6.

3.8.2. Working standards: Prepare cadmium working standards in the range of 0.2 to 20 ng/mL by making appropriate serial dilutions of the dilute stock solutions with the same diluting solution. A suggested method of preparation of the working standards is given below.

Working standard (ng/mL)	Std solution (ng/mL)	Aliquot (mL)	Final vol (mL)
0.2	10	2	100
0.5	10	5	100
1	10	10	100
2	100	2	100
5	100	2	100
10	100	10	100
20	1,000	2	100

Store the working standards in narrow-mouth polyethylene or glass bottles with leakproof caps. Prepare monthly.

3.9. Sample Preparation

3.9.1. Carefully transfer each sample filter with forceps from its filter cassette unit to a clean, separate 125-mL Phillips beaker along with any loose dust found in the cassette. Label each Phillips beaker with the appropriate sample number.

3.9.2. Digest the sample by adding 5 mL of concentrated nitric acid (HNO_3) to each Phillips beaker containing an air filter sample. Place the Phillips beakers on a hot plate in an exhaust hood and heat the samples until approximately 0.5 mL remains. The sample solution in each Phillips beaker should become clear. If it is not clear, digest the sample with another portion of concentrated nitric acid.

3.9.3. After completing the HNO_3 digestion and cooling the samples, add 40 µL (2 drops) of concentrated HCl to each air sample solution and then swirl the contents. Carefully add about 5 mL of deionized water by pouring it down the inside of each beaker.

3.9.4. Quantitatively transfer each cooled air sample solution from each Phillips beaker to a clean 10-mL volumetric flask. Dilute each flask to volume with deionized water and mix well.

3.10. Flame AAS Analysis

Analyze all of the air samples for their cadmium content by flame atomic absorption spectroscopy (AAS) according to the instructions given below.

3.10.1. Set up the atomic absorption spectrophotometer for the air/acetylene flame analysis of cadmium according to the SOP (5.8.) or the manufacturer's operational instructions. For the source lamp, use the cadmium hollow cathode or electrodeless discharge lamp operated at the manufacturer's recommended rating for continuous operation. Allow the lamp to warm up 10 to 20 min or until the energy output stabilizes. Optimize conditions such as lamp position, burner head alignment, fuel and oxidant flow rates, etc. See the SOP or specific instrument manuals for details. Instrumental parameters for the Perkin-Elmer Model 603 used in the validation of this method are given in Appendix A.

3.10.2. Aspirate and measure the absorbance of a standard solution of cadmium. The standard concentration should be within the linear range. For the

instrumentation used in the validation of this method a 2 μg/mL cadmium standard gives a net absorbance reading of about 0.350 abs. units (see Section 1.5.5.) when the instrument and the source lamp are performing to manufacturer specifications.

3.10.3. To increase instrument response, scale expand the absorbance reading of the aspirated 2 μg/mL working standard approximately four times. Increase the integration time to at least 3 seconds to reduce signal noise.

3.10.4. Autozero the instrument while aspirating a deionized water blank. Monitor the variation in the baseline absorbance reading (baseline noise) for a few minutes to insure that the instrument, source lamp and associated equipment are in good operating condition.

3.10.5. Aspirate the working standards and samples directly into the flame and record their absorbance readings. Aspirate the deionized water blank immediately after every standard or sample to correct for and monitor any baseline drift and noise. Record the baseline absorbance reading of each deionized water blank. Label each standard and sample reading and its accompanying baseline reading.

3.10.6. It is recommended that the entire series of working standards be analyzed at the beginning and end of the analysis of a set of samples to establish a concentration-response curve, ensure that the standard readings agree with each other and are reproducible. Also, analyze a working standard after every five or six samples to monitor the performance of the spectrophotometer. Standard readings should agree within ±10 to 15% of the readings obtained at the beginning of the analysis.

3.10.7. Bracket the sample readings with standards during the analysis. If the absorbance reading of a sample is above the absorbance reading of the highest working standard, dilute the sample with diluting solution and reanalyze. Use the appropriate dilution factor in the calculations.

3.10.8. Repeat the analysis of approximately 10% of the samples for a check of precision.

3.10.9. If possible, analyze quality control samples from an independent source as a check on analytical recovery and precision.

3.10.10. Record the final instrument settings at the end of the analysis. Date and label the output.

3.11. AAS–HGA Analysis

Initially analyze all of the air samples for their cadmium content by flame atomic absorption spectroscopy (AAS) according to the instructions given in Section 3.10. If the concentration of cadmium in a sample solution is less than three times the quantitative detection limit [0.04 μg/mL (40 ng/mL) for the instrumentation used in the validation] and the sample results are to be averaged with other samples for TWA calculations, proceed with the AAS–HGA analysis of the sample as described below.

3.11.1. Set up the atomic absorption spectrophotometer and HGA for flameless atomic absorption analysis of cadmium according to the SOP (5.9.) or the manufacturer's operational instructions and allow the instrument to stabilize. The graphite furnace atomizer is equipped with a pyrolytically coated graphite tube containing a pyrolytic platform. For the source lamp, use a cadmium hollow cathode or electrodeless discharge lamp operated at the manufacturer's recommended setting for graphite furnace operation. The Zeeman background corrector and EDL are recommended for use with the L'vov platform. Instrumental parameters for the Perkin-Elmer Model 5100 spectrophotometer and Zeeman HGA–600 graphite furnace used in the validation of this method are given in Appendix B.

3.11.2. Optimize the energy reading of the spectrophotometer at 228.8 nm by adjusting the lamp position and the wavelength according to the manufacturer's instructions.

3.11.3. Set up the autosampler to inject a 5-μL aliquot of the working standard, sample or reagent blank solution onto the L'vov platform along with a 10-μL overlay of the matrix modifier.

3.11.4. Analyze the reagent blank (diluting solution, Section 3.5.6.) and then autozero the instrument before starting the analysis of a set of samples. It is recommended that the reagent blank be analyzed several times during the analysis to assure the integrated absorbance (peak area) reading remains at or near zero.

3.11.5. Analyze a working standard approximately midway in the linear portion of the working standard range two or three times to check for reproducibility and sensitivity (see sections 1.5.5. and 1.5.6.) before starting the analysis of samples. Calculate the experimental characteristic mass value from the average integrated absorbance reading and injection volume of the analyzed working standard. Compare this value to the manufacturer's suggested value as a check of proper instrument operation.

3.11.6. Analyze the reagent blank, working standard, and sample solutions. Record and label the peak area (abs-sec) readings and the peak and background peak profiles on the printer/plotter.

3.11.7. It is recommended the entire series of working standards be analyzed at the beginning and end of the analysis of a set of samples. Establish a concentration-response curve and ensure standard readings agree with each other and are reproducible. Also, analyze a working standard after every five or six samples to monitor the performance of the system. Standard readings should agree within ±15% of the readings obtained at the beginning of the analysis.

3.11.8. Bracket the sample readings with standards during the analysis. If the peak area reading of a sample is above the peak area reading of the highest working standard, dilute the sample with the diluting solution and reanalyze. Use the appropriate dilution factor in the calculations.

3.11.9. Repeat the analysis of approximately 10% of the samples for a check of precision.

3.11.10. If possible, analyze quality control samples from an independent source as a check of analytical recovery and precision.

3.11.11. Record the final instrument settings at the end of the analysis. Date and label the output.

3.12. Calculations

Note: Standards used for HGA analysis are in ng/mL. Total amounts of cadmium from calculations will be in ng (not μg) unless a prior conversion is made.

3.12.1. Correct for baseline drift and noise in flame AAS analysis by subtracting each baseline absorbance reading from its corresponding working standard or sample absorbance reading to obtain the net absorbance reading for each standard and sample.

3.12.2. Use a least squares regression program to plot a concentration-response curve of net absorbance reading (or peak area for HGA analysis) versus concentration (μg/mL or ng/mL) of cadmium in each working standard.

3.12.3. Determine the concentration (μg/mL or ng/mL) of cadmium in each sample from the resulting concentration-response curve. If the concentration of cadmium in a sample solution is less than three times the quantitative detection limit [0.04 μg/mL (40 ng/mL) for the instrumentation used in the validation of the method] and if consecutive samples were taken on one employee and the sample results are to be averaged with other samples to determine a single TWA, reanalyze the sample by AAS–HGA as described in Section 3.11. and report the AAS–HGA analytical results.

3.12.4. Calculate the total amount (μg or ng) of cadmium in each sample from the sample solution volume (mL):

$$W = (C)(\text{sample vol, mL})(DF)$$

Where:

W = Total cadmium in sample
C = Calculated concentration of cadmium
DF = Dilution Factor (if applicable)

3.12.5. Make a blank correction for each air sample by subtracting the total amount of cadmium in the corresponding blank sample from the total amount of cadmium in the sample.

3.12.6. Calculate the concentration of cadmium in an air sample (mg/m^3 or $\mu g/m^3$) by using one of the following equations:

$$mg/m^3 = W_{bc}/(\text{Air vol sampled, L})$$

or

$$\mu g/m^3 = (W_{bc})(1{,}000\ ng/\mu g)/(\text{Air vol sampled, L})$$

Where:

W_{bc} = blank corrected total μg cadmium in the sample. (1μg = 1,000 ng)

4. Backup Data

4.1. Introduction

4.1.1. The purpose of this evaluation is to determine the analytical method recovery, working standard range, and qualitative and quantitative detection limits of the two atomic absorption analytical techniques included in this method. The evaluation consisted of the following experiments:

1. An analysis of 24 samples (six samples each at 0.1, 0.5, 1 and 2 times the TWA-PEL) for the analytical method recovery study of the flame AAS analytical technique.

2. An analysis of 18 samples (six samples each at 0.5, 1 and 2 times the Action Level TWA-PEL) for the analytical method

TABLE III.—CD DETECTION LIMIT STUDY

[AAS-HGA Analysis]

STD (ng/mL)	Peak area readings × 10^3 at 228.8 nm		Statistical analysis
Reagent blank	0	0	n=6.
	0	1	mean=0.167.
	0	0	std dev=0.41.
			CV=2.45.
0.1	6	6	n=6.
	5	7	mean=7.7.
	13	7	std dev=2.8.
			CV=0.366.
0.2	11	13	n=6.
	11	12	mean=11.8.
	12	12	std dev=0.75.
			CV=0.064.
0.5	28	33	n=6.
	26	28	mean=28.8.
	28	30	std dev=2.4.
			CV=0.083.
1.0	52	55	n=6.
	56	58	mean=54.8.
	54	54	std dev=2.0.
			CV=0.037.
2.0	101	112	n=6.
	110	110	mean=108.8.
	110	110	std dev=3.9.
			CV=0.036.

TABLE IV.—CD STANDARD WORKING RANGE STUDY

[AAS-HGA Analysis]

STD (ng/mL)	Peak area readings × 10^3 at 228.8 nm		Statistical analysis
0.2	11	13	n=6.
	11	12	mean=11.8.
	12	12	std dev=0.75.
			CV=0.064.
0.5	28	33	n=6.
	26	28	mean=28.8.
	28	30	std dev=2.4.
			CV=0.083.
1.0	52	55	n=6.
	56	58	mean=54.8.
	54	54	std dev=2.0.
			CV=0.037.
2.0	101	112	n=6.
	110	110	mean=108.8.
	110	110	std dev=3.9.
			CV=0.036.
5.0	247	265	n=6.
	268	275	mean=265.5.
	259	279	std dev=11.5.
			CV=0.044.

TABLE IV.—CD STANDARD WORKING RANGE STUDY—Continued

[AAS-HGA Analysis]

STD (ng/mL)	Peak area readings × 10^3 at 228.8 nm		Statistical analysis
10.0	495	520	n=6.
	523	513	mean=516.7.
	516	533	std dev=12.7.
			CV=0.025.
20.0	950	953	n=6.
	951	958	mean=941.8.
	949	890	std dev=25.6.
			CV=0.027.
30.0	1269	1291	n=6.
	1303	1307	mean=1293.
	1295	1290	std dev=13.3.
			CV=0.010.
40.0	1505	1567	n=6.
	1535	1567	mean=1552.
	1566	1572	std dev=26.6.
			CV=0.017.

TABLE V.—ANALYTICAL METHOD RECOVERY

[Flame AAS Analysis]

Test level	0.5×	Percent rec.	μg taken	1.0×	Percent rec.	μg taken	2.0×	Percent rec.
μg taken	μg found			μg found			μg found	
1.00	1.0715	107.2	2.00	2.0688	103.4	4.00	4.1504	103.8
1.00	1.0842	108.4	2.00	2.0174	100.9	4.00	4.1108	102.8
1.00	1.0842	108.4	2.00	2.0431	102.2	4.00	4.0581	101.5
1.00	*1.0081	*100.8	2.00	2.0431	102.2	4.00	4.0844	102.1
1.00	1.0715	107.2	2.00	2.0174	100.9	4.00	4.1504	103.8
1.00	1.0842	108.4	2.00	2.0045	100.2	4.00	4.1899	104.7
n=		5			6			6
mean=		107.9			101.6			103.1
std dev=		0.657			1.174			1.199
CV_1=		0.006			0.011			0.012

CV_1 (pooled)=0.010

* Rejected as an outlier—this value did not pass the outlier T-test at the 99% confidence level.

Test level	0.1×	Percent rec.
μg taken	μg found	
0.200	0.2509	125.5
0.200	0.2509	125.5
0.200	0.2761	138.1
0.200	0.2258	112.9
0.200	0.2258	112.9
0.200	0.1881	94.1
n=		6
mean=		118.2
std dev=		15.1
CV_1=		0.128

TABLE VI.—ANALYTICAL METHOD RECOVERY

[AAS-HGA analysis]

Test level	0.5×	Percent rec.	ng taken	1.0×	Percent rec.	ng taken	2.0×	Percent rec.
ng taken	ng found			ng found			ng found	
75	71.23	95.0	150	138.00	92.0	300	258.43	86.1
75	71.47	95.3	150	138.29	92.2	300	258.46	86.2
75	70.02	93.4	150	136.30	90.9	300	280.55	93.5
75	77.34	103.1	150	146.62	97.7	300	288.34	96.1
75	78.32	104.4	150	145.17	96.8	300	261.74	87.2
75	71.96	95.9	150	144.88	96.6	300	277.22	92.4
n=		6			6			6
mean=		97.9			94.4			90.3
std dev=		4.66			2.98			4.30
CV_t=		0.048			0.032			0.048
				CV_t(pooled)=0.043				

Attachment 1

Instrumental Parameters for Flame AAS Analysis

Atomic Absorption Spectrophotometer (Perkin-Elmer Model 603)

Flame: Air/Acetylene—lean, blue
Oxidant Flow: 55
Fuel Flow: 32
Wavelength: 228.8 nm
Slit: 4 (0.7 nm)
Range: UV
Signal: Concentration (4 exp)
Integration Time: 3 sec

Attachment 2

Instrumental Parameters for HGA Analysis

Atomic Absorption Spectrophotometer (Perkin-Elmer Model 5100)

Signal Type: Zeeman AA
Slitwidth: 0.7 nm
Wavelength: 228.8 nm
Measurement: Peak Area
Integration Time: 6.0 sec
BOC Time: 5 sec
BOC=Background Offset Correction.

ZEEMAN GRAPHITE FURNACE (PERKIN-ELMER MODEL HGA-600)

Step	Ramp time (sec)	Hold time (sec)	Temp. (°C)	Argon flow (mL/min)	Read (sec)
1) Predry	5	10	90	300	
2) Dry	30	10	140	300	
3) Char	10	20	900	300	
4) Cool Down	1	8	30	300	
5) Atomize	0	5	1600	0	−1
6) Burnout	1	8	2500	300	

Appendix F to § ____: Nonmandatory Protocol for Biological Monitoring

1.00 Introduction

Under the final OSHA cadmium rule (29 CFR part 1910), monitoring of biological specimens and several periodic medical examinations are required for eligible employees. These medical examinations are to be conducted regularly, and medical monitoring is to include the periodic analysis of cadmium in blood (CDB), cadmium in urine (CDU) and beta-2-microglobulin in urine (B2MU). As CDU and B2MU are to be normalized to the concentration of creatinine in urine (CRTU), then CRTU must be analyzed in conjunction with CDU and B2MU analyses.

The purpose of this protocol is to provide procedures for establishing and maintaining the quality of the results obtained from the analyses of CDB, CDU and B2MU by commercial laboratories. Laboratories conforming to the provisions of this nonmandatory protocol shall be known as "participating laboratories." The biological monitoring data from these laboratories will be evaluated by physicians responsible for biological monitoring to determine the conditions under which employees may continue to work in locations exhibiting airborne-cadmium concentrations at or above defined actions levels (see paragraphs (l)(3) and (l)(4) of the final rule). These results also may be used to support a decision to remove workers from such locations.

Under the medical monitoring program for cadmium, blood and urine samples must be collected at defined intervals from workers by physicians responsible for medical monitoring; these samples are sent to commerical laboratories that perform the required analyses and report results of these analyses to the responsible physicians. To ensure the accuracy and reliability of these laboratory analyses, the laboratories to which samples are submitted should participate in an ongoing and efficacious proficiency testing program. Availability of proficiency testing programs may vary with the analyses performed.

To test proficiency in the analysis of CDB, CDU and B2MU, a laboratory should participate either in the interlaboratory comparison program operated by the Centre de Toxicologie du Quebec (CTQ) or an equivalent program. (Currently, no laboratory in the U.S. performs proficiency testing on CDB, CDU or B2MU.) Under this program, CTQ sends participating laboratories 18 samples of each analyte (CDB, CDU and/or B2MU) annually for analysis. Participating laboratories must return the results of these analyses to CTQ within four to five weeks after receiving the samples.

The CTQ program pools analytical results from many participating laboratories to derive consensus mean values for each of the samples distributed. Results reported by each laboratory then are compared against these consensus means for the analyzed samples to determine the relative performance of each laboratory. The proficiency of a participating laboratory is a function of the extent of agreement between results submitted by the participating laboratory and the consensus values for the set of samples analyzed.

Proficiency testing for CRTU analysis (which should be performed with CDU and B2MU analyses to evaluate the results properly) also is recommended. In the U.S., only the College of American Pathologists (CAP) currently conducts CRTU proficiency testing; participating laboratories should be accredited for CRTU analysis by the CAP.

Results of the proficiency evaluations will be forwarded to the participating laboratory

by the proficiency-testing laboratory, as well as to physicians designated by the participating laboratory to receive this information. In addition, the participating laboratory should, on request, submit the results of their internal Quality Assurance/Quality Control (QA/QC) program for each analytic procedure (i.e., CDB, CDU and/or B2MU) to physicians designated to receive the proficiency results. For participating laboratories offering CDU and/or B2MU analyses, QA/QC documentation also should be provided for CRTU analysis. (Laboratories should provide QA/QC information regarding CRTU analysis directly to the requesting physician if they perform the analysis in-house; if CRTU analysis is performed by another laboratory under contract, this information should be provided to the physician by the contract laboratory.)

QA/QC information, along with the actual biological specimen measurements, should be provided to the responsible physician using standard formats. These physicians then may collate the QA/QC information with proficiency test results to compare the relative performance of laboratories, as well as to facilitate evaluation of the worker monitoring data. This information supports discretionary decisions made by the physician with regard to the biological monitoring program, and for mandating medical removal.

This protocol describes procedures that may be used by the responsible physicians to identify laboratories most likely to be proficient in the analysis of samples used in the biological monitoring of cadmium; also provided are procedures for record keeping and reporting by laboratories participating in proficiency testing programs, and recommendations to assist these physicians in interpreting analytical results determined by participating laboratories. As the collection and handling of samples affects the quality of the data, recommendations are made for these tasks. Specifications for analytical methods to be used in the medical monitoring program are included in this protocol as well.

In conclusion, this document is intended as a supplement to characterize and maintain the quality of medical monitoring data collected under the final cadmium rule promulgated by OSHA (29 CFR part 1910). OSHA has been granted authority under the Occupational Safety and Health Act of 1970 to protect workers from the effects of exposure to hazardous substances in the work place and to mandate adequate monitoring of workers to determine when adverse health effects may be occurring. This nonmandatory protocol is intended to provide guidelines and recommendations to improve the accuracy and reliability of the procedures used to analyze the biological samples collected as part of the medical monitoring program for cadmium.

2.0 Definitions

When the terms below appear in this protocol, use the following definitions.

Accuracy: A measure of the bias of a data set. Bias is a systematic error that is either inherent in a method or caused by some artifact or idiosyncracy of the measurement system. Bias is characterized by a consistent deviation (positive or negative) in the results from an accepted reference value.

Arithmetic Mean: The sum of measurements in a set divided by the number of measurements in a set.

Blind Samples: A quality control procedure in which the concentration of analyte in the samples should be unknown to the analyst at the time that the analysis is performed.

Coefficient of Variation: The ratio of the standard deviation of a set of measurements to the mean (arithmetic or geometric) of the measurements.

Compliance Samples: Samples from exposed workers sent to a participating laboratory for analysis.

Control Charts: Graphic representations of the results for quality control samples being analyzed by a participating laboratory.

Control Limits: Statistical limits which define when an analytic procedure exceeds acceptable parameters; control limits provide a method of assessing the accuracy of analysts, laboratories, and discrete analytic runs.

Control Samples: Quality control samples.

F/T: The measured amount of an analyte divided by the theoretical value (defined below) for that analyte in the sample analyzed; this ratio is a measure of the recovery for a quality control sample.

Geometric Mean: The natural antilog of the mean of a set of natural log-transformed data.

Geometric Standard Deviation: The antilog of the standard deviation of a set of natural log-transformed data.

Limit of Detection: Using a predefined level of confidence, this is the lowest measured value at which some of the measured material is likely to have come from the sample.

Mean: A central tendency of a set of data; in this protocol, this mean is defined as the *arithmetic mean* (see definition of *arithmetic mean* above) unless stated otherwise.

Performance: A measure of the overall quality of data reported by a laboratory.

Pools: Groups of quality-control samples to be established for each target value (defined below) of an analyte. For the protocol provided in attachment 3, for example, the theoretical value of the quality control samples of the pool must be within a range defined as plus or minus (±) 50% of the target value. Within each analyte pool, there must be quality control samples of at least 4 theoretical values.

Precision: The extent of agreement between repeated, independent measurements of the same quantity of an analyte.

Proficiency: The ability to satisfy a specified level of analyte performance.

Proficiency Samples: Specimens, the values of which are unknown to anyone at a participating laboratory, and which are submitted by a participating laboratory for proficiency testing.

Quality or Data Quality: A measure of the confidence in the measurement value.

Quality Control (QC) Samples: Specimens, the value of which is unknown to the analyst, but is known to the appropriate QA/QC personnel of a participating laboratory; when used as part of a laboratory QA/QC program, the theoretical values of these samples should not be known to the analyst until the analyses are complete. QC samples are to be run in sets consisting of one QC sample from each pool (see definition of "pools" above).

Sensitivity: For the purposes of this protocol, the limit of detection.

Standard Deviation: A measure of the distribution or spread of a data set about the mean; the standard deviation is equal to the positive square root of the variance, and is expressed in the same units as the original measurements in the data set.

Standards: Samples with values known by the analyst and used to calibrate equipment and to check calibration throughout an analytic run. In a laboratory QA/QC program, the values of the standards must exceed the values obtained for compliance samples such that the lowest standard value is near the limit of detection and the highest standard is higher than the highest compliance sample or QC sample. Standards of at least three different values are to be used for calibration, and should be constructed from at least 2 different sources.

Target Value: Those values of CDB, CDU or B2MU which trigger some action as prescribed in the medical surveillance section of the regulatory text of the final cadmium rule. For CDB, the target values are 5, 7, 10 and 15 μg/l. For CDU, the target values are 3, 5, 10 and 15 μg/g CRTU. For B2MU, the target values are 300, 500, 1000 and 1500 μg/g CRTU. (Note that target values may vary as a function of time.)

Theoretical Value (or Theoretical Amount): The reported concentration of a quality-control sample (or calibration standard) derived from prior characterizations of the sample.

Value or Measurement Value: The numerical result of a measurement.

Variance: A measure of the distribution or spread of a data set about the mean; the variance is the sum of the squares of the differences between the mean and each discrete measurement divided by one less than the number of measurements in the data set.

3.0 Protocol

This protocol provides procedures for characterizing and maintaining the quality of analytic results derived for the medical monitoring program mandated for workers under the final cadmium rule.

3.1 Overview

The goal of this protocol is to assure that medical monitoring data are of sufficient quality to facilitate proper interpretation. The data quality objectives (DQOs) defined for the medical monitoring program are summarized in Table 1. Based on available information, the DQOs presented in Table 1 should be achievable by the majority of laboratories offering the required analyses commercially; OSHA recommends that only laboratories meeting these DQOs be used for the analysis of biological samples collected for monitoring cadmium exposure.

TABLE 1.—RECOMMENDED DATA QUALITY OBJECTIVES (DQOS) FOR THE CADMIUM MEDICAL MONITORING PROGRAM

Analyte/concentration pool	Limit of detection	Precision (CV) (%)	Accuracy
Cadmium in blood	0.5 μg/l		±1 μg/l or 15% of the mean.
≤2 μg/l		40	
>2 μg/l		20	
Cadmium in urine	0.5 μg/g creatinine		±1 μg/l or 15% of the mean.
≤2 μg/l creatinine		40	
>2 μg/l creatinine		20	
β-2-microglobulin in urine: 100 μg/g creatine	100 μg/g creatinine	5	±15% of the mean.

To satisfy the DQOs presented in Table 1, OSHA provides the following guidelines:

1. Procedures for the collection and handling of blood and urine are specified (Section 3.4.1 of this protocol);

2. Preferred analytic methods for the analysis of CDB, CDU and B2MU are defined (and a method for the determination of CRTU also is specified since CDU and B2MU results are to be normalized to the level of CRTU).

3. Procedures are described for identifying laboratories likely to provide the required analyses in an accurate and reliable manner;

4. These guidelines (Sections 3.2.1 to 3.2.3, and Section 3.3) include recommendations regarding internal QA/QC programs for participating laboratories, as well as levels of proficiency through participation in an interlaboratory proficiency program;

5. Procedures for QA/QC record keeping (Section 3.3.2), and for reporting QC/QA results are described (Section 3.3.3); and,

6. Procedures for interpreting medical monitoring results are specified (Section 3.4.3).

Methods recommended for the biological monitoring of eligible workers are:

1. The method of Stoeppler and Brandt (1980) for CDB determinations (limit of detection: 0.5 μg/l);

2. The method of Pruszkowska et al. (1983) for CDU determinations (limit of detection: 0.5 μg/l of urine); and,

3. The Pharmacia Delphia test kit (Pharmacia 1990) for the determination of B2MU (limit of detection: 100 μg/l urine).

Because both CDU and B2MU should be reported in μg/g CRTU, an independent determination of CRTU is recommended. Thus, both the OSHA Salt Lake City Technical Center (OSLTC) method (OSHA, no date) and the Jaffe method (Du Pont, no date) for the determination of CRTU are specified under this protocol (i.e., either of these 2 methods may be used). Note that although detection limits are not reported for either of these CRTU methods, the range of measurements expected for CRTU (0.9-1.7 μg/l) are well above the likely limit of detection for either of these methods (Harrison, 1987).

Laboratories using alternate methods should submit sufficient data to the responsible physicians demonstrating that the alternate method is capable of satisfying the defined data quality objectives of the program. Such laboratories also should submit a QA/QC plan that documents the performance of the alternate method in a manner entirely equivalent to the QA/QC plans proposed in Section 3.3.1.

3.2 Duties of the Responsible Physician

The responsible physician will evaluate biological monitoring results provided by participating laboratories to determine whether such laboratories are proficient and have satisfied the QA/QC recommendations. A requirement of the medical monitoring program mandated under the cadmium rule is that responsible physicians have the duty to employ laboratories to perform the required CDB, CDU and B2MU analyses of biological samples collected from eligible workers (paragraph (l)(1)(iv) of the final rule). In determining which laboratories to employ for this purpose, these physicians should review proficiency and QA/QC data submitted to them by the participating laboratories.

Participating laboratories should demonstrate proficiency for each analyte (CDU, CDB and B2MU) sampled under the biological monitoring program. Participating laboratories involved in analyzing CDU and B2MU also should demonstrate proficiency for CRTU analysis, or provide evidence of a contract with a laboratory proficient in CRTU analysis.

3.2.1 Recommendations for Selecting Among Existing Laboratories

OSHA recommends that existing laboratories providing commercial analyses for CDB, CDU and/or B2MU for the medical monitoring program satisfy the following criteria:

1. Should have performed commercial analyses for the appropriate analyte (CDB, CDU and/or B2MU) on a regular basis over the last 2 years;

2. Should provide the responsible physician with an internal QA/QC plan;

3. If performing CDU or B2MU analyses, the participating laboratory should be accredited by the CAP for CRTU analysis, and should be enrolled in the corresponding CAP survey (note that alternate credentials may be acceptable, but acceptability is to be determined by the responsible physician); and,

4. Should have enrolled in the CTQ interlaboratory comparison program for the appropriate analyte (CDB, CDU and/or B2MU).

Participating laboratories should submit appropriate documentation demonstrating compliance with the above criteria to the responsible physician. To demonstrate compliance with the first of the above criteria, participating laboratories should submit the following documentation for each analyte they plan to analyze (note that each document should cover a period of at least 8 consecutive quarters, and that the period designated by the term "regular analyses" is at least once a quarter):

1. Copies of laboratory reports providing results from regular analyses of the appropriate analyte (CDB, CDU and/or B2MU);

2. Copies of 1 or more signed and executed contracts for the provision of regular analyses of the appropriate analyte (CDB, CDU and/or B2MU); or,

3. Copies of invoices sent to 1 or more clients requesting payment for the provision of regular analyses of the appropriate analyte (CDB, CDU and/or B2MU). Whatever the form of documentation submitted, the specific analytic procedures conducted should be identified directly. The forms that are copied for submission to the responsible physician also should identify the laboratory which provided these analyses.

To demonstrate compliance with the second of the above criteria, a laboratory should submit to the responsible physician an internal QA/QC plan detailing the standard operating procedures to be adopted for satisfying the recommended QA/QC procedures for the analysis of each specific analyte (CDB, CDU and/or B2MU). Procedures for internal QA/QC programs are detailed in Section 3.3.1 below.

To satisfy the third of the above criteria, laboratories analyzing for CDU or B2MU also should submit a QA/QC plan for creatinine analysis (CRTU); the QA/QC plan and characterization analyses for CRTU must come from the laboratory performing the CRTU analysis, even if the CRTU analysis is being performed by a contract laboratory.

Laboratories enrolling in the CTQ program (to satisfy the last of the above criteria) must remit, with the enrollment application, an initial fee of approximately $100 per analyte. (Note that this fee is only an estimate, and is subject to revision without notice.) Laboratories should indicate on the application that they agree to have proficiency test results sent by the CTQ directly to the physicians designated by participating laboratories.

Once a laboratory's application is processed by the CTQ, the laboratory will be assigned a code number which will be provided to the laboratory on the initial confirmation form, along with identification of the specific analytes for which the laboratory is participating. Confirmation of participation will be sent by the CTQ to physicians designated by the applicant laboratory.

3.2.2 Recommended Review of Laboratories Selected to Perform Analyses

Six months after being selected initially to perform analyte determinations, the status of participating laboratories should be reviewed by the responsible physicians. Such reviews should then be repeated every 6 months or whenever additional proficiency or QA/QC documentation is received (whichever occurs first).

As soon as the responsible physician has received the CTQ results from the first 3 rounds of proficiency testing (i.e., 3 sets of 3 samples each for CDB, CDU and/or B2MU) for a participating laboratory, the status of the laboratory's continued participation should be reviewed. Over the same initial 6-month period, participating laboratories also should provide responsible physicians the results of their internal QA/QC monitoring program used to assess performance for each analyte (CDB, CDU and/or B2MU) for which the laboratory performs determinations. This information should be submitted using appropriate forms and documentation.

The status of each participating laboratory should be determined for each analyte (i.e., whether the laboratory satisfies minimum proficiency guidelines based on the proficiency samples sent by the CTQ and the results of the laboratory's internal QA/QC program). To maintain competency for analysis of CDB, CDU and/or B2MU during the first review, the laboratory should satisfy performance requirements for at least 2 of the 3 proficiency samples provided in each of the 3 rounds completed over the 6-month period. Proficiency should be maintained for the analyte(s) for which the laboratory conducts determinations.

To continue participation for CDU and/or B2MU analyse, laboratories also should either maintain accreditation for CRTU analysis in the CAP program and participate in the CAP surveys, or they should contract the CDU and B2MU analyses to a laboratory which satisfies these requirements (or which can provide documentation of accreditation/participation in an equivalent program).

The performance requirement for CDB analysis is defined as an analytical result within ±1 μg/l blood or 15% of the consensus mean (whichever is greater). For samples exhibiting a consensus mean less than 1 μg/l, the performance requirement is defined as a concentration between the detection limit of the analysis and a maximum of 2 μg/l. The purpose for redefining the acceptable interval for low CDB values is to encourage proper reporting of the actual values obtained during measurement; laboratories, therefore, will not be penalized (in terms of a narrow range of acceptability) for reporting measured concentrations smaller than 1 μg/l.

The performance requirement for CDU analysis is defined as an analytical result within ±1 μg/l urine or 15% of the consensus mean (whichever is greater). For samples exhibiting a consensus mean less than 1 μg/l urine, the performance requirement is defined as a concentration between the detection limit of the analysis and a maximum of 2 μg/l urine. Laboratories also should demonstrate proficiency in creatinine analysis as defined by the CAP. Note that reporting CDU results, other than for the CTQ proficiency samples (i.e., compliance samples), should be accompanied with results of analyses for CRTU, and these 2 sets of results should be combined to provide a measure of CDU in units of μg/g CRTU.

The performance requirement for B2MU is defined as analytical results within ± 15% of the consensus mean. Note that reporting B2MU results, other than for CTQ proficiency samples (i.e., compliance samples), should be accompanied with results of analyses for CRTU, and these 2 sets of results should be combined to provide a measure of B2MU in units of μg/g CRTU.

There are no recommended performance checks for CRTU analyses. As stated previously, laboratories performing CRTU analysis in support of CDU or B2MU analyses should be accredited by the CAP, and participating in the CAP's survey for CRTU.

Following the first review, the status of each participating laboratory should be reevaluated at regular intervals (i.e., corresponding to receipt of results from each succeeding round of proficiency testing and submission of reports from a participating laboratory's internal QA/QC program).

After a year of collecting proficiency test results, the following proficiency criterion should be added to the set of criteria used to determine the participating laboratory's status (for analyzing CDB, CDU and/or B2MU): A participating laboratory should not fail performance requirements for more than 4 samples from the 6 most recent consecutive rounds used to assess proficiency for CDB, CDU and/or B2MU separately (i.e., a total of 18 discrete proficiency samples for each analyte). Note that this requirement does not replace, but supplements, the recommendation that a laboratory should satisfy the performance criteria for at least 2 of the 3 samples tested for each round of the program.

3.2.3 Recommendations for Selecting Among Newly-Formed Laboratories (or Laboratories that Previously Failed to Meet the Protocol Guidelines)

OSHA recommends that laboratories that have not previously provided commercial analyses of CDB, CDU and/or B2MU (or have done so for a period less than 2 years), or which have provided these analyses for 2 or more years but have not conformed previously with these protocol guidelines, should satisfy the following provisions for each analyte for which determinations are to be made prior to being selected to analyze biological samples under the medical monitoring program:

1. Submit to the responsible physician an internal QA/QC plan detailing the standard operating procedures to be adopted for satisfying the QA/QC guidelines (guidelines for internal QA/QC programs are detailed in Section 3.3.1);

2. Submit to the responsible physician the results of the initial characterization analyses for each analyte for which determinations are to be made;

3. Submit to the responsible physician the results, for the initial 6-month period, of the internal QA/QC program for each analyte for which determinations are to be made (if no commercial analyses have been conducted previously, a minimum of 2 mock standardization trials for each analyte should be completed per month for a 6-month period);

4. Enroll in the CTQ program for the appropriate analyte for which determinations are to be made, and arrange to have the CTQ program submit the initial confirmation of participation and proficiency test results directly to the designated physicians. Note that the designated physician should receive results from 3 completed rounds from the CTQ program before approving a laboratory for participation in the biological monitoring program;

5. Laboratories seeking participation for CDU and/or B2MU analyses should submit to the responsible physician documentation of accreditation by the CAP for CRTU analyses performed in conjunction with CDU and/or B2MU determinations (if CRTU analyses are conducted by a contract laboratory, this laboratory should submit proof of CAP accreditation to the responsible physician); and,

6. Documentation should be submitted on an appropriate form.

To participate in CDB, CDU and/or B2MU analyses, the laboratory should satisfy the above criteria for a minimum of 2 of the 3 proficiency samples provided in each of the 3 rounds of the CTQ program over a 6-month period; this procedure should be completed for each appropriate analyte. Proficiency should be maintained for each analyte to continue participation. Note that laboratories seeking participation for CDU or B2MU also should address the performance requirements for CRTU, which involves providing evidence of accreditation by the CAP and participation in the CAP surveys (or an equivalent program).

The performance requirement for CDB analysis is defined as an analytical result within ±1 μg/l or 15% of the consensus mean (whichever is greater). For samples exhibiting a consensus mean less than 1 μg/l, the performance requirement is defined as a concentration between the detection limit of the analysis and a maximum of 2 μg/l. The purpose of redefining the acceptable interval for low CDB values is to encourage proper reporting of the actual values obtained during measurement; laboratories, therefore, will not be penalized (in terms of a narrow range of acceptability) for reporting measured concentrations less than 1 μg/l.

The performance requirement for CDU analysis is defined as an analytical result within ±1 μg/l urine or 15% of the consensus mean (whichever is greater). For samples exhibiting a consensus mean less than 1 μg/l urine, the performance requirement is defined as a concentration that falls between the detection limit of the analysis and a maximum of 2 μg/l urine. Performance requirements for the companion CRTU analysis (defined by the CAP) also should be met. Note that reporting CDU results, other than for CTQ proficiency testing (i.e., compliance samples), should be accompanied with results of CRTU analyses, and these 2 sets of results should be combined to provide a measure of CDU in units of μg/g CRTU.

The performance requirement for B2MU is defined as an analytical result within ±15%

of the consensus mean. Note that reporting B2MU results, other than for CTQ proficiency testing (i.e., compliance samples), should be accompanied with results of CRTU analysis, these 2 sets of results should be combined to provide a measure of B2MU in units of μg/g CRTU.

Once a new laboratory has been approved by the responsible physician for conducting analyte determinations, the status of this approval should be reviewed periodically by the responsible physician as per the criteria presented under Section 3.2.2.

Laboratories which have failed previously to gain approval of the responsible physician for conducting determinations of 1 or more analytes due to lack of compliance with the criteria defined above for existing laboratories (Section 3.2.1), may obtain approval by satisfying the criteria for newly-formed laboratories defined under this section; for these laboratories, the second of the above criteria may be satisfied by submitting a new set of characterization analyses for each analyte for which determinations are to be made.

Reevaluation of these laboratories is discretionary on the part of the responsible physician. Reevaluation, which normally takes about 6 months, may be expedited if the laboratory can achieve 100% compliance with the proficiency test criteria using the 6 samples of each analyte submitted to the CTQ program during the first 2 rounds of proficiency testing.

For laboratories seeking reevaluation for CDU or B2MU analysis, the guidelines for CRTU analyses also should be satisfied, including accreditation for CRTU analysis by the CAP, and participation in the CAP survey program (or accreditation/participation in an equivalent program).

3.2.4 Future Modifications to the Protocol Guidelines

As participating laboratories gain experience with analyses for CDB, CDU and B2MU, it is anticipated that the performance achievable by the majority of laboratories should improve until it approaches that reported by the research groups which developed each method. OSHA, therefore, may choose to recommend stricter performance guidelines in the future as the overall performance of participating laboratories improves.

3.3 Guidelines for Record Keeping and Reporting

To comply with these guidelines, participating laboratories should satisfy the above-stated performance and proficiency recommendations, as well as the following internal QA/QC, record keeping, and reporting provisions.

If a participating laboratory fails to meet the provisions of these guidelines, it is recommended that the responsible physician disapprove further analyses of biological samples by that laboratory until it demonstrates compliance with these guidelines. On disapproval, biological samples should be sent to a laboratory that can demonstrate compliance with these guidelines, at least until the former laboratory is reevaluated by the responsible physician and found to be in compliance.

The following record keeping and reporting procedures should be practiced by participating laboratories.

3.3.1 Internal Quality Assurance/Quality Control Procedures

Laboratories participating in the cadmium monitoring program should develop and maintain an internal quality assurance/quality control (QA/QC) program that incorporates procedures for establishing and maintaining control for each of the analytic procedures (determinations of CDB, CDU and/or B2MU) for which the laboratory is seeking participation. For laboratories analyzing CDU and/or B2MU, a QA/QC program for CRTU also should be established.

Written documentation of QA/QC procedures should be described in a formal QA/QC plan; this plan should contain the following information: Sample acceptance and handling procedures (i.e., chain-of-custody); sample preparation procedures; instrument parameters; calibration procedures; and, calculations. Documentation of QA/QC procedures should be sufficient to identify analytical problems, define criteria under which analysis of compliance samples will be suspended, and describe procedures for corrective actions.

3.3.1.1 *QA/QC procedures for establishing control of CDB and CDU analyses*

The QA/QC program for CDB and CDU should address, at a minimum, procedures involved in calibration, establishment of control limits, internal QC analyses and maintaining control, and corrective-action protocols. Participating laboratory should develop and maintain procedures to assure that analyses of compliance samples are within control limits, and that these procedures are documented thoroughly in a QA/QC plan.

A nonmandatory QA/QC protocol is presented in Attachment 1. This attachment is illustrative of the procedures that should be addressed in a proper QA/QC program.

Calibration. Before any analytic runs are conducted, the analytic instrument should be calibrated. Calibration should be performed at the beginning of each day on which QC and/or compliance samples are run. Once calibration is established, QC or compliance samples may be run. Regardless of the type of samples run, about every fifth sample should serve as a standard to assure that calibration is being maintained.

Calibration is being maintained if the standard is within ±15% of its theoretical value. If a standard is more than + ±15% of its theoretical value, the run has exceeded control limits due to calibration error; the entire set of samples then should be reanalyzed after recalibrating or the results should be recalculated based on a statistical curve derived from that set of standards.

It is essential that the value of the highest standard analyzed be higher than the highest sample analyzed; it may be necessary, therefore, to run a high standard at the end of the run, which has been selected based on results obtained over the course of the run (i.e., higher than any standard analyzed to that point).

Standards should be kept fresh; as samples age, they should be compared with new standards and replaced if necessary.

Internal Quality Control Analyses. Internal QC samples should be determined interspersed with analyses of compliance samples. At a minimum, these samples should be run at a rate of 5% of the compliance samples or 2 samples per analytic run, whichever is greater. If only 2 samples are run, they should contain different levels of cadmium.

Internal QC samples may be obtained as commercially-available reference materials and/or they may be internally prepared. Internally-prepared samples should be well characterized and traced, or compared to a reference material for which a consensus value is available.

Levels of cadmium contained in QC samples should not be known to the analyst prior to reporting the results of the analysis.

Internal QC results should be plotted or charted in a manner which describes sample recovery and laboratory control limits.

Internal Control Limits. The laboratory protocol for evaluating internal QC analyses per control limits should be clearly defined. Limits may be based on statistical methods (e.g., as 2σ from the laboratory mean recovery), or on proficiency testing limits (e.g., ±2 μg or 15% of the mean, whichever is greater). Statistical limits that exceed ±40% should be reevaluated to determine the source error in the analysis.

When laboratory limits are exceeded, analytic work should terminate until the source of error is determined and corrected; compliance samples affected by the error should be reanalyzed. In addition, the laboratory protocol should address any unusual trends that develop which may be biasing the results. Numerous, consecutive results above or below laboratory mean recoveries, or outside laboratory statistical limits, indicate that problems may have developed.

Corrective Actions. The QA/QC plan should document in detail specific actions taken if control limits are exceeded or unusual trends develop. Corrective actions should be noted on an appropriate form, accompanied by supporting documentation.

In addition to these actions, laboratories should include whatever additional actions are necessary to assure that accurate data are reported to the responsible physicians.

Reference Materials. The following reference materials may be available:

Cadmium in Blood (CDB)

1. Centre de Toxicologie du Quebec, Le Centre Hospitalier de l'Universite Laval, 2705 boul. Laurier, Quebec, Que., Canada G1V 4G2. (Prepared 6 times per year at 1–15 μg Cd/l.)

2. H. Marchandise, Community Bureau of Reference-BCR, Directorate General XII, Commission of the European Communities, 200, rue de la Loi, B–1049, Brussels, Belgium. (Prepared as Bl CBM–1 at 5.37 μg Cd/l, and Bl CBM–2 at 12.38 μg Cd/l.)

3. Kaulson Laboratories Inc., 691 Bloomfield Ave., Caldwell, NJ 07006; tel: (201) 226–9494, FAX (201) 226–3244. (Prepared as #0141 [As, Cd, Hg, Pb] at 2 levels.)

Cadmium in Urine (CDU)

1. Centre de Toxicologie du Quebec, Le Centre Hospitalier de l'Universite Laval, 2705 boul. Laurier, Quebec, Que., Canada G1V 4G2. (Prepared 6 times per year.)

2. National Institute of Standards and Technology (NIST), Dept. of Commerce, Gaithersburg, MD; tel: (301) 975–6776. (Prepared as SRM 2670 freeze-dried urine [metals]; set includes normal and elevated levels of metals; cadmium is certified for elevated level of 88.0 μg/l in reconstituted urine.)

3. Kaulson Laboratories Inc., 691 Bloomfield Ave., Caldwell, NJ 07006; tel: (201) 226–9494, FAX (201) 226–3244. (Prepared as #0140 [As, Cd, Hg, Pb] at 2 levels.)

3.3.1.2 *QA/QC procedures for establishing control of B2MU*

A written, detailed QA/QC plan for B2MU analysis should be developed. The QA/QC plan should contain a protocol similar to those protocols developed for the CDB/CDU analyses. Differences in analyses may warrant some differences in the QA/QC protocol, but procedures to ensure analytical integrity should be developed and followed.

Examples of performance summaries that can be provided include measurements of accuracy (i.e., the means of measured values versus target values for the control samples) and precision (i.e., based on duplicate analyses). It is recommended that the accuracy and precision measurements be compared to those reported as achievable by the Pharmacia Delphia kit (Pharmacia 1990) to determine if and when unsatisfactory analyses have arisen. If the measurement error of 1 or more of the control samples is more than 15%, the run exceeds control limits. Similarly, this decision is warranted when the average CV for duplicate samples is greater than 5%.

3.3.2 Procedures for Record Keeping

To satisfy reporting requirements for commercial analyses of CDB, CDU and/or B2MU performed for the medical monitoring program mandated under the cadmium rule, participating laboratories should maintain the following documentation for each analyte:

1. For each analytic instrument on which analyte determinations are made, records relating to the most recent calibration and QC sample analyses;

2. For these instruments, a tabulated record for each analyte of those determinations found to be within and outside of control limits over the past 2 years;

3. Results for the previous 2 years of the QC sample analyses conducted under the internal QA/QC program (this information should be: Provided for each analyte for which determinations are made and for each analytic instrument used for this purpose, sufficient to demonstrate that internal QA/QC programs are being executed properly, and consistent with data sent to responsible physicians.

4. Duplicate copies of monitoring results for each analyte sent to clients during the previous 5 years, as well as associated information; supporting material such as chain-of-custody forms also should be retained; and,

5. Proficiency test results and related materials received while participating in the CTQ interlaboratory program over the past 2 years; results also should be tabulated to provide a serial record of relative error (derived per Section 3.3.3 below).

3.3.3 Reporting Procedures

Participating laboratories should maintain these documents: QA/QC program plans; QA/QC status reports; CTQ proficiency program reports; and, analytical data reports. The information that should be included in these reports is summarized in Table 2; a copy of each report should be sent to the responsible physician.

TABLE 2.—REPORTING PROCEDURES FOR LABORATORIES PARTICIPATING IN THE CADMIUM MEDICAL MONITORING PROGRAM

Report	Frequency (time frame)	Contents
1 QA/QC Program Plan	Once (initially)	A detailed description of the QA/QC protocol to be established by the laboratory to maintain control of analyte determinations.
2 QA/QC Status Report	Every 2 months	Results of the QC samples incorporated into regular runs for each instrument (over the period since the last report).
3 Proficiency Report	Attached to every data report	Results from the last full year of proficiency samples submitted to the CTQ program and Results of the 100 most recent QC samples incorporated into regular runs for each instrument.
4 Analytical Data Report	For all reports of data results	Date the sample was received; Date the sample was analyzed; Appropriate chain-of-custody information; Types of analyses performed; Results of the requested analyses and Copy of the most current proficiency report.

As noted in Section 3.3.1, a QA/QC program plan should be developed that documents internal QA/QC procedures (defined under Section 3.3.1) to be implemented by the participating laboratory for each analyte; this plan should provide a list identifying each instrument used in making analyte determinations.

A QA/QC status report should be written bimonthly for each analyte. In this report, the results of the QC program during the reporting period should be reported for each analyte in the following manner: The number (N) of QC samples analyzed during the period; a table of the target levels defined for each sample and the corresponding measured values; the mean of F/T value (as defined below) for the set of QC samples run during the period; and, use of $X \pm 2\sigma$ (as defined below) for the set of QC samples run during the period as a measure of precision.

As noted in Section 2, an F/T value for a QC sample is the ratio of the measured concentration of analyte to the established (i.e., reference) concentration of analyte for that QC sample. The equation below describes the derivation of the mean for F/T values, X:

$$\overline{X} = \frac{\sum (F/T)}{N}$$

The standard deviation, σ, for these measurements is derived using the following equation (note that 2σ is twice this value):

$$\sigma = \left[\frac{\sum (F/T - \overline{X})^2}{n-1} \right]^{\frac{1}{2}}$$

The nonmandatory QA/QC protocol (see Attachment 3) indicates that QC samples should be divided into several discrete pools, and a separate estimate of precision for each pools then should be derived. Several precision estimates should be provided for concentrations which differ in average value. These precision measures may be used to document improvements in performance with regard to the combined pool.

Participating laboratories should use the CTQ proficiency program for each analyte. Results of the this program will be sent by CTQ directly to physicians designated by the participating laboratories. Proficiency results from the CTQ program are used to establish the accuracy of results from each participating laboratory, and should be provided to responsible physicians for use in trend analysis. A proficiency report consisting of these proficiency results should accompany data reports as an attachment.

For each analyte, the proficiency report should include the results from the 6 previous proficiency rounds in the following format:

1. Number (N) of samples analyzed;

2. Mean of the target levels, $(1/N)\Sigma T_i$, with T_i being a consensus mean for the sample;

3. Mean of the measurements, $(1/N)\Sigma M_i$, with M_i being a sample measurement;

4. A measure of error defined by:

$(1/N)\Sigma(T_i - M_i)^2$

Analytical data reports should be submitted to responsible physicians directly. For each sample, report the following information: The date the sample was received; the date the sample was analyzed; appropriate chain-of-custody information; the type(s) of analyses performed; and, the results of the analyses. This information should be reported on a form similar to the form provided an appropriate form. The most

recent proficiency program report should accompany the analytical data reports (as an attachment).

Confidence intervals for the analytical results should be reported as $X \pm 2\sigma$, with X being the measured value and 2σ the standard deviation calculated as described above.

For CDU or B2MU results which are combined with CRTU measurements for proper reporting, the 95% confidence limits are derived from the limits for CDU or B2MU, (p), and the limits for CRTU, (q), as follows:

$$\frac{X}{Y} \pm \left(\frac{1}{Y^2}\right)(Y^2 \times p^2 + X^2 \times q^2)^{\frac{1}{2}}$$

For these calculations, $X \pm p$ is the measurement and confidence limits for CDU or B2MU, and $Y \pm q$ is the measurement and confidence limit for CRTU.

Participating laboratories should notify responsible physicians as soon as they receive information indicating a change in their accreditation status with the CTQ or the CAP. These physicians should not be expected to wait until formal notice of a status change has been received from the CTQ or the CAP.

3.4 Instructions to Physicians

Physicians responsible for the medical monitoring of cadmium-exposed workers must collect the biological samples from workers; they then should select laboratories to perform the required analyses, and should interpret the analytic results.

3.4.1 Sample Collection and Holding Procedures

Blood Samples. The following procedures are recommended for the collection, shipment and storage of blood samples for CDB analysis to reduce analytical variability; these recommendations were obtained primarily through personal communications with J.P. Weber of the CTQ (1991), and from reports by the Centers for Disease Control (CDC, 1986) and Stoeppler and Brandt (1980).

To the extent possible, blood samples should be collected from workers at the same time of day. Workers should shower or thoroughly wash their hands and arms before blood samples are drawn. The following materials are needed for blood sample collection: Alcohol wipes; sterile gauze sponges; band-aids; 20-gauge, 1.5-in. stainless steel needles (sterile); preprinted labels; tourniquets; vacutainer holders; 3-ml "metal free" vacutainer tubes (i.e., dark-blue caps), with EDTA as an anti-coagulant; and, styrofoam vacutainer shipping containers.

Whole blood samples are taken by venipuncture. Each blue-capped tube should be labeled or coded for the worker and company before the sample is drawn. (Blue-capped tubes are recommended instead of red-capped tubes because the latter may consist of red coloring pigment containing cadmium, which could contaminate the samples.) Immediately after sampling, the vacutainer tubes must be thoroughly mixed by inverting the tubes at least 10 times manually or mechanically using a Vortex device (for 15 sec). Samples should be refrigerated immediately or stored on ice until they can be packed for shipment to the participating laboratory for analysis.

The CDC recommends that blood samples be shipped with a "cool pak" to keep the samples cold during shipment. However, the CTQ routinely ships and receives blood samples for cadmium analysis that have not been kept cool during shipment. The CTQ has found no deterioration of cadmium in biological fluids that were shipped via parcel post without a cooling agent, even though these deliveries often take 2 weeks to reach their destination.

Urine Samples. The following are recommended procedures for the collection, shipment and storage of urine for CDU and B2MU analyses, and were obtained primarily through personal communications with J.P. Weber of the CTQ (1991), and from reports by the CDC (1986) and Stoeppler and Brandt (1980).

Single "spot" samples are recommended. As B2M can degrade in the bladder, workers should first empty their bladder and then drink a large glass of water at the start of the visit. Urine samples then should be collected within 1 hour. Separate samples should be collected for CDU and B2MU using the following materials: Sterile urine collection cups (250 ml); small sealable plastic bags; preprinted labels; 15-ml polypropylene or polyethylene screw-cap tubes; lab gloves ("metal free"); and, preservatives (as indicated).

The sealed collection cup should be kept in the plastic bag until collection time. The workers should wash their hands with soap and water before receiving the collection cup. The collection cup should not be opened until just before voiding and the cup should be sealed immediately after filling. It is important that the inside of the container and cap are not touched by, or come into contact with, the body, clothing or other surfaces.

For CDU analyzes, the cup is swirled gently to resuspend any solids, and the 15-ml tube is filled with 10-12 ml urine. The CDC recommends the addition of 100 µl concentrated HNO_3 as a preservative before sealing the tube and then freezing the sample. The CTQ recommends minimal handling and does not acidify their interlaboratory urine reference materials prior to shipment, nor do they freeze the sample for shipment. At the CTQ, if the urine sample has much sediment, the sample is acidified in the lab to free any cadmium in the precipitate.

For B2M, the urine sample should be collected directly into a polyethylene bottle previously washed with dilute nitric acid. The pH of the urine should be measured and adjusted to 8.0 with 0.1 N NaOH immediately following collection. Samples should be frozen and stored at –20°C until testing is performed. The B2M in the samples should be stable for 2 days when stored at 2–8°C, and for at least 2 months at –20°C. Repeated freezing and thawing should be avoided to prevent denaturing the B2M (Pharmacia 1990).

3.4.2 Recommendations for Evaluating Laboratories

Using standard error data and the results of proficiency testing obtained from CTQ, responsible physicians can make an informed choice of which laboratory to select to analyze biological samples. In general, laboratories with small standard errors and little disparity between target and measured values tend to make precise and accurate sample determinations. Estimates of precision provided to the physicians with each set of monitoring results can be compared to previously-reported proficiency and precision estimates. The latest precision estimates should be at least as small as the standard error reported previously by the laboratory. Moreover, there should be no indication that precision is deteriorating (i.e., increasing values for the precision estimates). If precision is deteriorating, physicians may decide to use another laboratory for these analyses. QA/QC information provided by the participating laboratories to physicians can, therefore, assist physicians in evaluating laboratory performance.

3.4.3 Use and Interpretation of Results

When the responsible physician has received the CDB, CDU and/or B2MU results, these results must be compared to the action levels discussed in the final rule for cadmium. The comparison of the sample results to action levels is straightforward. The measured value reported from the laboratory can be compared directly to the action levels; if the reported value exceeds an action level, the required actions must be initiated.

4.0 Background

Cadmium is a naturally-occurring environmental contaminant to which humans are continually exposed in food, water, and air. The average daily intake of cadmium by the U.S. population is estimated to be 10–20 µg/day. Most of this intake is via ingestion, for which absorption is estimated at 4–7% (Kowal et al. 1979). An additional nonoccupational source of cadmium is smoking tobacco; smoking a pack of cigarettes a day adds an additional 2–4 µg cadmium to the daily intake, assuming absorption via inhalation of 25–35% (Nordberg and Nordberg 1988; Friberg and Elinder 1988; Travis and Haddock 1980).

Exposure to cadmium fumes and dusts in an occupational setting where air concentrations are 20–50 $\mu g/m^3$ results in an additional daily intake of several hundred micrograms (Friberg and Elinder 1988, p. 563). In such a setting, occupational exposure to cadmium occurs primarily via inhalation, although additional exposure may occur through the ingestion of material via contaminated hands if workers eat or smoke without first washing. Some of the particles that are inhaled initially may be ingested when the material is deposited in the upper respiratory tract, where it may be cleared by mucociliary transport and subsequently swallowed.

Cadmium introduced into the body through inhalation or ingestion is transported by the albumin fraction of the blood plasma to the liver, where it accumulates and is stored principally as a bound form complexed with the protein metallothionein. Metallothionein-bound cadmium is the main form of cadmium subsequently transported to the kidney; it is these 2 organs, the liver and kidney, in which the majority of the cadmium body burden accumulates. As much as one half of the total

body burden of cadmium may be found in the kidneys (Nordberg and Nordberg 1988).

Once cadmium has entered the body, elimination is slow; about 0.02% of the body burden is excreted per day via urinary/fecal elimination. The whole-body half-life of cadmium is 10–35 years, decreasing slightly with increasing age (Travis and Haddock 1980).

The continual accumulation of cadmium is the basis for its chronic noncarcinogenic toxicity. This accumulation makes the kidney the target organ in which cadmium toxicity usually is first observed (Piscator 1964). Renal damage may occur when cadmium levels in the kidney cortex approach 200 μg/g wet tissue-weight (Travis and Haddock 1980).

The kinetics and internal distribution of cadmium in the body are complex, and depend on whether occupational exposure to cadmium is ongoing or has terminated. In general, cadmium in blood is related principally to recent cadmium exposure, while cadmium in urine reflects cumulative exposure (i.e., total body burden) (Lauwerys et al. 1976; Friberg and Elinder 1988).

4.1 Health Effects

Studies of workers in a variety of industries indicate that chronic exposure to cadmium may be linked to several adverse health effects including kidney dysfunction, reduced pulmonary function, chronic lung disease and cancer (Federal Register 1990). The primary sites for cadmium-associated cancer appear to be the lung and the prostate.

Cancer. Evidence for an association between cancer and cadmium exposure comes from both epidemiological studies and animal experiments. Pott (1985) found a statistically significant elevation in the incidence of prostate cancer among a cohort of cadmium workers. Other epidemiology studies also report an elevated incidence of prostate cancer; however, the increases observed in these other studies were not statistically significant (Meridian Research, Inc. 1989).

One study (Thun et al. 1985) contains sufficiently quantitative estimates of cadmium exposure to allow evaluation of dose-response relationships between cadmium exposure and lung cancer. A statistically significant excess of lung cancer attributed to cadmium exposure was found in this study, even after accounting for confounding variables such as coexposure to arsenic and smoking habits (Meridian Research, Inc. 1989).

Evidence for quantifying a link between lung cancer and cadmium exposure comes from a single study (Takenaka et al. 1983). In this study, dose-response relationships developed from animal data were extrapolated to humans using a variety of models. OSHA chose the multistage risk model for estimating the risk of cancer for humans using these animal data. Animal injection studies also suggest an association between cadmium exposure and cancer, particularly observations of an increased incidence of tumors at sites remote from the point of injection. The International Agency for Research on Cancer (IARC) (Supplement 7, 1987) indicates that this, and related, evidence is sufficient to classify cadmium as an animal carcinogen. However, the results of these injection studies cannot be used to quantify risks attendant to human occupational exposures due to differences in routes of exposure (Meridian Research, Inc. 1989).

Based on the above-cited studies, the U.S. Environmental Protection Agency (EPA) classifies cadmium as "B1," a probable human carcinogen (USEPA 1985). IARC in 1987 recommended that cadmium be listed as a probable human carcinogen.

Kidney Dysfunction. The most prevalent nonmalignant effect observed among workers chronically exposed to cadmium is kidney dysfunction. Initially, such dysfunction is manifested by proteinuria (Meridian Research, Inc. 1989; Roth Associates, Inc. 1989). Proteinuria associated with cadmium exposure is most commonly characterized by excretion of low-molecular weight proteins (15,000–40,000 MW), accompanied by loss of electrolytes, uric acid, calcium, amino acids, and phosphate. Proteins commonly excreted include β-2-microglobulin (B2M), retinol-binding protein (RBP), immunoglobulin light chains, and lysozyme. Excretion of low molecular weight proteins is characteristic of damage to the proximal tubules of the kidney (Iwao et al. 1980).

Exposure to cadmium also may lead to urinary excretion of high-molecular weight proteins such as albumin, immunoglobulin G, and glycoproteins (Meridian Research, Inc. 1989; Roth Associates, Inc. 1989). Excretion of high-molecular weight proteins is indicative of damage to the glomeruli of the kidney. Bernard et al. (1979) suggest that cadmium-associated damage to the glomeruli and damage to the proximal tubules of the kidney develop independently of each other, but may occur in the same individual.

Several studies indicate that the onset of low-molecular weight proteinuria is a sign of irreversible kidney damage (Friberg et al. 1974; Roels et al. 1982; Piscator 1984; Elinder et al. 1985; Smith et al. 1986). For many workers, once sufficiently elevated levels of B2M are observed in association with cadmium exposure, such levels do not appear to return to normal even when cadmium exposure is eliminated by removal of the worker from the cadmium-contaminated work environment (Friberg, exhibit 29, 1990).

Some studies indicate that cadmium-induced proteinuria may be progressive; levels of B2MU increase even after cadmium exposure has ceased (Elinder et al. 1985). Other researchers have reached similar conclusions (Frieburg testimony, OSHA docket exhibit 29, Elinder testimony, OSHA docket exhibit 55, and OSHA docket exhibits 8–86B). Such observations are not universal, however (Smith et al. 1986; Tsuchiya 1976). Studies in which proteinuria has not been observed, however, may have initiated the reassessment too early (Meridian Research, Inc.1989; Roth Associates, Inc. 1989; Roels 1989).

A quantitative assessment of the risks of developing kidney dysfunction as a result of cadmium exposure was performed using the data from Ellis et al. (1984) and Falck et al. (1983). Meridian Research, Inc. (1989) and Roth Associates, Inc. (1989) employed several mathematical models to evaluate the data from the 2 studies, and the results indicate that cumulative cadmium exposure levels between 5 and 100 μg-years/m³ correspond with a one-in-a-thousand probability of developing kidney dysfunction.

When cadmium exposure continues past the onset of early kidney damage (manifested as proteinuria), chronic nephrotoxicity may occur (Meridian Research, Inc. 1989; Roth Associates, Inc. 1989). Uremia, which is the loss of the glomerulus' ability to adequately filter blood, may result. This condition leads to severe disturbance of electrolyte concentrations, which may result in various clinical complications including atherosclerosis, hypertension, pericarditis, anemia, hemorrhagic tendencies, deficient cellular immunity, bone changes, and other problems. Progression of the disease may require dialysis or a kidney transplant.

Studies in which animals are chronically exposed to cadmium confirm the renal effects observed in humans (Friberg et al. 1986). Animal studies also confirm cadmium-related problems with calcium metabolism and associated skeletal effects, which also have been observed among humans. Other effects commonly reported in chronic animal studies include anemia, changes in liver morphology, immunosuppression and hypertension. Some of these effects may be associated with cofactors; hypertension, for example, appears to be associated with diet, as well as with cadmium exposure. Animals injected with cadmium also have shown testicular necrosis.

4.2 Objectives for Medical Monitoring

In keeping with the observation that renal disease tends to be the earliest clinical manifestation of cadmium toxicity, the final cadmium standard mandates that eligible workers must be medically monitored to prevent this condition (as well as cadmimum-induced cancer). The objectives of medical-monitoring, therefore, are to: Identify workers at significant risk of adverse health effects from excess, chronic exposure to cadmium; prevent future cases of cadmium-induced disease; detect and minimize existing cadmium-induced disease; and, identify workers most in need of medical intervention.

The overall goal of the medical monitoring program is to protect workers who may be exposed continuously to cadmium over a 45-year occupational lifespan. Consistent with this goal, the medical monitoring program should assure that:

1. Current exposure levels remain sufficiently low to prevent the accumulation of cadmium body burdens sufficient to cause disease in the future by monitoring CDB as an indicator of recent cadmium exposure;

2. Cumulative body burdens, especially among workers with undefined historical exposures, remain below levels potentially capable of leading to damage and disease by assessing CDU as an indicator of cumulative exposure to cadmium; and,

3. Health effects are not occurring among exposed workers by determining B2MU as an early indicator of the onset of cadmium-induced kidney disease.

4.3 Indicators of Cadmium Exposure and Disease

Cadmium is present in whole blood bound to albumin, in erythrocytes, and as a metallothionein-cadmium complex. The metallothionein-cadmium complex that represents the primary transport mechanism for cadmium delivery to the kidney. CDB concentrations in the general, nonexposed population average 1 μg Cd/l whole blood, with smokers exhibiting higher levels (see Section 5.1.6). Data presented in Section 5.1.6 shows that 95% of the general population not occupationally exposed to cadmium have CDB levels less than 5 μg Cd/l.

If total body burdens of cadmium remain low, CDB concentrations indicate recent exposure (i.e., daily intake). This conclusion is based on data showing that cigarette smokers exhibit CDB concentrations of 2–7 μg/l depending on the number of cigarettes smoked per day (Nordberg and Nordberg 1988), while CDB levels for those who quit smoking return to general population values (approximately 1 μg/l) within several weeks (Lauwerys et al. 1976). Based on these observations, Lauwerys et al. (1976) concluded that CDB has a biological half-life of a few weeks to less than 3 months. As indicated in Section 3.1.6, the upper 95th percentile for CDB levels observed among those who are not occupationally exposed to cadmium is 5 μg/l, which suggests that the absolute upper limit to the range reported for smokers by Nordberg and Nordberg may have been affected by an extreme value (i.e., beyond 2σ above the mean).

Among occupationally-exposed workers, the occupational history of exposure to cadmium must be evaluated to interpret CDB levels. New workers, or workers with low exposures to cadmium, exhibit CDB levels that are representative of recent exposures, similar to the general population. However, for workers with a history of chronic exposure to cadmium, who have accumulated significant stores of cadmium in the kidneys/liver, part of the CDB concentrations appear to indicate body burden. If such workers are removed from cadmium exposure, their CDB levels remain elevated, possibly for years, reflecting prior long-term accumulation of cadmium in body tissues. This condition tends to occur, however, only beyond some threshold exposure value, and possibly indicates the capacity of body tissues to accumulate cadmium which cannot be excreted readily (Friberg and Elinder 1988; Nordberg and Nordberg 1988).

CDU is widely used as an indicator of cadmium body burdens (Nordberg and Nordberg 1988). CDU is the major route of elimination and, when CDU is measured, it is commonly expressed either as μg Cd/l urine (unadjusted), μg Cd/l urine (adjusted for specific gravity), or μg Cd/g CRTU (see Section 5.2.1). The metabolic model for CDU is less complicated than CDB, since CDU is dependentin large part on the body (i.e., kidney) burden of cadmium. However, a small proportion of CDU still be attributed to recent cadmium exposure, particularly if exposure to high airborne concentrations of cadmium occurred. Note that CDU is subject to larger inperindividual and day-to-day variations than CDB, so repeated measurements are recommended for CDU evaluations.

CDU is bound principally to metallothionein, regardless of whether the cadmium originates from metallothionein in plasma or from the cadmium pool accumulated in the renal tubules. Therefore, measurement of metallothionein in urine may provide information similar to CDU, while avoiding the contamination problems that may occur during collection and handling urine for cadmium analysis (Nordberg and Nordberg 1988). However, a commercial method for the determination of metallothionein at the sensitivity levels required under the final cadmium rule is not currently available; therefore, analysis of CDU is recommended.

Among the general population not occupationally exposed to cadmium, CDU levels average less than 1 μg/l (see Section 5.2.7). Normalized for creatinine (CRTU), the average CDU concentration of the general population is less than 1 μg/g CRTU. As cadmium accumulates over the lifespan, CDU increases with age. Also, cigarette smokers may eventually accumulate twice the cadmium body burden of nonsmokers. CDU is slightly higher in smokers than in nonsmokers, even several years after smoking cessation (Nordberg and Nordberg 1988). Despite variations due to age and smoking habits, 95% of those not occupationally exposed to cadmium exhibit levels of CDU less than 3 μg/g CRTU (based on the data presented in Section 5.2.7).

About 0.02% of the cadmium body burden is excreted daily in urine. When the critical cadmium concentration (about 200 ppm) in the kidney is reached, or if there is sufficient cadmium-induced kidney dysfunction, dramatic increases in CDU are observed (Nordberg and Nordberg 1988). Above 200 ppm, therefore, CDU concentrations cease to be an indicator of cadmium body burden, and are instead an index of kidney failure.

Proteinuria is an index of kidney dysfunction, and is defined by OSHA to be a material impairment. Several small proteins may be monitored as markers for proteinuria. Below levels indicative of proteinuria, these small proteins may be early indicators of increased risk of cadmium-induced renal tubular disease. Analytes useful for monitoring cadmium-induced renal tubular damage include:

1. β-2-Microglobulin (B2M), currently the most widely used assay for detecting kidney dysfunction, is the best characterized analyte available (Iwao et al. 1980; Chia et al. 1989);

2. Retinol Binding Protein (RBP) is more stable than B2M in acidic urine (i.e., B2M breakdown occurs if urinary pH is less than 5.5; such breakdown may result in false (i.e., low) B2M values (Bernard and Lauwerys, 1990));

3. N-Acetyl-B-Glucosaminidase (NAG) is the analyte of an assay that is simple, inexpensive, reliable, and correlates with cadmium levels under 10 μg/g CRTU, but the assay is less sensitive than RBP or B2M (Kawada et al. 1989);

4. Metallothionein (MT) correlates with cadmium and B2M levels, and may be a better predictor of cadmium exposure than CDU and B2M (Kawada et al. 1989);

5. Tamm-Horsfall Glycoprotein (THG) increases slightly with elevated cadmium levels, but this elevation is small compared to increases in urinary albumin, RBP, or B2M (Bernard and Lauwerys 1990);

6. Albumin (ALB), determined by the biuret method, is not sufficiently sensitive to serve as an early indicator of the onset of renal disease (Piscator 1962);

7. Albumin (ALB), determined by the Amido Black method, is sensitive and reproducible, but involves a time-consuming procedure (Piscator 1962);

8. Glycosaminoglycan (GAG) increases among cadmium workers, but the significance of this effect is unknown because no relationship has been found between elevated GAG and other indices of tubular damage (Bernard and Lauwerys 1990);

9. Trehalase seems to increase earlier than B2M during cadmium exposure, but the procedure for analysis is complicated and unreliable (Iwata et al. 1988); and,

10. Kallikrein is observed at lower concentrations among cadmium-exposed workers than among normal controls (Roels et al. 1990).

Of the above analytes, B2M appears to be the most widely used and best characterized analyte to evaluate the presence/absence, as well as the extent of, cadmium-induced renal tubular damage (Kawada, Koyama, and Suzuki 1989; Shaikh and Smith 1984; Nogawa 1984). However, it is important that samples be collected and handled so as to minimize B2M degradation under acidic urine conditions.

The threshold value of B2MU commonly used to indicate the presence of kidney damage 300 μg/g CRTU (Kjellstrom et al. 1977a; Buchet et al. 1980; and Kowal and Zirkes 1983). This value represents the upper 95th or 97.5th percentile level of urinary excretion observed among those without tubular dysfunction (Elinder, exbt L–140–45, OSHA docket H057A). In agreement with these conclusions, the data presented in Section 5.3.7 of this protocol generally indicate that the level of 300 μg/g CRTU appears to define the boundary for kidney dysfunction. It is not clear, however, that this level represents the upper 95th percentile of values observed among those who fail to demonstrate proteinuria effects.

Although elevated B2MU levels appear to be a fairly specific indicator of disease associated with cadmium exposure, other conditions that may lead to elevated B2MU levels include high fevers from influenza, extensive physical exercise, renal disease unrelated to cadmium exposure, lymphomas, and AIDS (Iwao et al. 1980; Schardun and van Epps 1987). Elevated B2M levels observed in association with high fevers from influenza or from extensive physical exercise are transient, and will return to normal levels once the fever has abated or metabolic rates return to baseline values following exercise. The other conditions linked to elevated B2M levels can be diagnosed as part of a properly-designed medical examination. Consequently, monitoring B2M, when accompanied by regular medical examinations and CDB and CDU determinations (as indicators of present and past cadmium exposure), may serve as a

specific, early indicator of cadmium-induced kidney damage.

4.4 Criteria for Medical Monitoring of Cadmium Workers

Medical monitoring mandated by the final cadmium rule includes a combination of regular medical examinations and periodic monitoring of 3 analytes: CDB, CDU and B2MU. As indicated above, CDB is monitored as an indicator of current cadmium exposure, while CDU serves as an indicator of the cadmium body burden; B2MU is assessed as an early marker of irreversible kidney damage and disease.

The final cadmium rule defines a series of action levels that have been developed for each of the 3 analytes to be monitored. These action levels serve to guide the responsible physician through a decision-making process. For each action level that is exceeded, a specific response is mandated. The sequence of action levels, and the attendant actions, are described in detail in the final cadmium rule.

Other criteria used in the medical decision-making process relate to tests performed during the medical examination (including a determination of the ability of a worker to wear a respirator). These criteria, however, are not affected by the results of the analyte determinations addressed in the above paragraphs and, consequently, will not be considered further in these guidelines.

4.5 Defining to Quality and Proficiency of the Analyte Determinations

As noted above in Sections 2 and 3, the quality of a measurement should be defined along with its value to properly interpret the results. Generally, it is necessary to know the accuracy and the precision of a measurement before it can be properly evaluated. The precision of the data from a specific laboratory indicates the extent to which the repeated measurements of the same sample vary within that laboratory. The accuracy of the data provides an indication of the extent to which these results deviate from average results determined from many laboratories performing the same measurement (i.e., in the absence of an independent determination of the true value of a measurement). Note that terms are defined operationally relative to the manner in which they will be used in this protocol. Formal definitions for the terms in italics used in this section can be found in the list of definitions (Section 2).

Another data quality criterion required to properly evaluate measurement results is the limit of detection of that measurement. For measurements to be useful, the range of the measurement which is of interest for biological monitoring purposes must lie entirely above the limit of detection defined for that measurement.

The overall quality of a laboratory's results is termed the performance of that laboratory. The degree to which a laboratory satisfies a minimum performance level is referred to as the proficiency of the laboratory. A successful medical monitoring program, therefore, should include procedures developed for monitoring and recording laboratory performance; these procedures can be used to identify the most proficient laboratories.

5.0 Overview of Medical Monitoring Tests for CDB, CDU, B2MU and CRTU

To evaluate whether available methods for assessing CDB, CDU, B2MU and CRTU are adequate for determining the parameters defined by the proposed action levels, it is necessary to review procedures available for sample collection, preparation and analysis. A variety of techniques for these purposes have been used historically for the determination of cadmium in biological matrices (including CDB and CDU), and for the determination of specific proteins in biological matrices (including B2MU). However, only the most recent techniques are capable of satisfying the required accuracy, precision and sensitivity (i.e., limit of detection) for monitoring at the levels mandated in the final cadmium rule, while still facilitating automated analysis and rapid processing.

5.1 Measuring Cadmium in Blood (CDB)

Analysis of biological samples for cadmium requires strict analytical discipline regarding collection and handling of samples. In addition to occupational settings, where cadmium contamination would be apparent, cadmium is a ubiquitous environmental contaminant, and much care should be exercised to ensure that samples are not contaminated during collection, preparation or analysis. Many common chemical reagents are contaminated with cadmium at concentrations that will interfere with cadmium analysis; because of the widespread use of cadmium compounds as colored pigments in plastics and coatings, the analyst should continually monitor each manufacturer's chemical reagents and collection containers to prevent contamination of samples.

Guarding against cadmium contamination of biological samples is particularly important when analyzing blood samples because cadmium concentrations in blood samples from nonexposed populations are generally less than 2 $\mu g/l$ (2 ng/ml), while occupationally-exposed workers can be at medical risk to cadmium toxicity if blood concentrations exceed 5 $\mu g/l$ (ACGIH 1991 and 1992). This narrow margin between exposed and unexposed samples requires that exceptional care be used in performing analytic determinations for biological monitoring for occupational cadmium exposure.

Methods for quantifying cadmium in blood have improved over the last 40 years primarily because of improvements in analytical instrumentation. Also, due to improvements in analytical techniques, there is less need to perform extensive multi-step sample preparations prior to analysis. Complex sample preparation was previously required to enhance method sensitivity (for cadmium), and to reduce interference by other metals or components of the sample.

5.1.1 Analytical Techniques Used to Monitor Cadmium in Biological Matrices

TABLE 3.—COMPARISON OF ANALYTICAL PROCEDURES/INSTRUMENTATION FOR DETERMINATION OF CADMIUM IN BIOLOGICAL SAMPLES

Analytical procedure	Limit of detection (ng/(g or ml))	Specified biological matrix	Reference	Comments
Flame Atomic Absorption Spectroscopy (FAAS).	≥1.0	Any matrix	Perkin-Elmer (1982)	Not sensitive enough for biomonitoring without extensive sample digestion, metal chelation and organic solvent extraction.
Graphite Furnace Atomic Absorption Spectroscopy (GFAAS).	0.04	Urine	Pruszkowska et al. (1983)	Methods of choice for routine cadmium analysis.
	≥0.20	Blood	Stoeppler and Brandt (1980).	
Inductively-Coupled Argon-Plasma Atomic Emission Spectroscopy (ICAP AES).	2.0	Any matrix	NIOSH (1984A)	Requires extensive sample preparation and concentration of metal with chelating resin. Advantage is simultaneous analyses for as many as 10 metals from 1 sample.
Neutron Activation Gamma Spectroscopy (NA)	1.5	In vivo (liver)	Ellis et al. (1983)	Only available *in vivo* method for direct determination of cadmium body tissue burdens; expensive; absolute determination of cadmium in reference materials.
Isotope Dilution Mass Spectroscopy (IDMS)	<1.0	Any matrix	Michiels and DeBievre (1986).	Suitable for absolute determination of cadmium in reference materials; expensive.
Differential Pulse Anodic Stripping Voltammetry (DPASV).	<1.0	Any matrix	Stoeppler and Brandt (1980).	Suitable for absolute determination of cadmium in reference materials; efficient method to check accuracy of analytical method.

A number of analytical techniques have been used for determining cadmium concentrations in biological materials. A summary of the characteristics of the most widely employed techniques is presented in Table 3. The technique most suitable for medical monitoring for cadmium is atomic absorption spectroscopy (AAS).

To obtain a measurement using AAS, a light source (i.e., hollow cathode or lectrode-free discharge lamp) containing the element of interest as the cathode, is energized and the lamp emits a spectrum that is unique for that element. This light source is focused through a sample cell, and a selected wavelength is monitored by a monochrometer and photodetector cell. Any ground state atoms in the sample that match those of the lamp element and are in the path of the emitted light may absorb some of the light and decrease the amount of light that reaches the photodetector cell. The amount of light absorbed at each characteristic wavelength is proportional to the number of ground state atoms of the corresponding element that are in the pathway of the light between the source and detector.

To determine the amount of a specific metallic element in a sample using AAS, the sample is dissolved in a solvent and aspirated into a high-temperature flame as an aerosol. At high temperatures, the solvent is rapidly evaporated or decomposed and the solute is initially solidified; the majority of the sample elements then are transformed into an atomic vapor. Next, a light beam is focused above the flame and the amount of metal in the sample can be determined by measuring the degree of absorbance of the atoms of the target element released by the flame at a characteristic wavelength.

A more refined atomic absorption technique, flameless AAS, substitutes an electrothermal, graphite furnace for the flame. An aliquot (10–100 μl) of the sample is pipetted into the cold furnace, which is then heated rapidly to generate an atomic vapor of the element.

AAS is a sensitive and specific method for the elemental analysis of metals; its main drawback is nonspecific background absorbtion and scattering of the light beam by particles of the sample as it decomposes at high temperatures; nonspecific absorbance reduces the sensitivity of the analytical method. The problem of nonspecific absorbance and scattering can be reduced by extensive sample pretreatment, such as ashing and/or acid digestion of the sample to reduce its organic content.

Current AAS instruments employ background correction devices to adjust electronically for background absorbtion and scattering. A common method to correct for background effects is to use a deuterium arc lamp as a second light source. A continuum light source, such as the deuterium lamp, emits a broad spectrum of wavelengths instead of specific wavelengths characteristic of a particular element, as with the hollow cathode tube. With this system, light from the primary source and the continuum source are passed alternately through the sample cell. The target element effectively absorbs light only from the primary source (which is much brighter than the continuum source at the characteristic wavelengths), while the background matrix absorbs and scatters light from both sources equally. Therefore, when the ratio of the two beams is measured electronically, the effect of nonspecific background absorption and scattering is eliminated. A less common, but more sophisticated, background correction system is based on the Zeeman effect, which uses a magnetically-activated light polarizer to compensate electronically for nonspecific absorbtion and scattering.

Atomic emission spectroscopy with inductively-coupled argon plasma (AES–ICAP) is widely used to analyze for metals. With this instrument, the sample is aspirated into an extremely hot argon plasma flame, which excites the metal atoms; emission spectra specific for the sample element then are generated. The quanta of emitted light passing through a monochrometer are amplified by photomultiplier tubes and measured by a photodetector to determine the amount of metal in the sample. An advantage of AES–ICAP over AAS is that multi-elemental analyses of a sample can be performed by simultaneously measuring specific elemental emission energies. However, AES–ICAP lacks the sensitivity of AAS, exhibiting a limit of detection which is higher than the limit of detection for graphite-furnace AAS (Table 3).

Neutron activation (NA) analysis and isotope dilution mass spectrometry (IDMS) are 2 additional, but highly specialized, methods that have been used for cadmium determinations. These methods are expensive because they require elaborate and sophisticated instrumentation.

NA analysis has the distinct advantage over other analytical methods of being able to determine cadmium body burdens in specific organs (e.g., liver, kidney) in vivo (Ellis et al. 1983). Neutron bombardment of the target transforms cadmium-13 to cadmium-114, which promptly decays ($<10^{-14}$ sec) to its ground state, emitting gamma rays that are measured using large gamma detectors; appropriate shielding and instrumentation are required when using this method.

IDMS analysis, a definitive but laborious method, is based on the change in the ratio of 2 isotopes of cadmium (cadmium 111 and 112) that occurs when a known amount of the element (with an artificially altered ratio of the same isotopes [i.e., a cadmium 111 "spike"] is added to a weighed aliquot of the sample (Michiels and De Bievre 1986).

5.1.2 Methods Developed for CDB Determinations

A variety of methods have been used for preparing and analyzing CDB samples; most of these methods rely on one of the analytical techniques described above. Among the earliest reports, Princi (1947) and Smith et al. (1955) employed a colorimetric procedure to analyze for CDB and CDU. Samples were dried and digested through several cycles with concentrated mineral acids (HNO_3 and H_2SO_4) and hydrogen peroxide (H_2O_2). The digest was neutralized, and the cadmium was complexed with diphenylthiocarbazone and extracted with chloroform. The dithizone-cadmium complex then was quantified using a spectrometer.

Colorimetric procedures for cadmium analyses were replaced by methods based on atomic absorption spectroscopy (AAS) in the early 1960s, but many of the complex sample preparation procedures were retained. Kjellstrom (1979) reports that in Japanese, American and Swedish laboratories during the early 1970s, blood samples were wet ashed with mineral acids or ashed at high temperature and wetted with nitric acid. The cadmium in the digest was complexed with metal chelators including diethyl dithiocarbamate (DDTC), ammonium pyrrolidine dithiocarbamate (APDC) or diphenylthiocarbazone (dithizone) in ammonia-citrate buffer and extracted with methyl isobutyl ketone (MIBK). The resulting solution then was analyzed by flame AAS or graphite-furnace AAS forcadmium determinations using deuterium-lamp background correction.

In the late 1970s, researchers began developing simpler preparation procedures. Roels et al. (1978) and Roberts and Clark (1986) developed simplified digestion procedures. Using the Roberts and Clark method, a 0.5 ml aliquot of blood is collected and transferred to a digestion tube containing 1 ml concentrated HNO_3. The blood is then digested at 110 °C for 4 hours. The sample is reduced in volume by continued heating, and 0.5 ml 30% H_2O_2 is added as the sample dries. The residue is dissolved in 5 ml dilute (1%) HNO_3, and 20 µl of sample is then analyzed by graphite-furnace AAS with deuterium-background correction.

The current trend in the preparation of blood samples is to dilute the sample and add matrix modifiers to reduce background interference, rather than digesting the sample to reduce organic content. The method of Stoeppler and Brandt (1980), and the abbreviated procedure published in the American Public Health Association's (APHA) *Methods for Biological Monitoring* (1988), are straightforward and are nearly identical. For the APHA method, a small aliquot (50–300 µl) of whole blood that has been stabilized with ethylenediaminetetraacetate (EDTA) is added to 1.0 ml 1MHNO_3, vigorously shaken and centrifuged. Aliquots (10–25 µl) of the supernatant then are then analyzed by graphite-furnace AAS with appropriate background correction.

Using the method of Stoeppler and Brandt (1980), aliquots (50–200 µl) of whole blood that have been stabilized with EDTA are pipetted into clean polystyrene tubes and mixed with 150-600 µl of 1 M HNO_3. After vigorous shaking, the solution is centrifuged and a 10–25 µl aliquot of the supernatant then is analyzed by graphite-furnace AAS with appropriate background correction.

Claeys-Thoreau (1982) and DeBenzo et al. (1990) diluted blood samples at a ratio of 1:10 with a matrix modifier (0.2% Triton X–100, a wetting agent) for direct determinations of CDB. DeBenzo et al. also demonstrated that aqueous standards of cadmium, instead of spiked, whole-blood samples, could be used to establish calibration curves if standards and samples are treated with additional small volumes of matrix modifiers (i.e., 1% HNO_3, 0.2% ammonium hydrogenphosphate and 1 mg/ml magnesium salts).

These direct dilution procedures for CDB analysis are simple and rapid. Laboratories can process more than 100 samples a day using a dedicated graphite-furnace AAS, an auto-sampler, and either a Zeeman- or a deuterium-background correction system. Several authors emphasize using optimum settings for graphite-furnace temperatures during the drying, charring, and atomization processes associated with the flameless AAS method, and the need to run frequent QC samples when performing automated analysis.

5.1.3 Sample Collection and Handling

Sample collection procedures are addressed primarily to identify ways to minimize the degree of variability that may be introduced by sample collection during medical monitoring. It is unclear at this point the extent to which collection procedures contribute to variability among CDB samples. Sources of variation that may result from sampling procedures include time-of-day effects and introduction of external contamination during the collection process. To minimize these sources, strict adherence to a sample collection protocol is recommended. Such a protocol must include provisions for thorough cleaning of the site from which blood will be extracted; also, every effort should be made to collect samples near the same time of day. It is also important to recognize that under the recent OSHA blood-borne pathogens standard (29 CFR 1910.1030), blood samples and certain body fluids must be handled and treated as if they are infectious.

5.1.4 Best Achievable Performance

The best achievable performance using a particular method for CDB determinations is assumed to be equivalent to the performance reported by research laboratories in which the method was developed.

For their method, Roberts and Clark (1986) demonstrated a limit of detection of 0.4 µg Cd/l in whole blood, with a linear response curve from 0.4 to 16.0 µg Cd/l. They report a coefficient of variation (CV) of 6.7% at 8.0 µg/l.

The APHA (1988) reports a range of 1.0–25 µg/l, with a CV of 7.3% (concentration not stated). Insufficient documentation was available to critique this method.

Stoeppler and Brandt (1980) achieved a detection limit of 0.2 µg Cd/l whole blood, with a linear range of 0.4–12.0 µg Cd/l, and a CV of 15–30%, for samples at <1.0 µg/l. Improved precision (CV of 3.8%) was reported for CDB concentrations at 9.3 µg/l.

5.1.5 General Method Performance

For any particular method, the performance expected from commercial laboratories may be somewhat lower than that reported by the research laboratory in which the method was developed. With participation in appropriate proficiency programs and use of a proper in-house QA/QC program incorporating provisions for regular corrective actions, the performance of commercial laboratories is expected to approach that reported by research laboratories. Also, the results reported for existing proficiency programs serve as a gauge of the likely level of performance that currently can be expected from commercial laboratories offering these analyses.

Weber (1988) reports on the results of the proficiency program run by the Centre de Toxicologie du Quebec (CTQ). As indicated previously, participants in that program receive 1β blood samples per year having cadmium concentrations ranging from 0.2–20 µg/l. Currently, 76 laboratories are participating in this program. The program is established for several analytes in addition to cadmium, and not all of these laboratories participate in the cadmium proficiency-testing program.

Under the CTQ program, cadmium results from individual laboratories are compared against the consensus mean derived for each sample. Results indicate that after receiving 60 samples (i.e., after participation for approximately three years), 60% of the laboratories in the program are able to report results that fall within ±1 µg/l or 15% of the mean, whichever is greater. (For this procedure, the 15% criterion was applied to concentrations exceeding 7 µg/l.) On any single sample of the last 20 samples, the percentage of laboratories falling within the specified range is between 55 and 80%.

The CTQ also evaluates the performance of participating laboratories against a less severe standard: ±2 µg/l or 15% of the mean, whichever is greater (Weber 1988); 90% of participating laboratories are able to satisfy this standard after approximately 3 years in the program. (The 15% criterion is used for concentrations in excess of 13 µg/l.) On any single sample of the last 15 samples, the

percentage of laboratories falling within the specified range is between 80 and 95% (except for a single test for which only 60% of the laboratories achieved the desired performance).

Based on the data presented in Weber (1988), the CV for analysis of CDB is nearly constant at 20% for cadmium concentrations exceeding 5 μg/l, and increases for cadmium concentrations below 5 μg/l. At 2 μg/l, the reported CV rises to approximately 40%. At 1 μg/l, the reported CV is approximately 60%.

Participating laboratories also tend to overestimate concentrations for samples exhibiting concentrations less than 2 μg/l (see Figure 11 of Weber 1988). This problem is due in part to the proficiency evaluation criterion that allows reporting a minimum ±2.0 μg/l for evaluated CDB samples. There is currently little economic or regulatory incentive for laboratories participating in the CTQ program to achieve greater accuracy for CDB samples containing cadmium at concentrations less than 2.0 μg/l, even if the laboratory has the experience and competency to distinguish among lower concentrations in the samples obtained from the CTQ.

The collective experience of international agencies and investigators demonstrate the need for a vigorous QC program to ensure that CDB values reported by participating laboratories are indeed reasonably accurate. As Friberg (1988) stated:

"Information about the quality of published data has often been lacking. This is of concern as assessment of metals in trace concentrations in biological media are fraught with difficulties from the collection, handling, and storage of samples to the chemical analyses. This has been proven over and over again from the results of interlaboratory testing and quality control exercises. Large variations in results were reported even from 'experienced' laboratories."

The UNEP/WHO global study of cadmium biological monitoring set a limit for CDB accuracy using the maximum allowable deviation method at $Y=X\pm(0.1X+1)$ for a targeted concentration of 10 μg Cd/l (Friberg and Vahter 1983). The performance of participating laboratories over a concentration range of 1.5–12 μg/l was reported by Lind et al. (1987). Of the 3 QC runs conducted during 1982 and 1983, 1 or 2 of the 6 laboratories failed each run. For the years 1983 and 1985, between zero and 2 laboratories failed each of the consecutive QC runs.

In another study (Vahter and Friberg 1988), QC samples consisting of both external (unknown) and internal (stated) concentrations were distributed to laboratories participating in the epidemiology research. In this study, the maximum acceptable deviation between the regression analysis of reported results and reference values was set at $Y=X\pm(0.05X+0.2)$ for a concentration range of 0.3–5.0 μg Cd/l. It is reported that only 2 of 5 laboratories had acceptable data after the first QC set, and only 1 of 5 laboratories had acceptable data after the second QC set. By the fourth QC set, however, all 5 laboratories were judged proficient.

The need for high quality CDB monitoring is apparent when the toxicological and biological characteristics of this metal are considered; an increase in CDB from 2 to 4 μg/l could cause a doubling of the cadmium accumulation in the kidney, a critical target tissue for selective cadmium accumulation (Nordberg and Nordberg 1988).

Historically, the CDC's internal QC program for CDB cadmium monitoring program has found achievable accuracy to be ±≥10% of the true value at CDB concentrations ≥5.0 μg/l (Paschal 1990). Data on the performance of laboratories participating in this program currently are not available.

5.1.6 Observed CDB Concentrations

As stated in Section 4.3, CDB concentrations are representative of ongoing levels of exposure to cadmium. Among those who have been exposed chronically to cadmium for extended periods, however, CDB may contain a component attributable to the general cadmium body burden.

5.1.6.1 *CDB Concentrations Among Unexposed Samples*

Numerous studies have been conducted examining CDB concentrations in the general population, and in control groups used for comparison with cadmium-exposed workers. A number of reports have been published that present erroneously high values of CDB (Nordberg and Nordberg 1988). This problem was due to contamination of samples during sampling and analysis, and to errors in analysis. Early AAS methods were not sufficiently sensitive to accurately estimate CDB concentrations.

Table 4 presents results of recent studies reporting CDB levels for the general U.S. population not exposed occupationally to cadmium. Other surveys of tissue cadmium using U.S. samples and conducted as part of a cooperative effort among Japan, Sweden and the U.S., did not collect CDB data because standard analytical methodologies were unavailable, and because of analytic problems (Kjellstrom 1979; SWRI 1978).

TABLE 4.—BLOOD CADMIUM CONCENTRATIONS OF U.S. POPULATION NOT OCCUPATIONALLY EXPOSED TO CADMIUM [a]

Study No.	No. in study (n)	Sex	Age	Smoking habits [b]	Arithmetic mean (±S.D.) [c]	Absolute range or (95% CI) [d]	Geometric mean (±GSD) [e]	Lower 95th percentile of distribution [f]	Upper 95th percentile of distribution [f]	Reference
1	60	M	4 to 69	NS,S	1.13	0.35–3.3	0.98±1.71	0.4	2.4	Kowal et al. (1979).
	68	F	4 to 69	NS,S	1.03	0.21–3.3	0.91±1.63	0.4	2.0	
	115	M/F	4 to 69	NS	0.95	0.21–3.3	0.85±1.59	0.4	1.8	
	31	M/F	4 to 69	S	1.54	0.4–3.3	1.37±1.65	0.6	3.2	
2	10	M	Adults	(?)	2.0±2.1	(0.5–5.0)		[g] (0)	[g] (5.8)	Ellis et al. (1983).
3	24	M	Adults	NS			0.6±1/87	0.2	1.8	Frieberg and Vahter (1983).
	20	M	Adults	S			1.2±2.13	0.3	4.4	
	64	F	Adults	NS			0.5±1.85	0.2	1.4	
	39	F	Adults	S			0.8±2.22	0.2	3.1	
4	32	M	Adults	S,NS			1.2±2.0	0.4	3.9	Thun et al. (1989).
5	35	M	Adults	(?)	2.1±2.1	(0.5–7.3)		[g] (0)	[g] (5.6)	Mueller et al. (1989).

Arithmetic and/or geometric means and standard deviations are provided in Table 4 for measurements among the populations defined in each study listed. The range of reported measurements and/or the 95% upper and lower confidence intervals for the means are presented when this information was reported in a study. For studies reporting either an arithmetic or geometric standard deviation along with a mean, the lower and upper 95th percentile for the distribution also were derived and reported in the table.

The data provided in Table 4 from Kowal et al. (1979) are from studies conducted between 1974 and 1976 evaluating CDB levels for the general population in Chicago, and are considered to be representative of the U.S. population. These studies indicate that the average CDB concentration among those not occupationally exposed to cadmium is approximately 1 μg/l.

In several other studies presented in Table 4, measurements are reported separately for males and females, and for smokers and nonsmokers. The data in this table indicate that similar CDB levels are observed among males and females in the general population, but that smokers tend to exhibit higher CDB levels than nonsmokers. Based on the Kowal et al. (1979) study, smokers not occupationally exposed to cadmium exhibit an average CDB level of 1.4 μg/l.

In general, nonsmokers tend to exhibit levels ranging to 2 μg/l, while levels observed among smokers range to 5 μg/l. Based on the data presented in Table 4, 95% of those not occupationally exposed to cadmium exhibit CDB levels less than 5 μg/l.

5.1.6.2 CDB *Concentrations Among Exposed Workers*

Table 5 is a summary of results from studies reporting CDB levels among workers exposed to cadmium in the work place. As in Table 4, arithmetic and/or geometric means and standard deviations are provided if reported in the listed studies. The absolute range, or the 95% confidence interval around the mean, of the data in each study are provided when reported. In addition, the lower and upper 95th percentile of the distribution are presented for each study in which a mean and corresponding standard deviation were reported. Table 5 also provides estimates of the duration, and level, of exposure to cadmium in the work place if these data were reported in the listed studies. The data presented in Table 5 suggest that CDB levels are dose related. Sukuri et al. (1983) show that higher CDB levels are observed among workers experiencing higher work place exposure. This trend appears to be true of every one of the studies listed in the table.

CDB levels reported in Table 5 are higher among those showing signs of cadmium-related kidney damage than those showing no such damage. Lauwerys et al. (1976) report CDB levels among workers with kidney lesions that generally are above the levels reported for workers without kidney lesions. Ellis et al. (1983) report a similar observation comparing workers with and without renal dysfunction, although they found more overlap between the 2 groups than Lauwerys et al.

TABLE 5.—BLOOD CADMIUM IN WORKERS EXPOSED TO CADMIUM IN THE WORKPLACE

Study number	Work environment (worker population monitored)	Number in study	Employment in years (mean)	Mean concentration of cadmium in air (μg/m³)	Concentrations of Cadmium in blood[a]					Reference
					Arithmetic mean (±S.D.)[b]	Absolute range or (95% C.I.)[c]	Geometric mean (±GSD)[d]	Lower 95th percentile of range[e] ( )[f]	Upper 95th percentile of range[e] ( )[f]	
1	Ni-Cd battery plant and Cd production plant:		3–40	<90						Lauwerys et al. 1976.
	(Workers without kidney lesions).	96			21.4±1.9			(18)	(25)	
	(Workers with kidney lesions).	25			38.8±3.8			(32)	(45)	
2	Ni-Cd battery plant:									Adamsson et al. (1979).
	(Smokers)	7	(5)	10.1	22.7	7.3–67.2				
	(Nonsmokers).	8	(9)	7.0	7.0	4.9–10.5				
3	Cadmium alloy plant:									Sukuri et al. 1982.
	(High exposure group).	7	(10.6)	[1,000–5 yrs;	20.8±7.1			(7.3)	(34)	
	(Low exposure group).	9	(7.3)	40–5 yrs]	7.1±1.1			(5.1)	(9.1)	
4	Retrospective study of workers with renal problems:	19	15–41							Roels et al. 1982.
	(Before removal).		(27.2)		39.9±3.7	11–179		(34)	(46)	
	(After removal).		[g](4.2)		14.1±5.6	5.7–27.4		(4.4)	(24)	
5	Cadmium production plant:									Ellis et al. 1983.
	(Workers without renal dysfunction).	33	1–34		15±5.7	7–31		(5.4)	(25)	
	(Workers with renal dysfunction).	18	10–34		24±8.5	10–34		(9.3)	(39)	
6	Cd-Cu alloy plant.	75	Up to 39				8.8±1.1	7.5	10	Mason et al. 1988.

TABLE 5.—BLOOD CADMIUM IN WORKERS EXPOSED TO CADMIUM IN THE WORKPLACE—Continued

Study number	Work environment (worker population monitored)	Number in study	Employment in years (mean)	Mean concentration of cadmium in air (μg/m³)	Concentrations of Cadmium in blood[a]					Reference
					Arithmetic mean (±S.D.)[b]	Absolute range or (95% C.I.)[c]	Geometric mean (±GSD)[d]	Lower 95th percentile of range[e] ( )[f]	Upper 95th percentile of range[e] ( )[f]	
7	Cadmium recovery operation—Current (19) and former (26) workers.	45	(19.0)				7.9±2.0	2.5	25	Thun et al. 1989.
8	Cadmium recovery operation	40			10.2±5.3	2.2–18.8		(1.3)	(19)	Mueller et al. 1989.

The data in Table 5 also indicate that CDB levels are higher among those experiencing current occupational exposure than those who have been removed from such exposure. Roels et al. (1982) indicate that CDB levels observed among workers experiencing ongoing exposure in the work place are almost entirely above levels observed among workers removed from such exposure. This finding suggests that CDB levels decrease once cadmium exposure has ceased.

A comparison of the data presented in Tables 4 and 5 indicates that CDB levels observed among cadmium-exposed workers is significantly higher than levels observed among the unexposed groups. With the exception of 2 studies presented in Table 5 (1 of which includes former workers in the sample group tested), the lower 95th percentile for CDB levels among exposed workers are greater than 5 μg/l, which is the value of the upper 95th percentile for CDB levels observed among those who are not occupationally exposed. Therefore, a CDB level of 5 μg/l represents a threshold above which significant work place exposure to cadmium may be occurring.

5.1.7 Conclusions and Recommendations for CDB

Based on the above evaluation, the following recommendations are made for a CDB proficiency program.

5.1.7.1 *Recommended Method*

The method of Stoeppler and Brandt (1980) should be adopted for analyzing CDB. This method was selected over other methods for its straightforward sample-preparation procedures, and because limitations of the method were described adequately. It also is the method used by a plurality of laboratories currently participating in the CTQ proficiency program. In a recent CTQ interlaboratory comparison report (CTQ 1991), analysis of the methods used by laboratories to measure CDB indicates that 46% (11 of 24) of the participating laboratories used the Stoeppler and Brandt methodology (HNO_3 deproteinization of blood followed by analysis of the supernatant by GF-AAS). Other CDB methods employed by participating laboratories identified in the CTQ report include dilution of blood (29%), acid digestion (12%) and miscellaneous methods (12%).

Laboratories may adopt alternate methods, but it is the responsibility of the laboratory to demonstrate that the alternate methods meet the data quality objectives defined for the Stoeppler and Brandt method (see section 5.1.7.2 below).

5.1.7.2 *Data Quality Objectives*

Based on the above evaluation, the following data quality objectives (DQOs) should facilitate interpretation of analytical results.

Limit of Detection. 0.5 μg/l should be achievable using the Stoeppler and Brandt method. Stoeppler and Brandt (1980) report a limit of detection equivalent to ≤0.2 μg/l in whole blood using 25 μl aliquots of deproteinized, diluted blood samples.

Accuracy. Initially, some of the laboratories performing CDB measurements may be expected to satisfy criteria similar to the less severe criteria specified by the CTQ program, i.e., measurements within 2 μg/l or 15% (whichever is greater) of the target value. About 60% of the laboratories enrolled in the CTQ program could meet this criterion on the first proficiencey test (Weber 1988).

Currently, approximately 12 laboratories in the CTQ program are achieving an accuracy for CDB analysis within the more severe constraints of ±1 μg/l or 15% (whichever is greater). Later, as laboratories gain experience, they should achieve the level of accuracy exhibited by these 12 laboratories. The experience in the CTQ program has shown that, even without incentives, laboratories benefit from the feedback of the program; after they have analyzed 40–50 control samples from the program, performance improves to the point where about 60% of the laboratories can meet the stricter criterion of ±1 μg/l or 15% (Weber 1988). Thus, this stricter target accuracy is a reasonable DQO.

Precision. Although Stoeppler and Brandt (1980) suggest that a coefficient of variation (CV) near 1.3% (for a 10 μg/l concentration) is achievable for within-run reproducibility, it is recognized that other factors affecting within- and between-run comparability will increase the achievable CV. Stoeppler and Brandt (1980) observed CVs that were as high as 30% for low concentrations (0.4 μg/l), and CVs of less than 5% for higher concentrations.

For internal QC samples (see section 3.3.1), laboratories should to attain an overall precision near 25%. For CDB samples with concentrations less than 2 μg/l, a target precision of 40% is reasonable, while precisions of 20% should be achievable for concentrations greater than 2 μg/l. Although these values are more strict than values observed in the CTQ interlaboratory program reported by Webber (1988), they are within the achievable limits reported by Stoeppler and Brandt (1980).

5.1.7.3 *Quality Assurance/Quality Control*

Commercial laboratories providing measurement of CDB should adopt an internal QA/QC program that incorporates the following components: Strict adherence to the selected method, including all calibration requirements; regular incorporation of QC samples during actual runs; a protocol for corrective actions, and documentation of these actions; and, participation in an interlaboratory proficiency program. Note that the nonmandatory QA/QC program presented in Attachment 3 is based on the Stoeppler and Brandt method for CDB analysis. Should an alternate method be adopted, the laboratory should develop a QA/QC program satisfying the provisions of Section 3.3.1.

5.2 Measuring Cadmium in Urine (CDU)

As in the case of CDB measurement, proper determination of CDU requires strict analytical discipline regarding collection and handling of samples. Because cadmium is both ubiquitous in the environment and employed widely in coloring agents for industrial products that may be used during sample collection, preparation and analysis, care should be exercised to ensure that samples are not contaminated during the sampling procedure.

Methods for CDU determination share many of the same features as those employed for the determination of CDB. Thus, changes and improvements to methods for measuring CDU over the past 40 years parallel those used to monitor CDB. The direction of development has largely been toward the simplification of sample preparation

techniques made possible because of improvements in analytic techniques.

5.2.1 Units of CDU Measurement

Procedures adopted for reporting CDU concentrations are not uniform. In fact, the situation for reporting CDU is more complicated than for CDB, where concentrations are normalized against a unit volume of whole blood.

Concentrations of solutes in urine vary with several biological factors (including the time since last voiding and the volume of liquid consumed over the last few hours); as a result, solute concentrations should be normalized against another characteristic of urine that represents changes in solute concentrations. The 2 most common techniques are either to standardize solute concentrations against the concentration of creatinine, or to standardize solute concentrations against the specific gravity of the urine. Thus, CDU concentrations have been reported in the literature as "uncorrected" concentrations of cadmium per volume of urine (i.e., μg Cd/l urine), "corrected" concentrations of cadmium per volume of urine at a standard specific gravity (i.e., μg Cd/l urine at a specific gravity of 1.020), or "corrected" mass concentration per unit mass of creatinine (i.e., μg Cd/g creatinine). (CDU concentrations [whether uncorrected or corrected for specific gravity, or normalized to creatinine] occasionally are reported in nanomoles [i.e., nmoles] of cadmium per unit mass or volume. In this protocol, these values are converted to μg of cadmium per unit mass or volume using 89 nmoles of cadmium = 10 μg.)

While it is agreed generally that urine values of analytes should be normalized for reporting purposes, some debate exists over what correction method should be used. The medical community has long favored normalization based on creatinine concentration, a common urinary constituent. Creatinine is a normal product of tissue catabolism, is excreted at a uniform rate, and the total amount excreted per day is constant on a day-to-day basis (NIOSH 1984b). While this correction method is accepted widely in Europe, and within some occupational health circles, Kowals (1983) argues that the use of specific gravity [i.e., total solids per unit volume) is more straightforward and practical [than creatinine) in adjusting CDU values for populations that vary by age or gender.

Kowals (1983) found that urinary creatinine (CRTU) is lower in females than males, and also varies with age. Creatinine excretion is highest in younger males (20–30 years old), decreases at middle age (50–60 years), and may rise slightly in later years. Thus, cadmium concentrations may be underestimated for some workers with high CRTU levels.

Within a single void urine collection, urine concentration of any analyte will be affected by recent consumption of large volumes of liquids, and by heavy physical labor in hot environments. The absolute amount of analyte excreted may be identical, but concentrations will vary widely so that urine must be corrected for specific gravity (i.e., to normalize concentrations to the quantity of total solute) using a fixed value (e.g., 1.020 or 1.024). However, since heavy-metal exposure may increase urinary protein excretion, there is a tendency to underestimate cadmium concentrations in samples with high specific gravities when specific-gravity corrections are applied.

Despite some shortcomings, reporting solute concentrations as a function of creatinine concentration is accepted generally; OSHA therefore recommends that CDU levels be reported as the mass of cadmium per unit mass of creatinine (μg/g CTRU).

Reporting CDU as μg/g CRTU requires an additional analytical process beyond the analysis of cadmium: Samples must be analyzed independently for creatinine so that results may be reported as the ratio of cadmium to creatinine concentrations found in the urine sample. Consequently, the overall quality of the analysis depends on the combined performance by a laboratory on these 2 determinations. The analysis used for CDU determinations is addressed below in terms of μg Cd/l, with analysis of creatinine addressed separately. Techniques for assessing creatinine are discussed in Section 5.4.

Techniques for deriving cadmium as a ratio of CRTU, and the confidence limits for independent measurements of cadmium and CRTU, are provided in Section 3.3.3.

5.2.2 Analytical Techniques Used to Monitor CDU

Analytical techniques used for CDU determinations are similar to those employed for CDB determinations; these techniques are summarized in Table 3. As with CDB monitoring, the technique most suitable for CDU determinations is atomic absorption spectroscopy (AAS). AAS methods used for CDU determinations typically employ a graphite furnace, with background correction made using either the deuterium-lamp or Zeeman techniques; Section 5.1.1 provides a detailed description of AAS methods.

5.2.3 Methods Developed for CDU Determinations

Princi (1947), Smith et al. (1955), Smith and Kench (1957), and Tsuchiya (1967) used colorimetric procedures similar to those described in the CDB section above to estimate CDU concentrations. In these methods, urine (50 ml) is reduced to dryness by heating in a sand bath and digested (wet ashed) with mineral acids. Cadmium then is complexed with dithiazone, extracted with chloroform and quantified by spectrophotometry. These early studies typically report reagent blank values equivalent to 0.3 μg Cd/l, and CDU concentrations among nonexposed control groups at maximum levels of 10 μg Cd/l—erroneously high values when compared to more recent surveys of cadmium concentrations in the general population.

By the mid-1970s, most analytical procedures for CDU analysis used either wet ashing (mineral acid) or high temperatures [>400 °C) to digest the organic matrix of urine, followed by cadmium chelation with APDC or DDTC solutions and extraction with MIBK. The resulting aliquots were analyzed by flame or graphite-furnace AAS (Kjellstrom 1979).

Improvements in control over temperature parameters with electrothermal heating devices used in conjunction with flameless AAS techniques, and optimization of temperature programs for controlling the drying, charring, and atomization processes in sample analyses, led to improved analytical detection of diluted urine samples without the need for sample digestion or ashing. Roels et al. (1978) successfully used a simple sample preparation, dilution of 1.0 ml aliquots of urine with 0.1 N HNO_3, to achieve accurate low-level determinations of CDU.

In the method described by Pruszkowska et al. (1983), which has become the preferred method for CDU analysis, urine samples were diluted at a ratio of 1:5 with water; diammonium hydrogenphosphate in dilute HNO_3 was used as a matrix modifier. The matrix modifier allows for a higher charring temperature without loss of cadmium through volatilization during pre-atomization. This procedure also employs a stabilized temperature platform in a graphite furnace, while nonspecific background absorbtion is corrected using the Zeeman technique. This method allows for an absolute detection limit of approximately 0.04 μg Cd/l urine.

5.2.4 Sample Collection and Handling

Sample collection procedures for CDU may contribute to variability observed among CDU measurements. Sources of variation attendant to sampling include time-of-day, the interval since ingestion of liquids, and the introduction of external contamination during the collection process. Therefore, to minimize contributions from these variables, strict adherence to a sample-collection protocol is recommended. This a protocol should include provisions for normalizing the conditions under which urine is collected. Every effort also should be made to collect samples during the same time of day.

Collection of urine samples from an industrial work force for biological monitoring purposes usually is performed using "spot" (i.e., single-void) urine with the pH of the sample determined immediately. Logistic and sample-integrity problems arise when efforts are made to collect urine over long periods (e.g., 24 hrs). Unless single-void urines are used, there are numerous opportunities for measurement error because of poor control over sample collection, storage and environmental contamination.

To minimize the interval during which sample urine resides in the bladder, the following adaption to the "spot" collection procedure is recommended: The bladder should first be emptied, and then a large glass of water should be consumed; the sample may be collected within an hour after the water is consumed.

5.2.5 Best Achievable Performance

Performance using a particular method for CDU determinations is assumed to be equivalent to the performance reported by the research laboratories in which the method was developed. Pruszkowska et al. (1983) report a detection limit of 0.04 μg/l CDU, with a CV of <4% between 0–5 μg/l. The CDC reports a minimum CDU detection limit of 0.07 μg/l using a modified method based on Pruszkowska et al. (1983). No CV is

stated in this protocol; the protocol contains only rejection criteria for internal QC parameters used during accuracy determinations with known standards (Attachment 8 of exhibit 106 of OSHA docket H057A). Stoeppler and Brandt (1980) report a CDU detection limit of 0.2 μg/l for their methodology.

5.2.6 General Method Performance

For any particular method, the expected initial performance from commercial laboratories may be somewhat lower than that reported by the research laboratory in which the method was developed. With participation in appropriate proficiency programs, and use of a proper in-house QA/QC program incorporating provisions for regular corrective actions, the performance of commercial laboratories may be expected to improve and approach that reported by a research laboratories. The results reported for existing proficiency programs serve to specify the initial level of performance that likely can be expected from commercial laboratories offering analysis using a particular method.

Weber (1988) reports on the results of the CTQ proficiency program, which includes CDU results for laboratories participating in the program. Results indicate that after receiving 60 samples (i.e., after participating in the program for approximately 3 years), approximately 80% of the participating laboratories report CDU results ranging between ±2 μg/l or 15% of the consensus mean, whichever is greater. On any single sample of the last 15 samples, the proportion of laboratories falling within the specified range is between 75 and 95%, except for a single test for which only 60% of the laboratories reported acceptable results. For each of the last 15 samples, approximately 60% of the laboratories reported results within ±1 μg or 15% of the mean, whichever is greater. The range of concentrations included in this set of samples was not reported.

Another report from the CTQ (1991) summarizes preliminary CDU results from their 1991 interlaboratory program. According to the report, for 3 CDU samples with values of 9.0, 16.6, 31.5 μg/l, acceptable results (target ±2 μg/l) were achieved by only 44–52% of the 34 laboratories participating in the CDU program. The overall CVs for these 3 CDU samples among the 34 participating laboratories were 31%, 25%, and 49%, respectively. The reason for this poor performance has not been determined.

A more recent report from the CTQ (Weber, private communication) indicates that 36% of the laboratories in the program have been able to achieve the target of ±1 μg/l or 15% for more than 75% of the samples analyzed over the last 5 years, while 45% of participating laboratories achieved a target of ±2 μg/l or 15% for more than 75% of the samples analyzed over the same period.

Note that results reported in the interlaboratory programs are in terms of μg Cd/l of urine, unadjusted for creatinine. The performance indicated, therefore, is a measure of the performance of the cadmium portion of the analyses, and does not include variation that may be introduced during the analysis of CRTU.

5.2.7 Observed CDU Concentrations

Prior to the onset of renal dysfunction, CDU concentrations provide a general indication of the exposure history (i.e., body burden)(see Section 4.3). Once renal dysfunction occurs, CDU levels appear to increase and are no longer indicative solely of cadmium body burden (Friberg and Elinder 1988).

5.2.7.1 *Range of CDU Concentrations Observed Among Unexposed Samples*

Surveys of CDU concentrations in the general population were first reported from cooperative studies among industrial countries (i.e., Japan, U.S. and Sweden) conducted in the mid-1970s. In summarizing these data, Kjellstrom (1979) reported that CDU concentrations among Dallas, Texas men (age range: <9–59 years; smokers and nonsmokers) varied from 0.11–1.12 μg/l (uncorrected for creatinine or specific gravity). These CDU concentrations are intermediate between population values found in Sweden (range: 0.11–0.80 μg/l) and Japan (range: 0.14–2.32 μg/l).

Kowal and Zirkes (1983) reported CDU concentrations for almost 1,000 samples collected during 1978–79 from the general U.S. adult population (i.e., nine states; both genders; ages 20–74 years). They report that CDU concentrations are lognormally distributed; low levels predominated, but a small proportion of the population exhibited high levels. These investigators transformed the CDU concentrations values, and reported the same data 3 different ways: μg/l urine (unadjusted), μg/l (specific gravity adjusted to 1.020), and μg/g CRTU. These data are summarized in Tables 6 and 7.

Based on further statistical examination of these data, including the lifestyle characteristics of this group, Kowal (1988) suggested increased cadmium absorption (i.e., body burden) was correlated with low dietary intakes of calcium and iron, as well as cigarette smoking.

CDU levels presented in Table 6 are adjusted for age and gender. Results suggest that CDU levels may be slightly different among men and women (i.e., higher among men when values are unadjusted, but lower among men when the values are adjusted, for specific gravity or CRTU). Mean differences among men and women are small compared to the standard deviations, and therefore may not be significant. Levels of CDU also appear to increase with age. The data in Table 6 suggest as well that reporting CDU levels adjusted for specific gravity or as a function of CRTU results in reduced variability.

TABLE 6.—URINE CADMIUM CONCENTRATIONS IN THE U.S. ADULT POPULATION: NORMAL AND CONCENTRATION-ADJUSTED VALUES BY AGE AND SEX [1]

	Geometric means (and geometric standard deviations)		
	Unadjusted (μg/l)	SG-adjusted [2] (μg/l at 1.020)	Creatine-adjusted (μg/g)
Sex:			
Male (n=484)	0.55 (2.9)	0.73 (2.6)	0.55 (2.7)
Female (n=498)	0.49 (3.0)	0.86 (2.7)	0.78 (2.7)
Age:			
20–29 (n=222)	0.32 (3.0)	0.43 (2.7)	0.32 (2.7)
30–39 (n=141)	0.46 (3.2)	0.70 (2.8)	0.54 (2.7)
40–49 (n=142)	0.50 (3.0)	0.81 (2.6)	0.70 (2.7)
50–59 (n=117)	0.61 (2.9)	0.99 (2.4)	0.90 (2.3)
60–69 (n=272)	0.76 (2.6)	1.16 (2.3)	1.03 (2.3)

[1] From Kowal and Zirkes 1983.
[2] SC-adjusted is adjusted for specific gravity.

TABLE 7.—URINE CADMIUM CONCENTRATIONS IN THE U.S. ADULT POPULATION: CUMULATIVE FREQUENCY DISTRIBUTION OF URINARY CADMIUM (N=982) [1]

[In percentage]

Range of concentrations	Unadjusted (μg/l)	SG-adjusted (μg/l at 1.020)	Creatine-adjusted (μg/g)
<0.5	43.9	28.0	35.6
0.6–1.0	71.7	56.4	65.6
1.1–1.5	84.4	74.9	81.4
1.6–2.0	91.3	84.7	88.9
2.1–3.0	97.3	94.4	95.8
3.1–4.0	98.8	97.4	97.2
4.1–5.0	99.4	98.2	97.9
5.1–10.0	99.6	99.4	99.3
10.0–20.0	99.8	99.6	99.6

[1] Source: Kowal and Zirkes (1983).

The data in the Table 6 indicate the geometric mean of CDU levels observed among the general population is 0.52 μg Cd/l urine (unadjusted), with a geometric standard deviation of 3.0. Normalized for creatinine, the geometric mean for the population is 0.66 μg/g CRTU, with a geometric standard deviation of 2.7. Table 7 provides the distributions of CDU concentrations for the general population studied by Kowal and Zirkes. The data in this table indicate that 95% of the CDU levels observed among those not occupationally exposed to cadmium are below 3 μg/g CRTU.

5.2.7.2 *Range of CDU Concentrations Observed Among Exposed Workers*

Table 8 is a summary of results from available studies of CDU concentrations observed among cadmium-exposed workers. In this table, arithmetic and/or geometric means and standard deviations are provided if reported in these studies. The absolute range for the data in each study, or the 95% confidence interval around the mean of each study, also are provided when reported. The lower and upper 95th percentile of the distribution are presented for each study in which a mean and corresponding standard deviation were reported. Table 8 also provides estimates of the years of exposure, and the levels of exposure, to cadmium in the work place if reported in these studies. Concentrations reported in this table are in μg/g CRTU, unless otherwise stated.

TABLE 8.—URINE CADMIUM CONCENTRATION'S IN WORKERS EXPOSED TO CADMIUM IN THE WORKPLACE

Study number	Work environment (worker population monitored)	Number in Study (n)	Employment in years (mean)	Mean Concentration of cadmium in air (μg/m³)	Concentration of cadmium in Urine [a]					Reference
					Arithmetic mean (± S.D.) [b]	Absolute range or (95% C.I.) [c]	Geometric mean (±GSD) [d]	Lower 95th percentile of range [e] ( ) [f]	Upper 95th percentile of range [e] ( ) [f]	
1	Ni-Cd battery plant and Cd production plant.		3–40	≤ 80						Lauwerys et al. 1976.
	(Workers without kidney lesions).	98			16.3±16.7			(0)	(44)	
	(Workers with kidney lesions).	25			48.2±42.6			(0)	(120)	
2	Ni-Cd battery plant.									Adamsson et al. (1979).
	(Smokers)	7	(5)	10.1	5.5	1.0–14.7				
	(Nonsmokers).	8	(9)	7.0	3.8	0.5–9.3				
3	Cadmium salts production facility.	148	(15.4)		15.8	2–150				Butchet et al. 1980.
4	Retrospective study of workers with renal problems.	19	15–41							Roels et al. 1982.
	(Before removal).		(27.2)		39.4±28.1	10.8–117		(0)	(88)	
	(After removal).		(4.2) [g]		16.4±9.0	60–42.3		(1.0)	(32)	
5	Cadmium production plant.									Ellis et al. 1983.

TABLE 8.—URINE CADMIUM CONCENTRATION'S IN WORKERS EXPOSED TO CADMIUM IN THE WORKPLACE—Continued

Study number	Work environment (worker population monitored)	Number in Study (n)	Employment in years (mean)	Mean Concentration of cadmium in air (μg/m³)	Concentration of cadmium in Urine [a]					
					Arithmetic mean (± S.D.) [b]	Absolute range or (95% C.I.) [c]	Geometric mean (±GSD) [d]	Lower 95th percentile of range [e] ( ) [f]	Upper 95th percentile of range [e] ( ) [f]	Reference
	(Workers without renal dysfunction).	33	1–34		9.4±6.9	2-27		(0)	(21)	
	(Workers with renal dysfunction).	18	10–34		22.8±12.7	8–55		(1)	(45)	
6	Cd-Cu alloy plant.	75	Up to 39	Note h	6.9±9.4			(0)	(23)	Mason et al. 1988.
7	Cadmium recovery operation.	45	(19)	87	9.3±6.9			(0)	(21)	Thun et al. 1989.
8	Pigment manufacturing plant.	29	(12.8)	0.16–3.0		0.2–9.5	1.1			Mueller et al. 1989.
9	Pigment manufacturing plant.	26	(12.1)	≤3.0			1.25±2.45	0.3	6	Kawada et al. 1990.

Data in Table 8 from Lauwerys et al. (1978) and Ellis et al. (1983) indicate that CDU concentrations are higher among those exhibiting kidney lesions or dysfunction than among those lacking these symptoms. Data from the study by Roels et al. (1982) indicate that CDU levels decrease among workers removed from occupational exposure to cadmium in comparison to workers experiencing ongoing exposure. In both cases, however, the distinction between the 2 groups is not as clear as with CDB; there is more overlap in CDU levels observed among each of the paired populations than is true for corresponding CDB levels. As with CDB levels, the data in Table 8 suggest increased CDU concentrations among workers who experienced increased overall exposure.

Although a few occupationally-exposed workers in the studies presented in Table 8 exhibit CDU levels below 3 μg/g CRTU, most of those workers exposed to cadmium levels in excess of the PEL defined in the final cadmium rule exhibit CDU levels above 3 μg/g CRTU; this level represents the upper 95th percentile of the CDU distribution observed among those who are not occupationally exposed to cadmium (Table 7).

The mean CDU levels reported in Table 8 among occupationally-exposed groups studied (except 2) exceed 3 μg/g CRTU. Correspondingly, the level of exposure reported in these studies (with 1 exception) are significantly higher than what workers will experience under the final cadmium rule. The 2 exceptions are from the studies by Mueller et al. (1989) and Kawada et al. (1990); these studies indicate that workers exposed to cadmium during pigment manufacture do not exhibit CDU levels as high as those levels observed among workers exposed to cadmium in other occupations. Exposure levels, however, were lower in the pigment manufacturing plants studied. Significantly, workers removed from occupational cadmium exposure for an average of 4 years still exhibited CDU levels in excess of 3 μg/g CRTU (Roels et al. 1982). In the single-exception study with a reported level of cadmium exposure lower than levels proposed in the final rule (i.e., the study of a pigment manufacturing plant by Kawada et al. 1990), most of the workers exhibited CDU levels less than 3 μg/g CRTU (i.e., the mean value was only 1.3 μg/g CRTU). CDU levels among workers with such limited cadmium exposure are expected to be significantly lower than levels reported on Table 8.

Based on the above data, a CDU level of 3 μg/g CRTU appear to represent a threshold above which significant work place exposure to cadmium occurs over the work span of those being monitored. Note that this threshold is not as distinct as the corresponding threshold described for CDB. In general, the variability associated with CDU measurements among exposed workers appears to be higher than the variability associated with CDB measurements among similar workers.

5.2.8 Conclusions and Recommendations for CDU

The above evaluation supports the following recommendations for a CDU proficiency program. These recommendations address only sampling and analysis procedures for CDU determinations specifically, which are to be reported as an unadjusted μg Cd/l urine. Normalizing this result to creatinine requires a second analysis for CRTU so that the ratio of the 2 measurements can be obtained. Creatinine analysis is addressed in Section 5.4. Formal procedures for combining the 2 measurements to derive a value and a confidence limit for CDU in μg/g CRTU are provided in Section 3.3.3.

5.2.8.1 *Recommended Method*

The method of Pruszkowska et al. (1983) should be adopted for CDU analysis. This method is recommended because it is simple, straightforward and reliable (i.e., small variations in experimental conditions do not affect the analytical results).

A synopsis of the methods used by laboratories to determine CDU under the interlaboratory program administered by the CTQ (1991) indicates that more than 78% (24 of 31) of the participating laboratories use a dilution method to prepare urine samples for CDU analysis. Laboratories may adopt alternate methods, but it is the responsibility of the laboratory to demonstrate that the alternate methods provide results of comparable quality to the Pruszkowska method.

5.2.8.2 *Data Quality Objectives*

The following data quality objectives should facilitate interpretation of analytical results, and are achievable based on the above evaluation.

Limit of Detection. A level of 0.5 μg/l (i.e., corresponding to a detection limit of 0.5 μg/g CRTU, assuming 1 g CRT/l urine) should be achievable. Pruszkowska et al. (1983) achieved a limit of detection of 0.04 μg/l for CDU based on the slope the the curve for their working standards (0.35 pg Cd/0.0044. A signal=1% absorbance using GF-AAS).

The CDC reports a minimum detection limit for CDU of 0.07 μg/l using a modified Pruszkowska method. This limit of detection was defined as 3 times the standard deviation calculated from 10 repeated measurements of a "low level" CDU test sample (Attachment 8 of exhibit 108 of OSHA docket H057A).

Stoeppler and Brandt (1980) report a limit of detection for CDU of 0.2 μg/l using an aqueous dilution (1:2) of the urine samples.

Accuracy. A recent report from the CTQ (Weber, private communication) indicates that 36% of the laboratories in the program achieve the target of ±1 μg/l or 15% for more

than 75% of the samples analyzed over the last 5 years, while 45% of participating laboratories achieve a target of ±2 μg/l or 15% for more than 75% of the samples analyzed over the same period. With time and a strong incentive for improvement, it is expected that the proportion of laboratories successfully achieving the stricter level of accuracy should increase. It should be noted, however, these indices of performance do not include variations resulting from the ancillary measurement of CRTU (which is recommended for the proper recording of results). The low cadmium levels expected to be measured indicate that the analysis of creatinine will contribute relatively little to the overall variability observed among creatinine-normalized CDU levels (see Section 5.4). The initial target value for reporting CDU under this program, therefore, is set at ±1 μg/g CRTU or 15% (whichever is greater).

Precision. For internal QC samples (which are recommended as part of an internal QA/QC program, Section 3.3.1), laboratories should attain an overall precision of 25%. For CDB samples with concentrations less than 2 μg/l, a target precision of 40% is, while precisions of 20% should be achievable for CDU concentrations greater than 2 μg/l. Although these values are more stringent than those observed in the CTQ interlaboratory program reported by Webber (1988), they are well within limits expected to be achievable for the method as reported by Stoeppler and Brandt (1980).

5.2.8.3 *Quality Assurance/Quality Control*

Commercial laboratories providing CDU determinations should adopt an internal QA/QC program that incorporates the following components: Strict adherence to the selected method, including calibration requirements; regular incorporation of QC samples during actual runs; a protocol for corrective actions, and documentation of such actions; and, participation in an interlaboratory proficiency program. Note that the nonmandatory program presented in Attachment 1 as an example of an acceptable QA/QC program, is based on using the Pruszkowska method for CDU analysis. Should an alternate method be adopted by a laboratory, the laboratory should develop a QA/QC program equivalent to the nonmandatory program, and which satisfies the provisions of Section 3.3.1.

5.3 Monitoring β-2-Microglobulin in Urine (B2MU).

As indicated in Section 4.3, B2MU appears to be the best of several small proteins that may be monitored as early indicators of cadmium-induced renal damage. Several analytic techniques are available for measuring B2M.

5.3.1 Units of B2MU Measurement

Procedures adopted for reporting B2MU levels are not uniform. In these guidelines, OSHA recommends that B2MU levels be reported as μg/g CRTU, similar to reporting CDU concentrations. Reporting B2MU normalized to the concentration of CRTU requires an additional analytical process beyond the analysis of B2M: Independent analysis for creatinine so that results may be reported as a ratio of the B2M and creatinine concentrations found in the urine sample. Consequently, the overall quality of the analysis depends on the combined performance on these 2 analyses. The analysis used for B2MU determinations is described in terms of μg B2M/l urine, with analysis of creatinine addressed separately. Techniques used to measure creatinine are provided in Section 5.4. Note that Section 3.3.3 provides techniques for deriving the value of B2M as function of CRTU, and the confidence limits for independent measurements of B2M and CRTU.

5.3.2 Analytical Techniques Used to Monitor B2MU

One of the earliest tests used to measure B2MU was the radial immunodiffusion technique. This technique is a simple and specific method for identification and quantitation of a number of proteins found in human serum and other body fluids when the protein is not readily differentiated by standard electrophoretic procedures. A quantitative relationship exists between the concentration of a protein deposited in a well that is cut into a thin agarose layer containing the corresponding monospecific antiserum, and the distance that the resultant complex diffuses. The wells are filled with an unknown serum and the standard (or control), and incubated in a moist environment at room temperature. After the optimal point of diffusion has been reached, the diameters of the resulting precipition rings are measured. The diameter of a ring is related to the concentration of the constituent substance. For B2MU determinations required in the medical monitoring program, this method requires a process that may be insufficient to concentrate the protein to levels that are required for detection.

Radioimmunoassay (RIA) techniques are used widely in immunologic assays to measure the concentration of antigen or antibody in body-fluid samples. RIA procedures are based on competitive-binding techniques. If antigen concentration is being measured, the principle underlying the procedure is that radioactive-labeled antigen competes with the sample's unlabeled antigen for binding sites on a known amount of immobile antibody. When these 3 components are present in the system, an equilibrium exists. This equilibrium is followed by a separation of the free and bound forms of the antigen. Either free or bound radioactive-labeled antigen can be assessed to determine the amount of antigen in the sample. The analysis is performed by measuring the level of radiation emitted either by the bound complex following removal of the solution containing the free antigen, or by the isolated solution containing the residual-free antigen. The main advantage of the RIA method is the extreme sensitivity of detection for emitted radiation and the corresponding ability to detect trace amounts of antigen. Additionally, large numbers of tests can be performed rapidly.

The enzyme-linked immunosorbent assay (ELISA) techniques are similar to RIA techniques except that nonradioactive labels are employed. This technique is safe, specific and rapid, and is nearly as sensitive as RIA techniques. An enzyme-labeled antigen is used in the immunologic assay; the labeled antigen detects the presence and quantity of unlabeled antigen in the sample. In a representative ELISA test, a plastic plate is coated with antibody (e.g., antibody to B2M). The antibody reacts with antigen (B2M) in the urine and forms an antigen-antibody complex on the plate. A second anti-B2M antibody (i.e., labeled with an enzyme) is added to the mixture and forms an antibody-antigen-antibody complex. Enzyme activity is measured spectrophotometrically after the addition of a specific chromogenic substrate which is activated by the bound enzyme. The results of a typical test are calculated by comparing the spectrophotometric reading of a serum sample to that of a control or reference serum. In general, these procedures are faster and require less laboratory work than other methods.

In a fluorescent ELISA technique (such as the one employed in the Pharmacia Delphia test for B2M), the labeled enzyme is bound to a strong fluorescent dye. In the Pharmacia Delphia test, an antigen bound to a fluorescent dye competes with unlabeled antigen in the sample for a predetermined amount of specific, immobile antibody. Once equilibrium is reached, the immobile phase is removed from the labeled antigen in the sample solution and washed; an enhancement solution then is added that liberates the fluorescent dye from the bound antigen-antibody complex. The enhancement solution also contains a chelate that complexes with the fluorescent dye in solution; this complex increases the fluorescent properties of the dye so that it is easier to detect.

To determine the quantity of B2M in a sample using the Pharmacia Delphia test, the intensity of the fluorescence of the enhancement solution is measured. This intensity is proportional to the concentration of labeled antigen that bound to the immobile antibody phase during the initial competition with unlabeled antigen from the sample. Consequently, the intensity of the fluorescence is an inverse function of the concentration of antigen (B2M) in the original sample. The relationship between the fluorescence level and the B2M concentration in the sample is determined using a series of graded standards, and extrapolating these standards to find the concentration of the unknown sample.

5.3.3 Methods Developed for B2MU Determinations

B2MU usually is measured by radioimmunoassay (RIA) or enzyme-linked immunosorbent assay (ELISA); however, other methods (including gel electrophoresis, radial immunodiffusion, and nephelometric assays) also have been described (Schardun and van Epps 1987). RIA and ELISA methods are preferred because they are sensitive at concentrations as low as micrograms per liter, require no concentration processes, are highly reliable and use only a small sample volume.

Based on a survey of the literature, the ELISA technique is recommended for monitoring B2MU. While RIAs provide greater sensitivity (typically about 1 μg/l, Evrin et al. 1971), they depend on the use of

radioisotopes; use of radioisotopes requires adherence to rules and regulations established by the Atomic Energy Commission, and necessitates an expensive radioactivity counter for testing. Radioisotopes also have a relatively short half-life, which corresponds to a reduced shelf life, thereby increasing the cost and complexity of testing. In contrast, ELISA testing can be performed on routine laboratory spectrophotometers, do not necessitate adherence to additional rules and regulations governing the handling of radioactive substances, and the test kits have long shelf lives. Further, the range of sensitivity commonly achieved by the recommended ELISA test (i.e., the Pharmacia Delphia test) is approximately 100 μg/l (Pharmacia 1990), which is sufficient for monitoring B2MU levels resulting from cadmium exposure. Based on the studies listed in Table 7 (Section 5.3.7), the average range of B2M concentrations among the general, nonexposed population falls between 60 and 300 μg/g CRTU. The upper 95th percentile of distributions, derived from studies in Table 9 which reported standard deviations, range between 180 and 1,140 μg/g CRTU. Also, the Pharmacia Delphia test currently is the most widely used test for assessing B2MU.

5.3.4 Sample Collection and Handling

As with CDB or CDU, sample collection procedures are addressed primarily to identify ways to minimize the degree of variability introduced by sample collection during medical monitoring. It is unclear the extent to which sample collection contributes to B2MU variability. Sources of variation include time-of-day effects, the interval since consuming liquids and the quantity of liquids consumed, and the introduction of external contamination during the collection process. A special problem unique to B2M sampling is the sensitivity of this protein to degradation under acid conditions commonly found in the bladder. To minimize this problem, strict adherence to a sampling protocol is recommended. The protocol should include provisions for normalizing the conditions under which the urine is collected. Clearly, it is important to minimize the interval urine spends in the bladder. It also is recommended that every effort be made to collect samples during the same time of day.

Collection of urine samples for biological monitoring usually is performed using "spot" (i.e., single-void) urine. Logistics and sample integrity become problems when efforts are made to collect urine over extended periods (e.g., 24 hrs). Unless single-void urines are used, numerous opportunities exist for measurement error because of poor control over sample collection, storage and environmental contamination.

To minimize the interval that sample urine resides in the bladder, the following adaption to the "spot" collection procedure is recommended: The bladder should be emptied and then a large glass of water should be consumed; the sample then should be collected within an hour after the water is consumed.

5.3.5 Best Achievable Performance

The best achievable performance is assumed to be equivalent to the performance reported by the manufacturers of the Pharmacia Delphia test kits (Pharmacia 1990). According to the insert that comes with these kits, QC results should be within ±2 SDs of the mean for each control sample tested; a CV of less than or equal to 5.2% should be maintained. The total CV reported for test kits is less than or equal to 7.2%.

5.3.6 General Method Performance

Unlike analyses for CDB and CDU, the Pharmacia Delphia test is standardized in a commercial kit that controls for many sources of variation. In the absence of data to the contrary, it is assumed that the achievable performance reported by the manufacturer of this test kit will serve as an achievable performance objective. The CTQ proficiency testing program for B2MU analysis is expected to use the performance parameters defined by the test kit manufacturer as the basis of the B2MU proficiency testing program.

Note that results reported for the test kit are expressed in terms of μg B2M/l of urine, and have not been adjusted for creatinine. The indicated performance, therefore, is a measure of the performance of the B2M portion of the analyses only, and does not include variation that may have been introduced during the analysis of creatinine.

5.3.7 Observed B2MU Concentrations

As indicated in Section 4.3, the concentration of B2MU may serve as an early indicator of the onset of kidney damage associated with cadmium exposure.

5.3.7.1 *Range of B2MU Concentrations Among Unexposed Samples*

Most of the studies listed in Table 9 report B2MU levels for those who were not occupationally exposed to cadmium. Studies noted in the second column of this table (which contain the footnote "d") reported B2MU concentrations among cadmium-exposed workers who, nonetheless, showed no signs of proteinuria. These latter studies are included in this table because, as indicated in Section 4.3, monitoring B2MU is intended to provide advanced warning of the onset of kidney dysfunction associated with cadmium exposure, rather than to distinguish relative exposure. This table, therefore, indicates the range of B2MU levels observed among those who had no symptoms of renal dysfunction (including workers with none of these symptoms).

TABLE 9.—B-2-MICROGLOBULIN CONCENTRATIONS OBSERVED IN URINE AMONG THOSE NOT OCCUPATIONALLY EXPOSED TO CADMIUM

Study No.	No. in study	Geometric mean	Geometric standard deviation	Lower 95th percentile of distribution [a]	Upper 95th percentile of distribution [a]	Reference
1	133 m [b]	115 μg/g [c]	4.03	12	1,140 μg/g [c]	Ishizaki et al. 1989.
2	161 f [b]	146 μg/g [c]	3.11	23	940 μg/g [c]	Ishizaki et al. 1989.
3	10	84 μg/g				Ellis et al. 1983.
4	203	76 μg/l				Stewart and Hughes 1981.
5	9	103 μg/g				Chia et al. 1989.
6	47 [d]	86 μg/L	1.9	30 μg/l	250 μg/L	Kjellstrom et al. 1977.
7	1,000 [e]	68.1 μg/gr Cr [c]	3.1 m & f	<10 μg/gr Cr [b]	320 μg/gr Cr [b]	Kowal 1983.
8	87	71 μg/g [f]		7 [b]	200 [b]	Buchet et al. 1980.
9	10	0.073 mg/24h				Evrin et al. 1971.
10	59	158 μg/g	1.1 [f]	130	180	Mason et al. 1988.
11	8	118 μg/g				Iwao et al. 1980.
12	34	79 μg/g				Wibowo et al. 1982.
13	41 m				400 μg/gr Cr [b]	Falck et al. 1983.
14	35 [b]	67				Roels et al. 1991.
15	31 [d]	63				Roels et al. 1991.
16	36 [d]	77 [f]				Miksche et al. 1981.
17	18 [b]	130				Kawada et al. 1989.
18	32 [e]	122				Kawada et al. 1989.
19	18 [d]	295	1.4	170	510	Thun et al. 1989.

To the extent possible, the studies listed in Table 9 provide geometric means and geometric standard deviations for measurements among the groups defined in each study. For studies reporting a geometric standard deviation along with a mean, the

lower and upper 95th percentile for these distributions were derived and reported in the table.

The data provided from 15 of the 19 studies listed in Table 9 indicate that the geometric mean concentration of B2M observed among those who were not occupationally exposed to cadmium is 70–170 μg/g CRTU. Data from the 4 remaining studies indicate that exposed workers who exhibit no signs of proteinuria show mean B2MU levels of 60–300 μg/g CRTU. B2MU values in the study by Thun et al. (1989), however, appear high in comparison to the other 3 studies. If this study is removed, B2MU levels for those who are not occupationally exposed to cadmium are similar to B2MU levels found among cadmium-exposed workers who exhibit no signs of kidney dysfunction. Although the mean is high in the study by Thun et al., the range of measurements reported in this study is within the ranges reported for the other studies.

Determining a reasonable upper limit from the range of B2M concentrations observed among those who do not exhibit signs of proteinuria is problematic. Elevated B2MU levels are among the signs used to define the onset of kidney dysfunction. Without access to the raw data from the studies listed in Table 9, it is necessary to rely on reported standard deviations to estimate an upper limit for normal B2MU concentrations (i.e., the upper 95th percentile for the distributions measured). For the 8 studies reporting a geometric standard deviation, the upper 95th percentiles for the distributions are 180–1140 μg/g CRTU. These values are in general agreement with the upper 95th percentile for the distribution (i.e., 631 μg/g CRTU) reported by Buchet et al. (1980). These upper limits also appear to be in general agreement with B2MU values (i.e., 100–690 μg/g CRTU) reported as the normal upper limit by Iwao et al. (1980), Kawada et al. (1989), Wibowo et al. (1982), and Schardun and van Epps (1987). These values must be compared to levels reported among those exhibiting kidney dysfunction to define a threshold level for kidney dysfunction related to cadmium exposure.

5.3.7.2 *Range of B2MU Concentrations Among Exposed Workers*

Table 10 presents results from studies reporting B2MU determinations among those occupationally exposed to cadmium in the work place; in some of these studies, kidney dysfunction was observed among exposed workers, while other studies did not make an effort to distinguish among exposed workers based on kidney dysfunction. As with Table 9, this table provides geometric means and geometric standard deviations for the groups defined in each study if available. For studies reporting a geometric standard deviation along with a mean, the lower and upper 95th percentiles for the distributions are derived and reported in the table.

TABLE 10.—β_2-MICROGLOBULIN CONCENTRATIONS OBSERVED IN URINE AMONG OCCUPATIONALLY-EXPOSED WORKERS

Study number	N	Concentration of β_2-microglobulin in urine				Reference
		Geometric mean (μg/g) [a]	Geom. Std. Dev.	L 95% of range [b]	U 95% of range [b]	
1	1,424	160	6.19	8.1	3,300	Ishizaki et al. 1989.
2	1,754	260	6.50	12	5,600	Ishizaki et al. 1989.
3	33	210				Ellis et al. 1983.
4	65	210				Chia et al. 1989.
5	[c] 44	5,700	6.49	[d] 300	[d] 98,000	Kjellstrom et al. 1977.
6	148	[e] 180		[f] 110	[f] 280	Buchet et al. 1980.
7	37	160	3.90	17	1,500	Kenzaburo et al. 1979.
8	[c] 45	3,300	8.70	[d] 310	[d] 69,000	Mason et al. 1988.
9	[c] 10	6,100	5.99	[f] 650	[f] 57,000	Falck et al. 1983.
10	[c] 11	3,900	2.96	[d] 710	[d] 15,000	Elinder et al. 1985.
11	[c] 12	300				Roels et al. 1991.
12	[g] 8	7,400				Roels et al. 1991.
13	[c] 23	[h] 1,800				Roels et al. 1989.
14	10	690				Iwao et al. 1980.
15	34	71				Wibowo et al. 1982.
16	[c] 15	4,700	6.49	[d] 590	[d] 93,000	Thun et al. 1989.

[a] Unless otherwise stated.
[b] Based on an assumed lognormal distribution.
[c] Among workers diagnosed as having renal dysfunction; for Elinder this means β_2 levels greater than 300 micrograms per gram creatinine (μg/gr Cr); for Roels, 1991, range=31–35, 170 μgβ_2/gr Cr and geometric mean=63 among healthy workers; for Mason β_2>300 μg/gr Cr.
[d] Based on a detailed review of the data by OSHA.
[e] Arithmetic mean.
[f] Reported in the study.
[g] Retired workers.
[h] 1,800 μgβ_2/gr Cr for first survey; second survey=1,600; third survey=2,600; fourth survey=2,600; fifth survey=2,600.

The data provided in Table 10 indicate that the mean B2MU concentration observed among workers experiencing occupational exposure to cadmium (but with undefined levels of proteinuria) is 160–7400 μg/g CRTU. One of these studies reports geometric means lower than this range (i.e., as low as 71 μg/g CRTU); an explanation for this wide spread in average concentrations is not available.

Seven of the studies listed in Table 10 report a range of B2MU levels among those diagnosed as having renal dysfunction. As indicated in this table, renal dysfunction (proteinuria) is defined in several of these studies by B2MU levels in excess of 300 μg/g CRTU (see footnote "c" of Table 10); therefore, the range of B2MU levels observed in these studies is a function of the operational definition used to identify those with renal dysfunction. Nevertheless, a B2MU level of 300 μg/g CRTU appears to be a meaningful threshold for identifying those having early signs of kidney damage. While levels much higher than 300 μg/g CRTU have been observed among those with renal dysfunction, the vast majority of those not occupationally exposed to cadmium exhibit much lower B2MU concentrations (see Table 9). Similarly, the vast majority of workers not exhibiting renal dysfunction are found to have levels below 300 μg/g CRTU (Table 9).

The 300 μg/g CRTU level for B2MU proposed in the above paragraph has support among researchers as the threshold level that distinguishes between cadmium-exposed workers with and without kidney dysfunction. For example, in the guide for physicians who must evaluate cadmium-exposed workers written for the Cadmium Council by Dr. Lauwerys, levels of B2M greater than 200–300 μg/g CRTU are considered to require additional medical evaluation for kidney dysfunction (exhibit 8–447, OSHA docket H057A). The most widely used test for measuring B2M (i.e., the Pharmacia Delphia test) defines B2MU levels above 300 μg/l as abnormal (exhibit L–140–1, OSHA docket H057A).

Dr. Elinder, chairman of the Department of Nephrology at the Karolinska Institute, testified at the hearings on the proposed cadmium rule. According to Dr. Elinder (exhibit L–140–45, OSHA docket H057A), the normal concentration of B2MU has been well documented (Evrin and Wibell 1972; Kjellstrom et al. 1977a; Elinder et al. 1978, 1983; Buchet et al. 1980; Jawaid et al. 1983; Kowal and Zirkes, 1983). Elinder stated that the upper 95 or 97.5 percentiles for B2MU among those without tubular dysfunction is below 300 μg/g CRTU (Kjellstrom et al. 1977a; Buchet et al. 1980; Kowal and Zirkes,

1983). Elinder defined levels of B2M above 300 μg/g CRTU as "slight" proteinuria.

5.3.8 *Conclusions and Recommendations for B2MU*

Based on the above evaluation, the following recommendations are made for a B2MU proficiency testing program. Note that the following discussion addresses only sampling and analysis for B2MU determinations (i.e., to be reported as an unadjusted μg B2M/l urine). Normalizing this result to creatinine requires a second analysis for CRTU (see section 5.4) so that the ratio of the 2 measurements can be obtained.

5.3.8.1 *Recommended Method*

The Pharmacia Delphia method (Pharmacia 1990) should be adopted as the standard method for B2MU determinations. Laboratories may adopt alternate methods, but it is the responsibility of the laboratory to demonstrate that alternate methods provide results of comparable quality to the Pharmacia Delphia method.

5.3.8.2 *Data Quality Objectives*

The following data quality objectives should facilitate interpretation of analytical results, and should be achievable based on the above evaluation.

Limit of Detection. A limit of 100 μg/l urine should be achievable, although the insert to the test kit (Pharmacia 1990) cites a detection limit of 150 μg/l; private conversations with representatives of Pharmacia, however, indicate that the lower limit of 100 μg/l should be achievable provided an additional standard of 100 μg/l B2M is run with the other standards to derive the calibration curve (section 3.3.1.1). The lower detection limit is desirable due to the proximity of this detection limit to B2MU values defined for the cadmium medical monitoring program.

Accuracy. Because results from an interlaboratory proficiency testing program are not available currently, it is difficult to define an achievable level of accuracy. Given the general performance parameters defined by the insert to the test kits, however, an accuracy of ±15% of the target value appears achievable.

Due to the low levels of B2MU to be measured generally, it is anticipated that the analysis of creatinine will contribute relatively little to the overall variability observed among creatinine-normalized B2MU levels (see section 5.4). The initial level of accuracy for reporting B2MU levels under this program should be set at ±15%.

Precision. Based on precision data reported by Pharmacia (1990), a precision value (i.e., CV) of 5% should be achievable over the defined range of the analyte. For internal QC samples (i.e., recommended as part of an internal QA/QC program, section 3.3.1), laboratories should attain precision near 5% over the range of concentrations measured.

5.3.8.3 *Quality Assurance/Quality Control*

Commercial laboratories providing measurement of B2MU should adopt an internal QA/QC program that incorporates the following components: Strict adherence to the Pharmacia Delphiad method, including calibration requirements; regular use of QC samples during routine runs; a protocol for corrective actions, and documentation of these actions; and, participation in an interlaboratory proficiency program. Procedures that may be used to address internal QC requirements are presented in Attachment 1. Due to differences between analyses for B2MU and CDB/CDU, specific values presented in Attachment 1 may have to be modified. Other components of the program (including characterization runs), however, can be adapted to a program for B2MU.

5.4 *Monitoring Creatinine in Urine (CRTU)*

Because CDU and B2MU should be reported relative to concentrations of CRTU, these concentrations should be determined in addition CDU and B2MU determinations.

5.4.1 *Units of CRTU Measurement*

CDU should be reported as μg Cd/g CRTU, while B2MU should be reported as μg B2M/g CRTU. To derive the ratio of cadmium or B2M to creatinine, CRTU should be reported in units of g crtn/l of urine. Depending on the analytical method, it may be necessary to convert results of creatinine determinations accordingly.

5.4.2 *Analytical Techniques Used To Monitor CRTU*

Of the techniques available for CRTU determinations, an absorbance spectrophotometric technique and a high-performance liquid chromatography (HPLC) technique are identified as acceptable in this protocol.

5.4.3 *Methods Developed for CRTU Determinations*

CRTU analysis performed in support of either CDU or B2MU determinations should be performed using either of the following 2 methods:

1. The Du Pont method (i.e., Jaffe method), in which creatinine in a sample reacts with picrate under alkaline conditions, and the resulting red chromofore is monitored (at 510 nm) for a fixed interval to determine the rate of the reaction; this reaction rate is proportional to the concentration of creatinine present in the sample (a copy of this method is provided in Attachment 2 of this protocol); or

2. The OSHA SLC Technical Center (OSLTC) method, in which creatinine in an aliquot of sample is separated using an HPLC column equipped with a UV detector; the resulting peak is quantified using an electrical integrator (a copy of this method is provided in Attachment 3 of this protocol).

5.4.4 *Sample Collection and Handling*

CRTU samples should be segregated from samples collected for CDU or B2MU analysis. Sample-collection techniques have been described under section 5.2.4. Samples should be preserved either to stabilize CDU (with HNO_3) or B2MU (with NaOH). Neither of these procedures should adversely affect CRTU analysis (see Attachment 3).

5.4.5 *General Method Performance*

Data from the OSLTC indicate that a CV of 5% should be achievable using the OSLTC method (Septon, I. private communication). The achievable accuracy of this method has not been determined.

Results reported in surveys conducted by the CAP (CAP 1991a, 1991b and 1992) indicate that a CV of 5% is achievable. The accuracy achievable for CRTU determinations has not been reported.

Laboratories performing creatinine analysis under this protocol should be CAP accredited and should be active participants in the CAP surveys.

5.4.6 *Observed CRTU Concentrations*

Published data suggest the range of CRTU concentrations is 1.0–1.6 g in 24-hour urine samples (Harrison 1987). These values are equivalent to about 1 g/l urine.

5.4.7 *Conclusions and Recommendations for CRTU*

5.4.7.1 *Recommended Method*

Use either the Jaffe method (Attachment 2) or the OSLTC method (Attachment 3). Alternate methods may be acceptable provided adequate performance is demonstrated in the CAP program.

5.4.7.2 *Data Quality Objectives*

Limit of Detection. This value has not been formally defined; however, a value of 0.1 g/l urine should be readily achievable.

Accuracy. This value has not been defined formally; accuracy should be sufficient to retain accreditation from the CAP.

Precision. A CV of 5% should be achievable using the recommended methods.

6.0 *References*

Adamsson E, Piscator M, and Nogawa K. (1979). Pulmonary and gastrointestinal exposure to cadmium oxide dust in a battery factory. *Environmental Health Perspectives, 28,* 219–222.

American Conference of Governmental Industrial Hygienists (ACGIH). (1980). *Documentation of the Threshold Limit Values and Biological Exposure Indices.* 5th edition. p. BEI–55.

Bernard A, Buchet J, Roels H, Masson P, and Lauwerys R. (1979). Renal excretion of proteins and enzymes in workers exposed to cadmium. *European Journal of Clinical Investigation, 9,* 11–22.

Bernard A and Lauwerys R. (1990). Early markers of cadmium nephrotoxicity: Biological significance and predictive value. *Toxocological and Environmental Chemistry, 27,* 65–72.

Braunwald E, Isselbacher K, Petersdorf R, Wilson J, Martin J, and Fauci A (Eds.). (1987). *Harrison's Principles of Internal Medicine.* New York: McGraw-Hill Book Company.

Buchet J, Roels H, Bernard I, and Lauwerys R. (1980). Assessment of renal funcion of workers exposed to inorganic lead, cadmium, or mercury vapor. *Journal of Occupational Medicine, 22,* 741–750.

CAP. (1991). Urine Chemistry, Series 1: Survey (Set U–B). College of American Pathologists.

CAP. (1991). Urine Chemistry, Series 1: Survey (Set U–C). College of American Pathologists.

CAP. (1992). Urine Chemistry, Series 1: Survey (Set U–A). College of American Pathologists.

CDC. (1980). Centers for Disease Control, Division of Environmental Health Laboratory

Sciences, Center for Environmental Health, Atlanta, Georgia. Docket No. 106A. Lake Couer d'Alene, Idaho cadmium and lead study: 86–0330, Specimen collection and shipping protocol.

CDC. (1990). Centers for Disease Control, Nutritional Biochemistry Branch. 4/27/90 Draft SOP for Method 0360A "Determination of cadmium in urine by graphite furnace atomic absorption spectrometry with Zeeman background correction."

Centre de Toxicologie du Quebec. (1991). Interlaboratory comparison program report for run #2. Shipping date 3/11/91. Addition BLR 9/19.

Chia K, Ong C, Ong H, and Endo G. (1989). Renal tubular function of workers exposed to low levels of cadmium. *British Journal of Industrial Medicine, 46,* 165–170.

Claeys-Thoreau F. (1982). Determination of low levels of cadmium and lead in biological fluids with simple dilution by atomic absorption spectrophotometry using Zeeman effect background absorption and the L'Vov platform. *Atomic Spectroscopy, 3,* 188–191.

DeBenzo Z, Fraile R, and Carrion N. (1990). Electrothermal atomization atomic absorption spectrometry with stabilized aqueous standards for the determination of cadmium in whole blood. *Analytica Chimica Acta, 231,* 283-288.

Elinder C, Edling C, Lindberg E, Kagedal B, and Vesterberg O. (1985). Assessment of renal function in workers previously exposed to cadmium. *British Journal of Internal Medicine, 42,* 754.

Ellis K, Cohn S, and Smith T. (1985). Cadmium inhalation exposure estimates: Their significance with respect to kidney and liver cadmium burden. *Journal of Toxicology and Environmental Health, 15,* 173–187.

Ellis K, Yasumura S, Vartsky D, and Cohn S. (1983). Evaluation of biological indicators of body burden of cadmium in humans. *Fundamentals and Applied Toxicology, 3,* 169–174.

Ellis K, Yeun K, Yasumura S, and Cohn S, (1984). Dose-response analysis of cadmium in man: Body burden vs kidney function. *Environmental Research, 33,* 216–226.

Evrin P, Peterson A, Wide I, and Berggard I. (1971). Radioimmunoassay of B–2-microglobulin in human biological fluids. *Scandanavian Journal of Clinical Laboratory Investigation, 28,* 439–443.

Falck F, Fine L, Smith R, Garvey J, Schork A, England B, McClatchey K, and Linton J. (1983). Metallothionein and occupational exposure to cadmium. *British Journal of Industrial Medicine, 40,* 305–313.

Federal Register. (1990). Occupational exposure to cadmium: Proposed rule. 55/22/4052–4147, February 6.

Friberg, Exhibit 29, (1990). Exhibit No. 29 of the OSHA Federal Docket H057A. Washington, D.C.

Friberg L. (1988). Quality assurance. In T. Clarkson (Ed.), *Biological Monitoring of Toxic Metals* (pp. 103–105). New York: Plenum Press.

Friberg L. and Elinder C. (1986). Cadmium toxicity in humans. In *Essential and Trace Elements in Human Health and Disease* (pp. 559–587). Docket Number 8–660.

Friberg L., Elinder F., et al. (1986). *Cadmium and Health: A Toxicological and Epidemiological Appraisal. Volume II, Effects and Response.* Boca Raton, FL: CRC Press.

Friberg L., Piscator M., Nordberg G., and Kjellstrom T. (1974). *Cadmium in the Environment* (2nd ed.). Cleveland: CRC

Friberg L., and Vahter M. (1983). Assessment of exposure to lead and cadmium through biological monitoring: Results of a UNEP/WHO global study. *Environmental Research, 30,* 95–128.

Gunter E., and Miller D. (1986). Laboratory procedures used by the division of environmental health laboratory sciences center for environmental health, Centers for Disease Control for the Hispanic health and nutrition examination survey (HHANES). Atlanta, GA: Centers for Disease Control.

Harrison. (1987). Harrison's Principles of Internal Medicine. Braunwald, E; Isselbacher, KJ; Petersdorf, RG; Wilson, JD; Martin, JB; and Fauci, AS Eds. Eleventh Ed. McGraw Hill Book Company. San Francisco.

Henry J. (1991). *Clinical Diagnosis and Management by Laboratory Methods* (18th edition). Philadelphia: WB Saunders Company.

IARC. (1987). *IRAC Monographs on the Evaluation of Carcinogenic Risks to Humans. Overall Evaluation of Carcinogenicity: Update of Volume 1–42.* Supplemental 7, 1987.

Ishizaki M., Kido T., Honda R., Tsuritani I., Yamada Y., Nakagawa H., and Nogawa K. (1989). Dose-response relationship between urinary cadmium and B–2-microglobulin in a Japanese environmentally cadmium exposed population. *Toxicology, 58,* 121–131.

Iwao S., Tsuchiya K., and Sakurai H. (1980). Serum and urinary B–2-microglobulin among cadmium-exposed workers. *Journal of Occupational Medicine, 22,* 399–402.

Iwata K., Katoh T., Morikawa Y., Aoshima K., Nishijo M., Teranishi H., and Kasuya M. (1988). Urinary trehalase activity as an indicator of kidney injury due to environmental cadmium exposure. *Archives of Toxicology, 62,* 435–439.

Kawada T., Koyama H., and Suzuki S. (1989). Cadmium, NAG activity, and B–2-microglobulin in the urine of cadmium pigment workers. *British Journal of Industrial Medicine, 46,* 52–55.

Kawada T., Tohyama C., and Suzuki S. (1990). Significance of the excretion of urinary indicator proteins for a low level of occupational exposure to cadmium. *International Archives of Occupational Environmental Health, 62,* 95–100.

Kjellstrom T. (1979). Exposure and accumulation of cadmium in populations from Japan, the United States, and Sweden. *Environmental Health Perspectives, 28,* 169–197.

Kjellstrom T., Evrin P., and Rahnster B. (1977). Dose-response analysis of cadmium-induced tubular proteinuria. *Environmental Research, 13,* 303–317.

Kjellstrom T., Shiroishi K., and Evrin P. (1977). Urinary B–2-microglobulin excretion among people exposed to cadmium in the general environment. *Environmental Research, 13,* 318–344.

Kneip T., & Crable J. (Eds.). (1988). Method 107. Cadmium in blood. *Methods for biological monitoring* (pp.161–164). Washington, DC: American Public Health Association.

Kowal N. (1988). Urinary cadmium and B–2–microglobulin: Correlation with nutrition and smoking history. *Journal of Toxicology and Environmental Health, 25,* 179–183.

Kowal N., Johnson D., Kraemer D., and Pahren H. (1979). Normal levels of cadmium in diet, urine, blood, and tissues of inhabitants of the United States. *Journal of Toxicology and Environmental Health, 5,* 995–1014.

Kowal N. and Zirkes M. (1983). Urinary cadmium and B–2–microglobulin: Normal values and concentration adjustment. *Journal of Toxicology and Environmental Health, 11,* 607–624.

Lauwerys R., Buchet J., and Roels H. (1976). The relationship between cadmium exposure or body burden and the concentration of cadmium in blood and urine in man. *International Archives of Occupational and Environmental Health, 36,* 275–285.

Lauwerys R, Roels H, Regniers, Buchet J, and Bernard A. (1979). Significance of cadmium concentration in blood and in urine in workers exposed to cadmium. *Environmental Research, 20,* 375–391.

Lind B, Elinder C, Friberg L, Nilsson B, Svartengren M, and Vahter M. (1987). Quality control in the analysis of lead and cadmium in blood. *Fresenius' Zeitschrift fur Analytical Chemistry, 326,* 647–655.

Mason H, Davison A, Wright A, Guthrie C, Fayers P, Venables K, Smith N, Chettle D, Franklin D, Scott M, Holden H, Gompertz D, and Newman-Taylor A. (1988). Relations between liver cadmium, cumulative exposure, and renal function in cadmium alloy workers. *British Journal of Industrial Medicine, 45,* 793–802.

Meridian Research, Inc. (1989). *Quantitative Assessment of Cancer Risks Associated with Occupational Exposure to Cd.* Prepared by Meridian Research, Inc. and Roth Associates, Inc. for the Occupational Safety & Health Administration. June 12, 1989.

Meridian Research, Inc and Roth Associates, Inc. (1989). *Quantitative Assessment of the Risk of Kidney Dysfunction Associated with Occupational Exposure to Cd.* Prepared by Meridian Research, Inc. and Roth Associates, Inc. for the Occupational Safety & Health Administration. July 31 1989.

Micheils E and DeBievre P. (1986). Method 25—Determination of cadmium in whole blood by isotope dilution mass spectrometry. O'Neill I, Schuller P, and Fishbein L (Eds.), *Environmental Carcinogens Selected Methods of Analysis* (Vol. 8). Lyon, France: International Agency for Research on Cancer.

Mueller P, Smith S, Steinberg K, and Thun M. (1989). Chronic renal tubular effects in relation to urine cadmium levels. *Nephron, 52,* 45–54.

NIOSH. (1984a). Elements in blood or tissues. Method 8005 issued 5/15/85 and Metals in urine. Method 8310 issued 2/15/84 In P. Eller (Ed.), *NIOSH Manual of Analytical Methods* (Vol. 1, Ed. 3). Cincinnati, Ohio: US–DHHS.

NIOSH. (1984b). Lowry L. Section F: Special considerations for biological samples in *NIOSH Manual of Analytical Methods*

(Vol. 1, 3rd ed). P. Eller (Ed.). Cincinnati, Ohio: US–DHHS.

Nordberg G and Nordberg M. (1988). Biological monitoring of cadmium. In T. Clarkson, L. Friberg, G. Nordberg, and P. Sager (Eds.), *Biological Monitoring of Toxic Metals*, New York: Plenum Press.

Nogawa K. (1984). Biologic indicators of cadmium nephrotoxicity in persons with low-level cadmium exposure. *Environmental Health Perspectives, 54,* 163–169.

OSLTC (no date). Analysis of Creatinine for the Normalization of Cadmium and Beta-2-Microglobulin Concentrations in Urine. OSHA Salt Lake Technical Center. Salt Lake City, UT.

Paschal. (1990). Attachment 8 of exhibit 108 of the OSHA docket H057A.

Perkin-Elmer Corporation. (1982). *Analytical Methods for Atomic Absorption Spectroscopy.*

Perkin-Elmer Corporation. (1977). *Analytical Methods Using the HGA Graphite Furnace.*

Pharmacia Diagnostics. (1990). Pharmacia DELFIA system B-2-microglobulin kit insert. Uppsala, Sweden: Pharmacia Diagnostics.

Piscator M. (1962). Proteinuria in chronic cadmium poisoning. *Archives of Environmental Health, 5,* 55–62.

Potts, C.L. (1965). Cadmium Proteinuria—The Health Battery Workers Exposed to Cadmium Oxide dust. Ann Occup Hyg, 3:55–61, 1965.

Princi F. (1947). A study of industrial exposures to cadmium. *Journal of Industrial Hygiene and Toxicology, 29,* 315–320.

Pruszkowska E, Carnick G, and Slavin W. (1983). Direct determination of cadmium in urine with use of a stabillized temperature platform furnace and Zeeman background correction. *Clinical Chemistry, 29,* 477–480.

Roberts C and Clark J. (1986). Improved determination of cadmium in blood and plasma by flameless atomic absorption spectroscopy. *Bulletin of Environmental Contamination and Toxicology, 36,* 496–499.

Roelandts I. (1989). Biological reference materials. *Soectrochimica Acta, 44B,* 281–290.

Roels H, Buchet R, Lauwerys R, Bruaux P, Clays-Thoreau F, Laafontaine A, Overschelde J, and Verduyn J. (1978). Lead and cadmium absorption among children near a nonferrous metal plant. *Environmental Research, 15,* 290–308.

Roels H, Djubgang J, Buchet J, Bernard A, and Lauwerys R. (1982). Evolution of cadmium-induced renal dysfunction in workers removed from exposure. *Scandanavian Journal of Work and Environmental Health, 8,* 191–200.

Roels H, Lauwerys R, and Buchet J. (1989). Health significance of cadmium induced renal dysfunction: A five year follow-up. *British Journal of Industrial Medicine, 46,* 755–764.

Roels J, Lauwerys R, Buchet J, Bernard A, Chettle D, Harvey T, and Al–Haddad I. (1981). In vivo measurements of liver and kidney cadmium in workers exposed to this metal: Its significance with respect to cadmium in blood and urine. *Environmental Research, 26,* 217–240.

Roels H, Lauwerys R, Buchet J, Bernard A, Lijnen P, and Houte G. (1990). Urinary kallikrein activity in workers exposed to cadmium, lead, or mercury vapor. *British Journal of Industrial Medicine, 47,* 331–337.

Sakurai H, Omae K, Toyama T, Higashi T, and Nakadate T. (1982). Cross-sectional study of pulmonary function in cadmium alloy workers. *Scandanavian Journal of Work and Environmental Health, 8,* 122–130.

Schardun G and van Epps L. (1987). B–2–microglobulin: Its significance in the evaluation of renal function. *Kidney International, 32,* 635–641.

Shaikh Z, and Smith L. (1984). Biological indicators of cadmium exposure and toxicity. *Experentia, 40,* 36–43.

Smith J and Kench J. (1957). Observations on urinary cadmium and protein excretion in men exposed to cadmium oxide dust and fume. *British Journal of Industrial Medicine, 14,* 240–245.

Smith J, Kench J, and Lane R. (1955). Determination of Cadmium in urine and observations on urinary cadmium and protein excretion in men exposed to cadmium oxide dust. *British Journal of Industrial Medicine, 12,* 698–701.

SWRI (Southwest Research Institute). (1978). The distribution of cadmium and other metals in human tissues. Health Effects Research Lab, Research Triangle Park, NC, Population Studies Division. NTIS No. PB–285–200.

Stewart M and Hughes E. (1981). Urinary B–2–microglobulin in the biological monitoring of cadmium workers. *British Journal of Industrial Medicine, 38,* 170–174.

Stoeppler K and Brandt M. (1980). Contributions to automated trace analysis. Part V. Determination of cadmium in whole blood and urine by electrothermal atomic absorption spectrophotometry. *Fresenius' Zeitschrift fur Analytical Chemistry, 300,* 372–380.

Takenaka et al. (1983). *Carcinogencity of Cd Chloride Aerosols in White Rats.* INCI 70: 367–373, 1983.

Thun M, Osorio A, Schober S, Hannon W, Lewis B, and Halperin W. (1989). Nephropathy in cadmium workers: Assessment of risk from airborne occupational exposure to cadmium. *British Journal of Industrial Medicine, 46,* 689–697.

Thun M, Schnorr T, Smith A, Halperin W, and Lemen R. (1985). Mortality among a cohort of US cadmium production workers—an update. *Journal of the National Cancer Institute, 74,* 325–333.

Travis D and Haddock A. (1980). Interpretation of the observed age-dependency of cadmium body burdens in man. *Environmental Research, 22,* 46–60.

Tsuchiya K. (1967). Proteinuria of workers exposed to cadmium fume. *Archives of Environmental Health, 14,* 875–880.

Tsuchiya K. (1976). Proteinuria of cadmium workers. *Journal of Occupational Medicine, 18,* 463–470.

Tsuchiya K, Iwao S, Sugita M, Sakurai H. (1979). Increased urinary B-2-microglobulin in cadmium exposure: Dose-effect relationship and biological significance of B-2-microglobulin. *Environmental Health Perspectives, 28,* 147–153.

USEPA. (1985). Updated Mutagenicity and Carcinogenicity Assessments of Cd: Addendum to the Health Assessment Document for Cd (May 1981). Final Report. June 1985.

Vahter M and Friberg L. (1986). Quality control in integrated human exposure monitoring of lead and cadmium. *Fresenius' Zeitschrift fur Analytical Chemistry, 332,* 728–731.

Weber J. (1980). An interlaboratory comparison programme for several toxic substances in blood and urine. *The Science of the Total Environment, 71,* 111–123.

Weber J. (1991a). Accuracy and precision of trace metal determinations in biological fluids. In K. Subramanian, G. Iyengar, and K. Okamot (Eds.), *Biological Trace Element Research-Multidisciplinary Perspectives,* ACS Symposium Series 445. Washington, DC: American Chemical Society.

Weber J. (1991b). Personal communication about interlaboratory program and shipping biological media samples for cadmium analyses.

Wibowo A, Herber R, van Deyck W, and Zielhuis R. (1982). Biological assessment of exposure in factories with second degree usage of cadmium compounds. *International Archives of Occupational Environmental Health, 49,* 265–273.

Attachment 1—Nonmandatory Protocol for an Internal Quality Assurance/Quality Control Program

The following is an example of the type of internal quality assurance/quality control program that assures adequate control to satisfy mandatory OSHA requirements under this protocol. However, other approaches may also be acceptable.

As indicated in Section 3.3.1 of the protocol, the mandatory QA/QC program for CDB and CDU should address, at a minimum, the following:

- Calibration;
- Establishment of control limits;
- Internal QC analyses and maintaining control; and
- Corrective action protocols.

This illustrative program includes both initial characterization runs to establish the performance of the method and ongoing analysis of quality control samples intermixed with compliance samples to maintain control.

Calibration

Before any analytical runs are conducted, the analytic instrument must be calibrated. This is to be done at the beginning of each day on which quality control samples and/or compliance samples are run. Once calibration is established, quality control samples or compliance samples may be run. Regardless of the type of samples run, every fifth sample must be a standard to assure that the calibration is holding.

Calibration is defined as holding if every standard is within plus or minus (±) 15% of its theoretical value. If a standard is more than plus or minus 15% of its theoretical value, then the run is out of control due to calibration error and the entire set of samples must either be reanalyzed after recalibrating or results should be recalculated based on a statistical curve derived from the measurement of all standards.

It is essential that the highest standard run is higher than the highest sample run. To assure that this is the case, it may be necessary to run a high standard at the end of

the run, which is selected based on the results obtained over the course of the run.

All standards should be kept fresh, and as they get old, they should be compared with new standards and replaced.

Initial Characterization Runs and Establishing Control

A participating laboratory should establish four pools of quality control samples for each of the analytes for which it wishes to be accredited. The concentrations of quality control samples within each pool are to be centered around each of the four target levels for the particular analyte identified in Section 4.4 of the protocol.

Within each pool, at least 4 quality control samples need to be established with varying concentrations ranging between plus or minus 50% of the target value of that pool. Thus for the medium-high cadmium in blood pool, the theoretical values of the quality control samples may range from 5 to 15 μg/l, (the target value is 10 μg/l). At least 4 unique theoretical values must be represented in this pool.

The range of theoretical values of plus or minus 50% of the target value of a pool means that there will be overlap of the pools. For example, the range of values for the medium-low pool for cadmium in blood is 3.5 to 10.5 μg/l while the range of values for the medium-high pool is 5 to 15 μg/l. Therefore, it is possible for a quality control sample from the medium-low pool to have a higher concentration of cadmium than a quality control sample from the medium-high pool.

Quality control samples may be obtained as commercially available reference materials, internally prepared, or both. Internally prepared samples should be well characterized and traced or compared to a reference material for which a consensus value for concentration is available. Levels of analyte in the quality control samples must be concealed from the analyst prior to the reporting of analytical results. Potential sources of materials that may be used to construct quality control samples are listed in Section 3.3.1 of the protocol.

Before any compliance samples are analyzed, control limits must be established. Control limits should be calculated for every pool of each analyte for which a laboratory seeks accreditation, and control charts should be kept for each pool of each analyte. A separate set of control charts and control limits should be established for each analytical instrument in a laboratory that will be used for analysis of compliance samples.

At the beginning of this QA/QC program, control limits should be based on the results of the analysis of 20 quality control samples from each pool of each analyte. For any given pool, the 20 quality control samples should be run on 20 different days. Although no more than one sample should be run from any single pool on a particular day, a laboratory may run quality control samples from different pools on the same day. This constitutes a set of initial characterization runs.

For each quality control sample analyzed, the value F/T (defined in the glossary) should be calculated. To calculate the control limits for a pool of an analyte, it is first necessary to calculate the mean, $\bar{X}$, of the F/T values for each quality control sample in a pool and then to calculate its standard deviation, $\hat{\sigma}$. Thus, for the control limit for a pool, $\bar{X}$ is calculated as:

$$\frac{\left(\Sigma \frac{F}{T}\right)}{N}$$

and $\hat{\sigma}$ is calculated as

$$\left[\frac{\sum \left(\frac{F}{T} - \bar{X}\right)^2}{(N-1)}\right]^{\frac{1}{2}}$$

where N is the number of quality control samples run for a pool.

The control limit for a particular pool is then given by the mean plus or minus 3 standard deviations ($\bar{X} \pm 3\hat{\sigma}$). The control limits may be no greater than 40% of the mean F/T value. If three standard deviations are greater than 40% of the mean F/T value, then analysis of compliance samples may not begin.[1] Instead, an investigation into the causes of the large standard deviation should begin, and the inadequacies must be remedied. Then, control limits must be reestablished which will mean repeating the running 20 quality control samples from each pool over 20 days.

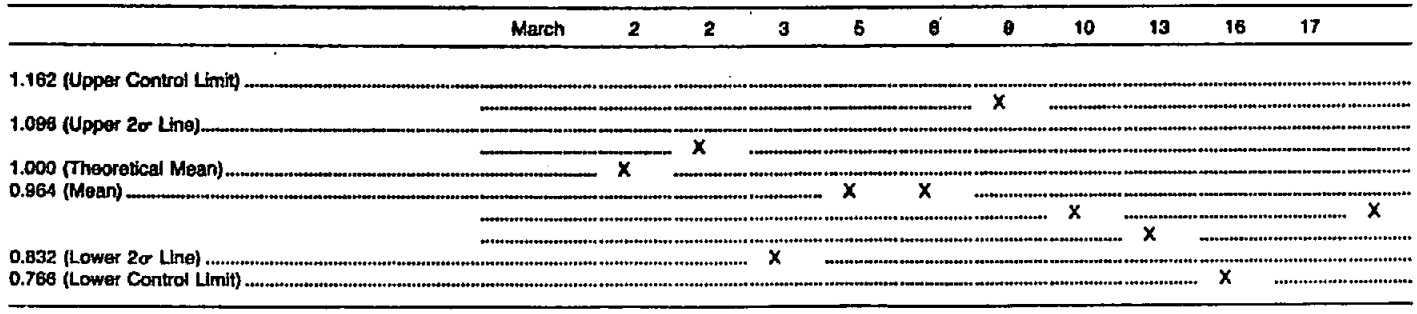
Internal Quality Control Analyses and Maintaining Control

Once control limits have been established for each pool of an analyte, analysis of compliance samples may begin. During any run of compliance samples, quality control samples are to be interspersed at a rate of no less than 5% of the compliance sample workload. When quality control samples are run, however, they should be run in sets consisting of one quality control sample from each pool. Therefore, it may be necessary, at times, to intersperse quality control samples at a rate greater than 5%.

There should be at least one set of quality control samples run with any analysis of compliance samples. At a minimum, for example, 4 quality control samples should be run even if only 1 compliance sample is run. Generally, the number of quality control samples that should be run are a multiple of four with the minimum equal to the smallest multiple of four that is greater than 5% of the total number of samples to be run. For example, if 300 compliance samples of an analyte are run, then at least 16 quality control samples should be run (16 is the smallest multiple of four that is greater than 15, which is 5% of 300).

Control charts for each pool of an analyte (and for each instrument in the laboratory to be used for analysis of compliance samples) should be established by plotting F/T versus date as the quality control sample results are reported. On the graph there should be lines representing the control limits for the pool, the mean F/T limits for the pool, and the theoretical F/T of 1.000. Lines representing plus or minus (±) 2σ should also be represented on the charts. A theoretical example of a control chart is presented in Figure 1.

FIGURE 1.—THEORETICAL EXAMPLE OF A CONTROL CHART FOR A POOL OF AN ANALYTE



[1] Note that the value, "40%" may change over time as experience is gained with the program.

All quality control samples should be plotted on the chart, and the charts should be checked for visual trends. If a quality control sample falls above or below the control limits for its pool, then corrective steps must be taken (see the section on corrective actions below). Once a laboratory's program has been established, control limits should be updated every 2 months, prior to sending OSHA the updated data required to maintain accreditation.

The updated control limits should be calculated from the results of the last 100 quality control samples run for each pool. If 100 quality control samples from a pool have not been run at the time of the update, then the limits should be based on as many as have been run provided at least 20 quality control samples from each pool have been run over 20 different days.

The trends that should be looked for on the control charts are:

1. 10 consecutive quality control samples falling above or below the mean;
2. 3 consecutive quality control samples falling more than 2S from the mean (above or below the 2S lines of the chart); or
3. the mean calculated to update the control limits falls more than 10% above or below the theoretical mean of 1.000.

If any of these trends is observed, then all analysis must be stopped, and an investigation into the causes of the errors must begin. Before the analysis of compliance samples may resume, the inadequacies must be remedied and the control limits must be reestablished for that pool of an analyte. Reestablishment of control limits will entail running 20 sets of quality control samples over 20 days.

Note that alternative procedures for defining internal quality control limits may also be acceptable. Limits may be based, for example, on proficiency testing, such as ± 1 μg or 15% of the mean (whichever is greater). These should be clearly defined.

Corrective Actions

Corrective action is the term used to describe the identification and remediation of errors occurring within an analysis. Corrective action is necessary whenever the result of the analysis of any quality control sample falls outside of the established control limits. The steps involved may include simple things like checking calculations of basic instrument maintenance, or it may involve more complicated actions like major instrument repair. Whatever the source of error, it must be identified and corrected (and a Corrective Action Report (CAR) must be completed and sent to OSHA with the next reaccreditation).

To maintain accreditation, laboratories must report corrective actions to the OSHA Salt Lake Technical Center. A form to be used for reporting corrective actions is provided in Attachment 5 of the protocol.

Attachment 2

Creatinine in Urine [JAFFE PROCEDURE].

Intended Use: The CREA pack is used in the Du Pont ACA® discrete clinical analyzer to quantitatively measure creatinine in serum and urine.

Summary The CREA method employs a modification of the kinetic Jaffe reaction reported by Larsen. This method has been reported to be less susceptible than conventional methods to interference from non-creatinine, Jaffe-positive compounds.[1]

A split sample comparison between the CREA method and a conventional Jaffe procedure on Autoanalyzer® showed a good correlation. [See Specific Performance Characteristics].

Autoanalyzer,® is a registered trademark of Technicon Corp., Tarrytown, NY.

Principles of Procedure: In the presence of a strong base such as NaOH, picrate reacts with creatinine to form a red chromophore. The rate of increasing absorbance at 510 nm due to the formation of this chromophore during a 17.07-second measurement period is directly proportional to the creatinine concentration in the sample.

$$\text{Creatinine} + \text{Picrate} \xrightarrow{\text{NaOH}} \text{Red chromophore (absorbs at 510 nm)}$$

Reagents:

Compartment [a]	Form	Ingredient	Quantity [b]
No. 2, 3, & 4	Liquid	Picrate	0.11 mmol
No. 6	Liquid	NaOH (for pH adjustment) [c]	

[a] Compartments are numbered 1–7, with compartment No. 7 located closest to pack fill position No. 2.
[b] Nominal value at manufacture.
[c] See Precautions.

Precautions: Compartment No. 6 contains 75μL of 10 N NaOH; avoid contact; skin irritant; rinse contacted area with water.

Used packs contain human body fluids; handle with appropriate care.

For In Vitro Diagnostic Use.

Mixing and Diluting: Mixing and diluting are automatically performed by the ACA® discrete clinical analyzer. The sample cup must contain sufficient quantity to accommodate the sample volume plus the "dead volume"; precise cup filling is not required.

SAMPLE CUP VOLUMES (μL)

Analyzer	Standard		Microsystem	
	Dead	Total	Dead	Total
II, III	120	3000	10	500
IV, SX	120	3000	30	500
V	90	3000	10	500

Storage of Unprocessed Packs: Store at 2–8 °C. Do not freeze. Do not expose to temperatures above 35 °C or to direct sunlight.

Expiration: Refer to expiration date on the tray label.

Specimen Collection: Serum or urine can be collected and stored by normal procedures.[2]

Known Interfering Substances: [3] Serum Protein Influence. Serum protein levels exert a direct influence on the CREA assay. The following should be taken into account when this method is used for urine samples and when it is calibrated:

Aqueous creatinine standards or urine specimens will give CREA results depressed by approximately 0.7 mg/dL [62 μmol/L] [4] and will be less precise than samples containing more than 3 g/dL [30 g/L] protein.

All urine specimens should be diluted with an albumin solution to give a final protein concentration of at least 3 g/dL [30 g/L]. Du Pont Enzyme Diluent (Cat. #790035–901) may be used for this purpose.

- High concentration of endrogenous bilirubin (>20 mg/dL [>342 μmol/L]) will give depressed CREA results [average depression 0.8 mg/dL [71 μmol/L]).[4]
- Grossly hemolyzed (hemoglobin >100 mg/dL [>62 μmol/L]) or visibly lipemic specimens may cause falsely elevated CREA results.[5,6]
- The following cephalosporin antibiotics do not interfere with the CREA method when present at the concentrations indicated. Systematic inaccuracies (bias) due to these substances are less than or equal to 0.1 mg/dL [8.84 μmol/L] at CREA concentrations of approximately 1 mg/dL [88 μmol/L].

[4] Systeme International d'unites (S.I. Units) are in brackets.

Antibiotic	Peak serum level [a,e,g]		Drug concentration	
	mg/dL	[mmol/L]	mg/dL	[mmol/L]
Cephaloridine	1.4	0.3	25	6.0
Cephalexin	0.6–2.0	0.2–0.6	25	7.2
Cephamandole	1.3–2.5	0.3–0.5	25	4.9
Cephapirin	2.0	0.4	25	5.6
Cephradine	1.5–2.0	0.4–0.6	25	7.1
Cefazolin	2.5–5.0	0.55–1.1	50	11.0

• The following cephalosporin antibiotics have been shown to affect CREA results when present at the indicated concentrations. System inaccuracies (bias) due to these substances are greater that 0.1 mg/dL [8.84 μmol/L] at CREA concentrations of:

Antibiotic	Peak serum level [a,g]		Drug concentration		Effect
	mg/dL [mmol/L]	mg/dL [mmol/L]	mg/dL	[mmol/L]	
Cephalothin	1–6	0.2–1.5	100	25.2	↓ 20–25%
Cephoxitin	2.0	0.5	5.0	1.2	↑ 35–40%

• The single wavelength measurement used in this method eliminates interference from chromophores whose 510 nm absorbance is constant throughout the measurement period.

• Each laboratory should determine the acceptability of its own blood collection tubes and serum separation products. Variations in these products may exist between manufacturers and, at times, from lot to lot.

Procedure

TEST MATERIALS

Item	II, III, Du Pont cat. No.	IV, SX, Du Pont cat. No.	V, Du Pont cat. No.
ACA® CREA analytical test pack	701976901	701976901	701976901
Sample system kit, or	710642901	710642901	713697901
Micro sample system kit, and	702694901	710356901	NA
Micro sample system holders	702785000	NA	NA
DYLUX® photosensitive printer paper	700036000	NA	NA
Thermal printer paper	NA	710639901	713645901
Du Pont purified water	704209901	710615901	710815901

TEST MATERIALS—Continued

Item	II, III, Du Pont cat. No.	IV, SX, Du Pont cat. No.	V, Du Pont cat. No.
Cell wash solution	701864901	710664901	710864901

Test Steps

The operator need only load the sample kit and appropriate test pack(s) into a properly prepared ACA® discrete clinical analyzer. It automatically advances the pack(s) through the test steps and prints a result(s). See the Instrument Manual of the ACA® analyzer for details of mechanical travel of the test pack(s).

Preset Creatinine (CREA) Test Conditions

- Sample volume: 200 μL.
- Diluent: purified water.
- Temperature: 37.0±0.1 °C.
- Reaction period: 29 seconds.
- Type of measurement: rate.
- Measurement period: 17.07 seconds.
- Wavelength: 510 nm.
- Units: mg/dL [μmol/L].

Calibration

The general calibration procedure is described in the Calibration/Verification chapter of the Manuals.

The following information should be considered when calibrating the CREA method.

- Assay range: 0–20 mg/mL [0–1768 μmol/L][e].
- Reference material: Protein containing primary standards[f] or secondary calibrators such as Du Pont Elevated Chemistry Control (Cat.[f] #790035903) and Normal Chemistry Control (Cat. #790035905)[g].
- Suggested calibration levels: 1,5,20, mg/mL, [88, 442, 1768 μmol/L].
- Calibration scheme: 3 levels, 3 packs per level.
- Frequency: Each new pack lot. Every 3 months for any one pack lot.

e. For the results in S.I. units [μmol/L] the conversion factory is 88.4.

f. Refer to the Creatinine Standard Preparation and Calibration Procedure available on request from a Du Pont Representative.

g. If the Du Pont Chemistry Controls are being used, prepare them according to the instructions on the product insert sheets.

PRESET CREATININE (CREA) TEST CONDITIONS

Item	ACA®, II, analyzer	ACA®, III, IV, SX, V, analyzer
Count by	One (1) [Five (5)]	NA.
Decimal point location.	0.0 mg/dL [000. μmol/L]	000.0 mg/dL [000 μmol/L].
Assigned starting point or offset C_0.	999.8 [9823.]	−1.000 E1 [−8.840 E2].
Scale factor or assigned.	0.2000 mg/dL/count[h]	2.004 E−1[h].
Linear term C_1[h]	[0.3536 μmol/L/count]	[1.772E1].

h. The preset scale factor (linear term) was derived from the molar absorptivity of the indicator and is based on an absorbance to activity relationship (sensitivity) of 0.596 (mA/min)/(U/L). Due to small differences in filters and electronic components between instruments, the actual scale factor (linear term) may differ slightly from that given above.

Quality Control

Two types of quality control procedures are recommended:

- **General instrument check.** Refer to the Filter Balance Procedure and the Absorbance Test Method described in the Instrument

Manual. Refer also to the ABS Test Methodology literature.

• **Creatinine method check.** At least once daily run a CREA test on a solution of known creatinine activity such as an assayed control or calibration standard other than that used to calibrate the CREA method. For further details review the Quality Assurance Section of the Chemistry Manual. The result obtained should fall within acceptable limits defined by the day-to-day variability of the system as measured in the user's laboratory. (See SPECIFIC PERFORMANCE CHARACTERISTICS for guidance.) If the result falls outside the laboratory's acceptable limits, follow the procedure outlined in the Chemistry Troubleshooting Section of the Chemistry Manual.

A possible system malfunction is indicated when analysis of a sample with five consecutive test packs gives the following results:

Level	SD
1 mg/dL	>0.15 mg/dL.
[88 μmol/L]	[>13 μmol/L].
20 mg/dL	>0.68 mg/dL.
[1768 μmol/L]	[>60 μmol/L].

Refer to the procedure outlined in the Trouble Shooting Section of the Manual.

Results

The ACA® analyzer automatically calculates and prints the CREA result in mg/dL [μmol/L].

Limitation of Procedure

Results >20 mg/dL [1768 μmol/L]:

• Dilute with suitable protein base diluent. Reassay. Correct for diluting before reporting.

The reporting system contains error messages to warn the operator of specific malfunctions. Any report slip containing a letter code or word immediately following the numerical value should not be reported. Refer to the Manual for the definition of error codes.

Reference Interval

Serum: [11] Males—0.6–1.3 md/dL [71–115 μmol/L].
Females: 0.6–1.0 md/dL [53–88 μmol/L]
Urine: [12] Males—0.6–2.5 g/24 hr [53–221 mmol/24 hr]
Females: 0.6–1.5 g/24 hr [53–133 mmol/24 hr]

Each laboratory should establish its own reference intervals for CREA as performed on the analyzer.

i. Reference interval data obtained from 200 apparently healthy individuals (71 males, 129 females) between the ages of 19 and 72.

Specific Performance Characteristics

REPRODUCIBILITY [K]

Material	Mean	Standard deviation (% CV)	
		Within-run	Between-day
Lyophilized Control	1.3 [115]	0.05 (3.7) [4.4]	0.05 (3.7) [4.4]
Lyophilized Control	20.6 [1821]	0.12 (0.6) [10.6]	0.37 (1.8) [32.7]

CORRELATION—REGRESSION STATISTICS [l]

Comparative method	Slope	Intercept	Correlation coefficient	n
Autoanalyzer®	1.03	0.03[2.7]	0.997	260

j. ALL SPECIFIC PERFORMANCE CHARACTERISTICS tests were run after normal recommended equipment quality control checks were performed (see Instrument Manual).

k. Specimens at each level were analyzed in duplicate for twenty days. The within-run and between-day standard deviations were calculated by the analysis of variance method.

l. Model equation for regression statistics is:

Result of ACA® Analyzer = Slope (Comparative method result) + intercept

Assay Range [m]

0.0–20.0 mg/dl [0–1768 μmol]

m. See REPRODUCIBILITY for method performance within the assay range.

Analytical Specificity

See KNOWN INTERFERING SUBSTANCES section for details.

Bibliography:

[1] Larsen, K., *Clin Chem Acta* 41, 209 (1972).
[2] Tietz, NW, *Fundamentals of Clinical Chemistry*, W. B. Saunders Co., Philadelphia, PA, 1976, pp 47–52, 1211.
[3] Supplementary information pertaining to the effects of various drugs and patient conditions on in vivo or in vitro diagnostic levels can be found in "Drug Interferences with Clinical Laboratory Tests," *Clin. Chem* 21 (5) (1975), and "Effects of Disease on Clinical Laboratory Tests," *Clin Chem*, 26 (4) 1D–476D (1980).
[4] Watkins, R. Fieldkamp, SC, Thibert, RJ, and Zak, B, *Clin Chem*, 21, 1002 (1975).
[5] Kawas, EE, Richards, AH, and Bigger, R, *An Evaluation of a Kinetic Creatinine Test for the Du Pont ACA*, Du Pont Company, Wilmington, DE (February 1973).[n]
[6] Westgard, JO, *Effects of Hemolysis and Lipemia* on ACA *Creatinine Method*, 0.200 μL, *Sample Size*, Du Pont Company, Wilmington, DE (October 1972).
[7] *Physicians' Desk Reference*, Medical Economics Company, 33 Edition, 1979.
[8] Henry, JB, *Clinical Diagnosis and Management by Laboratory Methods*, W.B. Saunders Co., Philadelphia, PA 1979, Vol. III.
[9] Krupp, MA, Tierney, LM Jr., Jawetz, E, Roe, RI, Camargo, CA, *Physicians Handbook*, Lange Medical Publications, Los Altos, CA, 1982 pp 635–636.
[10] Sarah, AJ, Koch, TR, Drusano, GL, Celoxitin Falsely Elevates Creatinine Levels, JAMA 247, 205–206 (1982).
[11] Gadsden, RH, and Phelps, CA, *A Normal Range Study of Amylase in Urine and Serum on the Du Pont ACA*, Du Pont Company, Wilmington, DE (March 1978 [n]
[12] Dicht, JJ, Reference Intervals for Serum Amylase and Urinary Creatinine on the Du Pont ACA® Discrete Clinical Analyzer, Du Pont Company, Wilmington, DE (November 1984).
n. Reprints available from Du Pont Company, Diagonostic Systems.

Attachment 3

Analysis of Creatinine for the Normalization of Cadmium and Beta–2–Microglobulin Concentrations in Urine

Matrix: Urine
Target Concentration: 1.1 g/L (this amount is representative of creatinine concentrations found in urine).
Procedure: A 1.0 mL aliquot of urine is passed through a C18 SEP-PAK® (Waters Associates). Approximately 30 mL of HPLC (high performance liquid chromatography) grade water is then run through the SEP-PAK. The resulting solution is diluted to volume in a 100–mL volumetric flask and analyzed by HPLC using an ultraviolet (UV) detector.
Special Requirements: After collection, samples should be appropriately stabilized for cadmium (Cd) analysis by using 10% high purity (with low Cd background levels) nitric acid (exactly 1.0 mL of 10% nitric acid per 10 mL of urine) or stabilized for *Beta–2–*Microglobulin (B2M) by taking to pH 7 with dilute NaOH (exactly 1.0 mL of 0.11 N NaOH per 10 mL of urine). If not immediately analyzed, the samples should be frozen and shipped by overnight mail in an insulated container.
Date: January 1992.
Chemists: David B. Armitage,
Duane Lee,
Organic Service Branch II, OSHA Technical Center, Salt Lake City, Utah.

1. General Discussion

1.1. Background

1.1.1. History of procedure

Creatinine has been analyzed by several methods in the past. The earliest methods were of the wet chemical type. As an example, creatinine reacts with sodium picrate in basic solution to form a red complex, which is then analyzed colorimetrically (Refs. 5.1. and 5.2.).

Since industrial hygiene laboratories will be analyzing for Cd and B2M in urine, they will be normalizing those concentrations to the concentration of creatinine in urine. A literature search revealed several HPLC methods (Refs. 5.3., 5.4., 5.5. and 5.6.) for creatinine in urine and because many industrial hygiene laboratories have HPLC equipment, it was desirable to develop an industrial hygiene HPLC method for creatinine in urine. The method of

Hausen, Fuchs, and Wachter was chosen as the starting point for method development. SEP-PAKs were used for sample clarification and cleanup in this method to protect the analytical column. The urine aliquot which has been passed through the SEP-PAK is then analyzed by reverse-phase HPLC using ion-pair techniques.

This method is very similar to that of Ogata and Taguchi (Ref. 5.6.), except they used centrifugation for sample clean-up. It is also of note that they did a comparison of their HPLC results to those of the Jaffe method (a picric acid method commonly used in the health care industry) and found a linear relationship of close to 1:1. This indicates that either HPLC or colorimetric methods may be used to measure creatinine concentrations in urine.

1.1.2. Physical properties (Ref. 5.7.)

Molecular weight: 113.12

Molecular formula: C_4–H_7–N_3–O

Chemical name: 2–amino–1,5–dihydro–1–methyl–4H–imidazol–4–one

CAS#: 60–27–5

Melting point: 300 °C (decomposes)

Appearance: white powder

Solubility: soluble in water; slightly soluble in alcohol; practically insoluble in acetone, ether, and chloroform

Synonyms: 1–methylglycocyamidine, 1–methylhydation–2–imide

Structure: see Figure #1

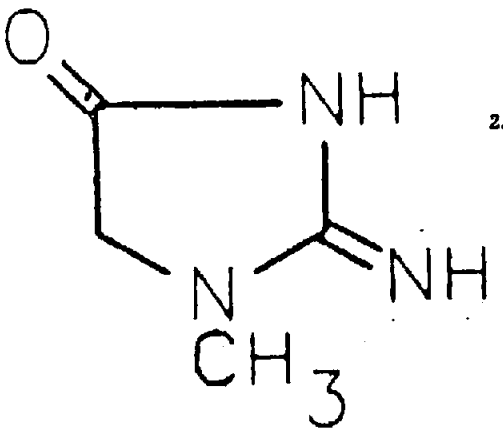


Figure #1

1.2 Advantages

1.2.1. This method offers a simple, straightforward, and specific alternative method to the Jaffe method.

1.2.2. HPLC instrumentation is commonly found in many industrial hygiene laboratories.

2. Sample Stabilization Procedure

2.1. Apparatus

Metal-free plastic container for urine sample.

2.2. Reagents

2.2.1. Stabilizing Solution—1) Nitric acid (10%, high purity with low Cd background levels) for stabilizing urine for Cd analysis or 2) NaOH, 0.11 N, for stabilizing urine for B2M analysis.

2.2.2. HPLC grade water

2.3. Technique

2.3.1. Stabilizing solution is added to the urine sample (see section 2.2.1.). The stabilizing solution should be such that for each 10 mL of urine, add exactly 1.0 mL of stabilizer solution. (Never add water or urine to acid or base. Always add acid or base to water or urine.) Exactly 1.0 mL of 0.11 N NaOH added to 10 mL of urine should result in a pH of 7. Or add 1.0 mL of 10% nitric acid to 10 mL of urine.

2.3.2. After sample collection seal the plastic bottle securely and wrap it with an appropriate seal. Urine samples should be frozen and then shipped by overnight mail (if shipping is necessary) in an insulated container. (Do not fill plastic bottle too full. This will allow for expansion of contents during the freezing process.)

2.4. The Effect of Preparation and Stabilization Techniques on Creatinine Concentrations

Three urine samples were prepared by making one sample acidic, not treating a second sample, and adjusting a third sample to pH 7. The samples were analyzed in duplicate by two different procedures. For the first procedure a 1.0 mL aliquot of urine was put in a 100-mL volumetric flask, diluted to volume with HPLC grade water, and then analyzed directly on an HPLC. The other procedure used SEP–PAKs. The SEP–PAK was rinsed with approximately 5 mL of methanol followed by approximately 10 mL of HPLC grade water and both rinses were discarded. Then, 1.0 mL of the urine sample was put through the SEP–PAK, followed by 30 mL of HPLC grade water. The urine and water were transferred to a 100-mL volumetric flask, diluted to volume with HPLC grade water, and analyzed by HPLC. These three urine samples were analyzed on the day they were obtained and then frozen. The results show that whether the urine is acidic, untreated or adjusted to pH 7, the resulting answer for creatinine is essentially unchanged. The purpose of stabilizing the urine by making it acidic or neutral is for the analysis of Cd or B2M respectively.

COMPARISON OF PREPARATION AND STABILIZATION TECHNIQUES

Sample	w/o SEP-PAK (g/L creatinine)	with SEP-PAK (g/L creatinine)
Acid	1.10	1.10
Acid	1.11	1.10
Untreated	1.12	1.11
Untreated	1.11	1.12
pH7	1.08	1.02
pH7	1.11	1.08

2.5. Storage

After 4 days and 54 days of storage in a freezer, the samples were thawed, brought to room temperature and analyzed using the same procedures as in section 2.4. The results of several days of storage show that the resulting answer for creatinine is essentially unchanged.

STORAGE DATA

Sample	4 days		54 days	
	w/o SEP-PAK (g/L creatinine)	with SEP-PAK (g/L creatinine)	w/o SEP-PAK (g/L creatinine)	with SEP-PAK (g/L creatinine)
Acid	1.09	1.09	1.08	1.09
Acid	1.10	1.10	1.09	1.10
Acid			1.09	1.09
Untreated	1.13	1.14	1.09	1.11
Untreated	1.15	1.14	1.10	1.10
Untreated			1.09	1.10

STORAGE DATA—Continued

Sample	4 days		54 days	
	w/o SEP-PAK (g/L creatinine)	with SEP-PAK (g/L creatinine)	w/o SEP-PAK (g/L creatinine)	with SEP-PAK (g/L creatinine)
pH 7	1.14	1.13	1.12	1.12
pH 7	1.14	1.13	1.12	1.12
pH 7			1.12	1.12

2.6. Interferences

None.

2.7. Safety precautions

2.7.1. Make sure samples are properly sealed and frozen before shipment to avoid leakage.

2.7.2. Follow the appropriate shipping procedures.

The following modified special safety precautions are based on those recommended by the Centers for Disease Control (CDC)(Ref. 5.8.).

2.7.3. Wear gloves, lab coat, and safety glasses while handling all human urine products. Disposable plastic, glass, and paper (pipet tips, gloves, etc.) that contact urine should be placed in a biohazard autoclave bag. These bags should be kept in appropriate containers until sealed and autoclaved. Wipe down all work surfaces with 10% sodium hypochlorite solution when work is finished.

2.7.4. Dispose of all biological samples and diluted specimens in a biohazard autoclave bag at the end of the analytical run.

2.7.5. Special care should be taken when handling and dispensing nitric acid. Always remember to add acid to water (or urine). Nitric acid is a corrosive chemical capable of severe eye and skin damage. Wear metal-free gloves, a lab coat, and safety glasses. If the nitric acid comes in contact with any part of the body, quickly wash with copious quantities of water for at least 15 minutes.

2.7.6. Special care should be taken when handling and dispensing NaOH. Always remember to add base to water (or urine). NaOH can cause severe eye and skin damage. Always wear the appropriate gloves, a lab coat, and safety glasses. If the NaOH comes in contact with any part of the body, quickly wash with copious quantities of water for at least 15 minutes.

3. Analytical Procedure

3.1. Apparatus

3.1.1. A high performance liquid chromatograph equipped with pump, sample injector and UV detector.

3.1.2. A C18 HPLC column; 25 cm × 4.6 mm I.D.

3.1.3. An electronic integrator, or some other suitable means of determining analyte response.

3.1.4. Stripchart recorder.

3.1.5. C18 SEP-PAKs (Waters Associates) or equivalent.

3.1.6. Luer-lock syringe for sample preparation (5 mL or 10 mL).

3.1.7. Volumetric pipettes and flasks for standard and sample preparation.

3.1.8. Vacuum system to aid sample preparation (optional).

3.2. Reagents

3.2.1. Water, HPLC grade.

3.2.2. Methanol, HPLC grade.

3.2.3. PIC B-7® (Waters Associates) in small vials.

3.2.4. Creatinine, anhydrous, Sigma Chemical Corp., purity not listed.

3.2.5. 1-Heptanesulfonic acid, sodium salt monohydrate.

3.2.6. Phosphoric acid.

3.2.7. Mobile phase. It can be prepared by mixing one vial of PIC B-7 into a 1 L solution of 50% methanol and 50% water. The mobile phase can also be made by preparing a solution that is 50% methanol and 50% water with 0.005M heptanesulfonic acid and adjusting the pH of the solution to 3.5 with phosphoric acid.

3.3. Standard preparation

3.3.1. Stock standards were prepared by weighing 10 to 15 mg of creatinine. This is transferred to a 25-mL volumetric flask and diluted to volume with HPLC grade water.

3.3.2. Dilutions to a working range of 3 to 35 μg/mL are made in either HPLC grade water or HPLC mobile phase (standards give the same detector response in either solution).

3.4. Sample preparation

3.4.1. The C18 SEP-PAK is connected to a Luer-lock syringe. It is rinsed with 5 mL HPLC grade methanol and then 10 mL of HPLC grade water. These rinses are discarded.

3.4.2. Exactly 1.0 mL of urine is pipetted into the syringe. The urine is put through the SEP-PAK into a suitable container using a vacuum system.

3.4.3. The walls of the syringe are rinsed in several stages with a total of approximately 30 mL of HPLC grade water. These rinses are put through the SEP-PAK into the same container. The resulting solution is transferred to a 100-mL volumetric flask and then brought to volume with HPLC grade water.

3.5. Analysis (conditions and hardware are those used in this evaluation.]

3.5.1. Instrument conditions

Column	Zorbax® ODS, 5-6 μm particle size; 25 cm × 4.6 mm I.D.
Mobile phase	See Section 3.2.7.
Detector	Dual wavelength UV; 229 nm (primary) 254 nm (secondary).
Flow rate	0.7 mL/minute.
Retention time	7.2 minutes.
Sensitivity	0.05 AUFS.
Injection volume.	20 μL.

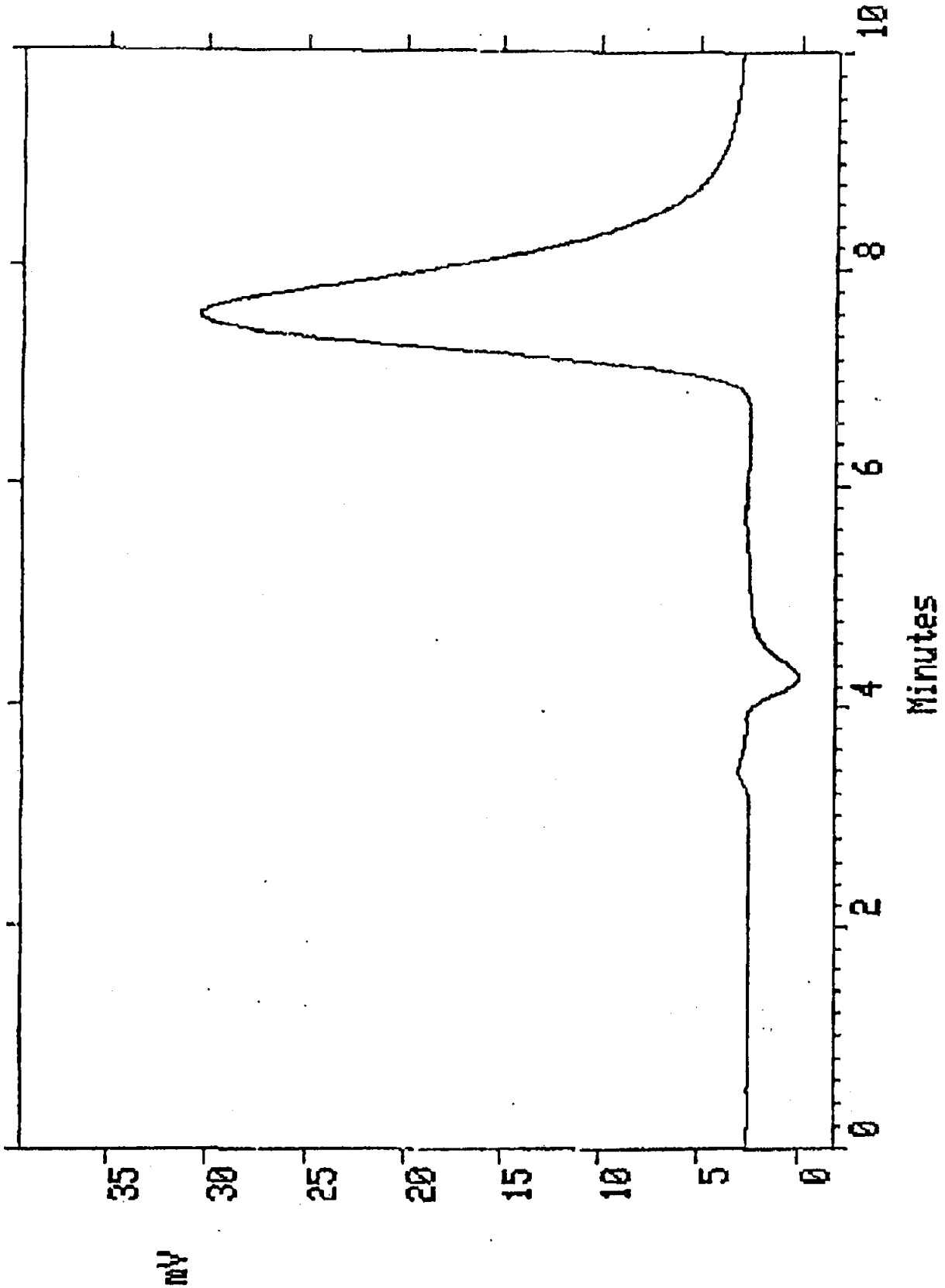
3.5.2. Chromatogram (See Figure #2).

3.6. Interferences

3.6.1. Any compound that has the same retention time as creatinine and absorbs at 229 nm is an interference.

3.6.2. HPLC conditions may be varied to circumvent interferences. In addition, analysis at another UV wavelength (i.e. 254 nm) would allow a comparison of the ratio of response of a standard to that of a sample. Any deviations would indicate an interference.

BILLING CODE 4510-26-M



BILLING CODE 4510-29-C

Chromatogram of a creatinine standard
Figure #2

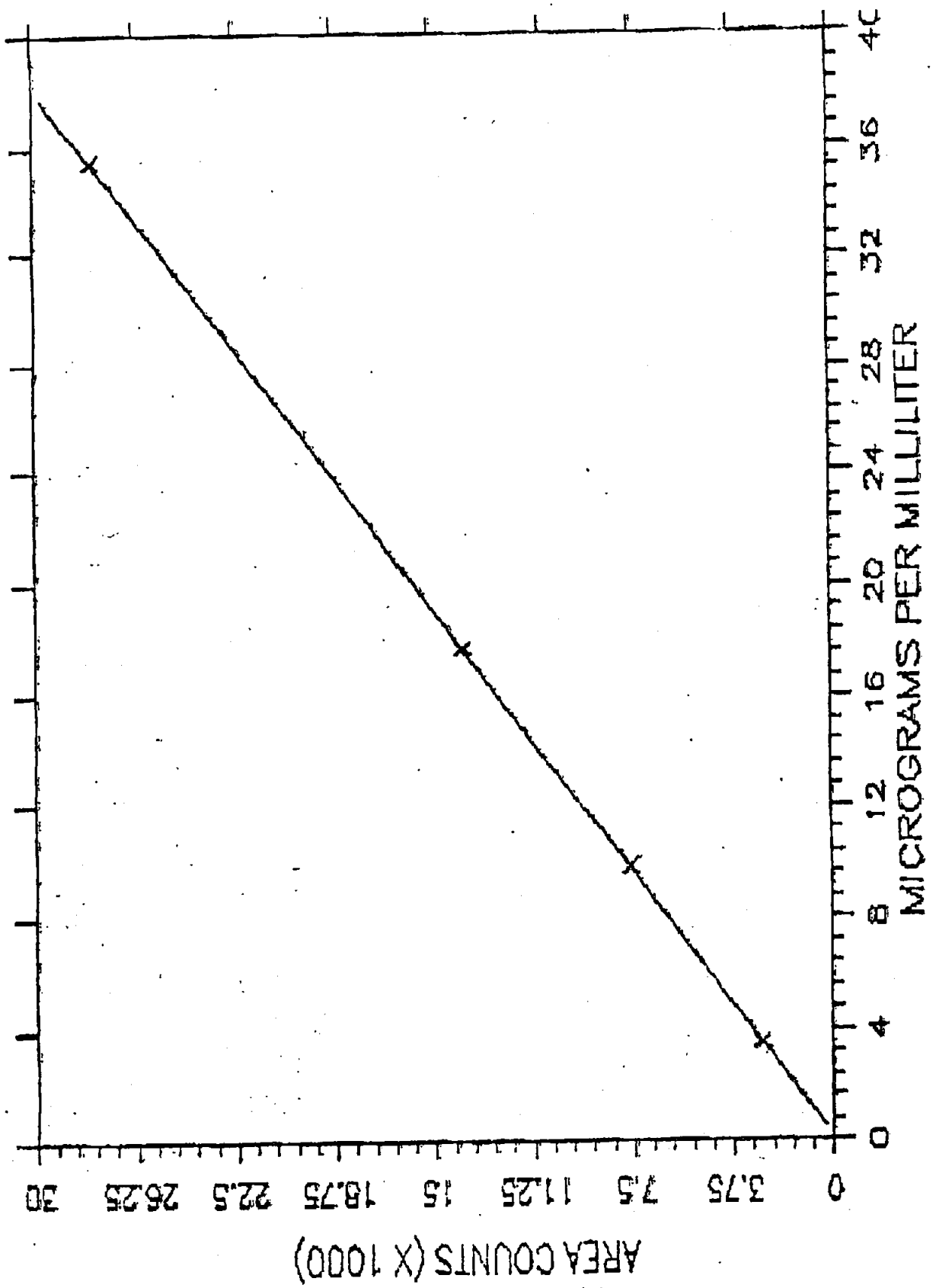
3.7. Calculations

3.7.1. A calibration curve is constructed by plotting detector response versus standard concentration (See Figure #3).

3.7.2. The concentration of creatinine in a sample is determined by finding the concentration corresponding to its detector response. (See Figure #3).

3.7.3. The μg/mL creatinine from section 3.7.2. is then multiplied by 100 (the dilution factor). This value is equivalent to the micrograms of creatinine in the 1.0 mL stabilized urine aliquot or the milligrams of creatinine per liter of urine. The desired unit, g/L, is determined by the following relationship:

BILLING CODE 4510-26-M



Calibration curve for creatinine
Figure #3

BILLING CODE 4510-29-C

$$g/L = \frac{\mu g/mL}{1000} = \frac{mg/L}{1000}$$

3.7.4. The resulting value for creatinine is used to normalize the urinary concentration of the desired analyte [A] (Cd or B2M) by using the following formula.

$$\mu g\ A/g\ creatinine = \frac{\mu g\ A/L\ (experimental)}{g/L\ creatinine}$$

Where A is the desired analyte. The protocol of reporting such normalized results is μg A/g creatinine.

3.8. Safety precautions. See section 2.7.

4. Conclusions

The determination of creatinine in urine by HPLC is a good alternative to the Jaffe method for industrial hygiene laboratories. Sample clarification with SEP-PAKs did not change the amount of creatinine found in urine samples. However, it does protect the analytical column. The results of this creatinine in urine procedure are unaffected by the pH of the urine sample under the conditions tested by this procedure. Therefore, no special measures are required for creatinine analysis whether the urine sample has been stabilized with 10% nitric acid for the Cd analysis or brought to a pH of 7 with 0.11 NaOH for the B2M analysis.

5. References

5.1. Clark, L.C.; Thompson, H.L.; *Anal. Chem.* 1949, 21, 1218.

5.2. Peters, J.H.; *J. Biol. Chem.* 1942, 146, 176.

5.3. Hausen, V.A.; Fuchs, D.; Wachter, H.; *J. Clin. Chem. Clin. Biochem.* 1981, 19, 373–378.

5.4. Clark, P.M.S.; Kricka, L.J.; Patel, A.; *J. Liq. Chrom.* 1980, 3(7), 1031–1046.

5.5. Ballerini, R.; Chinol, M.; Cambi, A.; *J. Chrom.* 1979, 179, 365–369.

5.6. Ogata, M.; Taguchi, T.; *Industrial Health* 1987, 25, 225–228.

5.7. "Merck Index", 11th ed.; Windholz, Martha Ed.; Merck: Rahway, N.J., 1989; p. 403.

5.8. Kimberly, M.; "*Determination of Cadmium in Urine by Graphite Furnace Atomic Absorption Spectrometry with Zeeman Background Correction.*" Centers for Disease Control, Atlanta, Georgia, unpublished, update 1990.

XI. Final Standard (Construction)

PART 1926—[AMENDED]

9. The authority citation for 29 CFR part 1926, Subpart D is revised as follows:

Authority: Sec. 107, Contract Work Hours and Safety Standards Act (Construction Safety Act) (40 U.S.C. 333); sec. 4, 6, 8 Occupational Safety and Health Act of 1970 (29 U.S.C. 653, 655, 657); Secretary of Labor's Order No. 12–71 (36 FR 8754), 8–76 (41 FR 25059), 9–83 (48 FR 35736) or 1–90 (55 FR 9033) as applicable.

Sections 1926.58, 1926.59, and 1926.60 also issued under 5 U.S.C. 553 and 29 CFR part 1911.

10. A new § 1926.63 with appendices A, B, C, D, E, and F are added to subpart D to read as set forth below. The text of appendices A, B, C, D, E, and F is identical to the text of appendices A, B, C, D, E, and F of § 1910.1027 of subpart 2 of part 1910.

§ 1926.63 Cadmium.

(a) *Scope.* This standard applies to all occupational exposures to cadmium and cadmium compounds, in all forms, in all construction work where an employee may potentially be exposed to cadmium. Construction work is defined as work involving construction, alteration and/or repair, including but not limited to the following:

(1) Wrecking, demolition or salvage of structures where cadmium or materials containing cadmium are present;

(2) Use of cadmium containing-paints and cutting, brazing, burning, grinding or welding on surfaces that were painted with cadmium-containing paints;

(3) Construction, alteration, repair, maintenance, or renovation of structures, substrates, or portions thereof, that contain cadmium, or materials containing cadmium;

(4) Cadmium welding; cutting and welding cadmium-plated steel; brazing or welding with cadmium alloys;

(5) Installation of products containing cadmium;

(6) Electrical grounding with cadwelding, or electrical work using cadmium-coated conduit;

(7) Maintaining or retrofitting cadmium-coated equipment;

(8) Cadmium contamination/emergency cleanup; and

(9) Transportation, disposal, storage, or containment of cadmium or materials containing cadmium on the site or location at which construction activities are performed.

(b) *Definitions.*

Action level (AL) is defined as an airborne concentration of cadmium of 2.5 micrograms per cubic meter of air (2.5 $\mu g/m^3$), calculated as an 8-hour time-weighted average (TWA).

Assistant Secretary means the Assistant Secretary of Labor for Occupational Safety and Health, U.S. Department of Labor, or designee.

Authorized person means any person authorized by the employer and required by work duties to be present in regulated areas or any person authorized by the OSH Act or regulations issued under it to be in regulated areas.

Competent person, in accordance with 29 CFR 1926.32(f), means a person designated by the employer to act on the employer's behalf who is capable of identifying existing and potential cadmium hazards in the workplace and the proper methods to control them in order to protect workers, and has the authority necessary to take prompt corrective measures to eliminate or control such hazards. The duties of a competent person include at least the following: Determining prior to the performance of work whether cadmium is present in the workplace; establishing, where necessary, regulated areas and assuring that access to and from those areas is limited to authorized employees; assuring the adequacy of any employee exposure monitoring required by this standard; assuring that all employees exposed to air cadmium levels above the PEL wear appropriate personal protective equipment and are trained in the use of appropriate methods of exposure control; assuring that proper hygiene facilities are provided and that workers are trained to use those facilities; and assuring that the engineering controls required by this standard are implemented, maintained in proper operating condition, and functioning properly.

Director means the Director of the National Institute for Occupational Safety and Health (NIOSH), U.S. Department of Health and Human Services, or designee.

Employee exposure and similar language referring to the air cadmium level to which an employee is exposed

means the exposure to airborne cadmium that would occur if the employee were not using respiratory protective equipment.

Final medical determination is the written medical opinion of the employee's health status by the examining physician under paragraphs (l)(3)-(12) of this section or, if multiple physician review under paragraph (l)(13) of this section or the alternative physician determination under paragraph (l)(14) of this section is invoked, it is the final, written medical finding, recommendation or determination that emerges from that process.

High-efficiency particulate absolute (HEPA) air filter means a filter capable of trapping and retaining at least 99.97 percent of mono-dispersed particles of 0.3 micrometers in diameter.

Regulated area means an area demarcated by the employer where an employee's exposure to airborne concentrations of cadmium exceeds, or can reasonably be expected to exceed the permissible exposure limit (PEL).

This section means this cadmium standard.

(c) *Permissible Exposure Limit (PEL).* The employer shall assure that no employee is exposed to an airborne concentration of cadmium in excess of five micrograms per cubic meter of air (5 $\mu g/m^3$), calculated as an eight-hour time-weighted average exposure (TWA).

(d) *Exposure Monitoring—(1) General.* (i) Prior to the performance of any construction work where employees may be potentially exposed to cadmium, the employer shall establish the applicability of this standard by determining whether cadmium is present in the workplace and whether there is the possibility that employee exposures will be at or above the action level. The employer shall designate a competent person who shall make this determination. Investigation and material testing techniques shall be used, as appropriate, in the determination. Investigation shall include a review of relevant plans, past reports, material safety data sheets, and other available records, and consultations with the property owner and discussions with appropriate individuals and agencies.

(ii) Where cadmium has been determined to be present in the workplace, and it has been determined that there is a possibility the employee's exposure will be at or above the action level, the competent person shall identify employees potentially exposed to cadmium at or above the action level.

(iii) Determinations of employee exposure shall be made from breathing-zone air samples that reflect the monitored employee's regular, daily 8-hour TWA exposure to cadmium.

(iv) Eight-hour TWA exposures shall be determined for each employee on the basis of one or more personal breathing-zone air samples reflecting full shift exposure on each shift, for each job classification, in each work area. Where several employees perform the same job tasks, in the same job classification, on the same shift, in the same work area, and the length, duration, and level of cadmium exposures are similar, an employer may sample a representative fraction of the employees instead of all employees in order to meet this requirement. In representative sampling, the employer shall sample the employee(s) expected to have the highest cadmium exposures.

(2) *Specific.* (i) Initial monitoring. Except as provided for in paragraph (d)(2)(iii) of this section, where a determination conducted under paragraph (d)(1)(i) of this section shows the possibility of employee exposure to cadmium at or above the action level, the employer shall conduct exposure monitoring as soon as practicable that is representative of the exposure for each employee in the workplace who is or may be exposed to cadmium at or above the action level.

(ii) In addition, if the employee periodically performs tasks that may expose the employee to a higher concentration of airborne cadmium, the employee shall be monitored while performing those tasks.

(iii) Where the employer has objective data, as defined in paragraph (n)(2) of this section, demonstrating that employee exposure to cadmium will not exceed airborne concentrations at or above the action level under the expected conditions of processing, use, or handling, the employer may rely upon such data instead of implementing initial monitoring.

(iv) Where a determination conducted under paragraphs (d)(1) or (d)(2) of this section is made that a potentially exposed employee is not exposed to airborne concentrations of cadmium at or above the action level, the employer shall make a written record of such determination. The record shall include at least the monitoring data developed under paragraphs (d)(2)(i)–(iii) of this section, where applicable, and shall also include the date of determination, and the name and social security number of each employee.

(3) *Monitoring frequency (periodic monitoring).* (i) If the initial monitoring or periodic monitoring reveals employee exposures to be at or above the action level, the employer shall monitor at a frequency and pattern needed to assure that the monitoring results reflect with reasonable accuracy the employee's typical exposure levels, given the variability in the tasks performed, work practices, and environmental conditions on the job site, and to assure the adequacy of respiratory selection and the effectiveness of engineering and work practice controls.

(ii) If the initial monitoring or the periodic monitoring indicates that employee exposures are below the action level and that result is confirmed by the results of another monitoring taken at least seven days later, the employer may discontinue the monitoring for those employees whose exposures are represented by such monitoring.

(4) *Additional monitoring.* The employer also shall institute the exposure monitoring required under paragraphs (d)(2)(i) and (d)(3) of this section whenever there has been a change in the raw materials, equipment, personnel, work practices, or finished products that may result in additional employees being exposed to cadmium at or above the action level or in employees already exposed to cadmium at or above the action level being exposed above the PEL, or whenever the employer or competent person has any reason to suspect that any other change might result in such further exposure.

(5) *Employee notification of monitoring results.* (i) No later than five working days after the receipt of the results of any monitoring performed under this section, the employer shall notify each affected employee individually in writing of the results. In addition, within the same time period, the employer shall post the results of the exposure monitoring in an appropriate location that is accessible to all affected employees.

(ii) Wherever monitoring results indicate that employee exposure exceeds the PEL, the employer shall include in the written notice a statement that the PEL has been exceeded and a description of the corrective action being taken by the employer to reduce employee exposure to or below the PEL.

(6) *Accuracy of measurement.* The employer shall use a method of monitoring and analysis that has an accuracy of not less than plus or minus 25 percent (± 25%), with a confidence level of 95 percent, for airborne concentrations of cadmium at or above the action level and the permissible exposure limit.

(e) *Regulated areas—(1) Establishment.* The employer shall establish a regulated area wherever an

employee's exposure to airborne concentrations of cadmium is, or can reasonably be expected to be in excess of the permissible exposure limit (PEL).

(2) *Demarcation.* Regulated areas shall be demarcated from the rest of the workplace in any manner that adequately establishes and alerts employees of the boundaries of the regulated area, including employees who are or may be incidentally in the regulated areas, and that protects persons outside the area from exposure to airborne concentrations of cadmium in excess of the PEL.

(3) *Access.* Access to regulated areas shall be limited to authorized persons.

(4) *Provision of respirators.* Each person entering a regulated area shall be supplied with and required to use a respirator, selected in accordance with paragraph (g)(2) of this section.

(5) *Prohibited activities.* The employer shall assure that employees do not eat, drink, smoke, chew tobacco or gum, or apply cosmetics in regulated areas, or carry the products associated with any of these activities into regulated areas or store such products in those areas.

(f) *Methods of compliance*—(1) *Compliance hierarchy.* (i) Except as specified in paragraph (f)(1)(ii) of this section, the employer shall implement engineering and work practice controls to reduce and maintain employee exposure to cadmium at or below the PEL, except to the extent that the employer can demonstrate that such controls are not feasible.

(ii) The requirement to implement engineering controls to achieve the PEL does not apply where the employer demonstrates the following:

(A) The employee is only intermittently exposed; and

(B) The employee is not exposed above the PEL on 30 or more days per year (12 consecutive months).

(iii) Wherever engineering and work practice controls are not sufficient to reduce employee exposure to or below the PEL, the employer nonetheless shall implement such controls to reduce exposures to the lowest levels achievable. The employer shall supplement such controls with respiratory protection that complies with the requirements of paragraph (g) of this section and the PEL.

(iv) The employer shall not use employee rotation as a method of compliance.

(2) *Specific operations*—(i) *Abrasive blasting.* Abrasive blasting on cadmium or cadmium-containing materials shall be conducted in a manner that will provide adequate protection.

(ii) *Heating cadmium and cadmium-containing materials.* Welding, cutting, and other forms of heating of cadmium or cadmium-containing materials shall be conducted in accordance with the requirements of 29 CFR 1926.353 and 29 CFR 1926.354, where applicable.

(3) *Prohibitions.* (i) High speed abrasive disc saws and similar abrasive power equipment shall not be used for work on cadmium or cadmium-containing materials unless they are equipped with appropriate engineering controls to minimize emissions, if the exposure levels are above the PEL.

(ii) Materials containing cadmium shall not be applied by spray methods, if exposures are above the PEL, unless employees are protected with supplied-air respirators with full facepiece, hood, helmet, suit, operated in positive pressure mode and measures are instituted to limit overspray and prevent contamination of adjacent areas.

(4) *Mechanical ventilation.* (i) When ventilation is used to control exposure, measurements that demonstrate the effectiveness of the system in controlling exposure, such as capture velocity, duct velocity, or static pressure shall be made as necessary to maintain its effectiveness.

(ii) Measurements of the system's effectiveness in controlling exposure shall be made as necessary within five working days of any change in production, process, or control that might result in a significant increase in employee exposure to cadmium.

(iii) Recirculation of air. If air from exhaust ventilation is recirculated into the workplace, the system shall have a high efficiency filter and be monitored to assure effectiveness.

(iv) Procedures shall be developed and implemented to minimize employee exposure to cadmium when maintenance of ventilation systems and changing of filters is being conducted.

(5) *Compliance program.* (i) Where the PEL is exceeded, the employer shall establish and implement a written compliance program to reduce employee exposure to or below the PEL by means of engineering and work practice controls, as required by paragraph (f)(1) of this section. To the extent that engineering and work practice controls cannot reduce exposures to or below the PEL, the employer shall include in the written compliance program the use of appropriate respiratory protection to achieve compliance with the PEL.

(ii) Written compliance programs shall be reviewed and updated as often and as promptly as necessary to reflect significant changes in the employer's compliance status or significant changes in the lowest air cadmium level that is technologically feasible.

(iii) A competent person shall review the comprehensive compliance program initially and after each change.

(iv) Written compliance programs shall be provided upon request for examination and copying to the Assistant Secretary, the Director, affected employees, and designated employee representatives.

(g) *Respirator protection*—(1) *General.* Where respirators are required by this section, the employer shall provide them at no cost to the employee and shall assure that they are used in compliance with the requirements of this section. Respirators shall be used in the following circumstances:

(i) Where exposure levels exceed the PEL, during the time period necessary to install or implement feasible engineering and work practice controls;

(ii) In those maintenance and repair activities and during those brief or intermittent operations where exposures exceed the PEL and engineering and work practice controls are not feasible, or are not required;

(iii) In regulated areas, as prescribed in paragraph (e) of this section;

(iv) Where the employer has implemented all feasible engineering and work practice controls and such controls are not sufficient to reduce exposures to or below the PEL;

(v) In emergencies;

(vi) Wherever an employee who is exposed to cadmium at or above the action level requests a respirator; and

(vii) Wherever an employee is exposed to cadmium above the PEL and engineering controls are not required under paragraph (f)(1)(ii) of this section.

(2) *Respirator selection.* (i) Where respirators are required under this section, the employer shall select and provide the appropriate respirator as specified in Table 1. The employer shall select respirators from among those jointly approved as acceptable protection against cadmium dust, fume, and mist by the Mine Safety and Health Administration (MSHA) and by the National Institute for Occupational Safety and Health (NIOSH) under the provisions of 30 CFR part 11.

TABLE 1.—RESPIRATORY PROTECTION FOR CADMIUM

Airborne concentration or condition of use [a]	Required respirator type [b]
10 × or less	A half mask, air-purifying respirator equipped with a HEPA [c] filter.[d]
25 × or less	A powered air-purifying respirator ("PAPR" with a loose-fitting hood or helmet equipped with a HEPA filter, or a supplied-air respirator with a loose-fitting hood or helmet facepiece operated in the continuous flow mode.
50 × or less	A full facepiece air-purifying respirator equipped with a HEPA filter, or a powered air-purifying respirator with a tight-fitting half mask equipped with a HEPA filter, or a supplied air respirator with a tight-fitting half mask operated in the continuous flow mode.
250 × or less	A powered air-purifying respirator with a tight-fitting full facepiece equipped with a HEPA filter, or a supplied-air respirator with a tight-fitting full facepiece operated in the continuous flow mode.
1000 × or less	A supplied-air respirator with half mask or full facepiece operated in the pressure demand or other positive pressure mode.
>1000 × or unknown concentrations	A self-contained breathing apparatus with unknown concentrations a full facepiece operated in the pressure demand or other positive pressure mode, or a supplied-air respirator with a full facepiece operated in the pressure demand or other positive pressure mode and equipped with an auxiliary escape type self contained breathing apparatus operated in the pressure demand mode.
Fire fighting	A self-contained breathing apparatus with full facepiece operated in the pressure demand or other positive pressure mode.

[a] Concentrations expressed as multiple of the PEL.
[b] Respirators assigned for higher environmental concentrations may be used at lower exposure levels. Quantitative fit testing is required for all tight-fitting air purifying respirators where airborne concentration of cadmium exceeds 10 times the TWA PEL (10×5 μg/m³=50 μg/m³). A full facepiece respirator is required when eye irritation is experienced.
[c] HEPA means High Efficiency Particulate Absolute.
[d] Fit testing, qualitative or quantitative, is required.
Source: *Respiratory Decision Logic*, NIOSH, 1987.

(ii) The employer shall provide a powered, air-purifying respirator (PAPR) in lieu of a negative pressure respirator wherever:

(A) An employee entitled to a respirator chooses to use this type of respirator; and

(B) This respirator will provide adequate protection to the employee.

(3) *Respirator program.* (i) Where respiratory protection is required, the employer shall institute a respirator protection program in accordance with 29 CFR 1910.134.

(ii) The employer shall permit each employee who is required to use an air purifying respirator to leave the regulated area to change the filter elements or replace the respirator whenever an increase in breathing resistance is detected and shall maintain an adequate supply of filter elements for this purpose.

(iii) The employer shall also permit each employee who is required to wear a respirator to leave the regulated area to wash his or her face and the respirator facepiece whenever necessary to prevent skin irritation associated with respirator use.

(iv) If an employee exhibits difficulty in breathing while wearing a respirator during a fit test or during use, the employer shall make available to the employee a medical examination in accordance with paragraph (l)(6)(ii) of this section to determine if the employee can wear a respirator while performing the required duties.

(v) No employee shall be assigned a task requiring the use of a respirator if, based upon his or her most recent examination, an examining physician determines that the employee will be unable to continue to function normally while wearing a respirator. If the physician determines the employee must be limited in, or removed from his or her current job because of the employee's inability to wear a respirator, the limitation or removal shall be in accordance with paragraphs (l) (11) and (12) of this section.

(4) *Respirator fit testing.* (i) The employer shall assure that the respirator issued to the employee is fitted properly and exhibits the least possible facepiece leakage.

(ii) For each employee wearing a tight-fitting, air purifying respirator (either negative or positive pressure) who is exposed to airborne concentrations of cadmium that do not exceed 10 times the PEL ($10 \times 5\ \mu g/m^3 = 50\ \mu g/m^3$), the employer shall perform either quantitative or qualitative fit testing at the time of initial fitting and at least annually thereafter. If quantitative fit testing is used for a negative pressure respirator, a fit factor that is at least 10 times the protection factor for that class of respirators (Table 1 in paragraph (g)(2)(i) of this section) shall be achieved at testing.

(iii) For each employee wearing a tight-fitting air purifying respirator (either negative or positive pressure) who is exposed to airborne concentrations of cadmium that exceed 10 times the PEL ($10 \times 5\ \mu g/m^3 = 50\ \mu g/m^3$), the employer shall perform quantitative fit testing at the time of initial fitting and at least annually thereafter. For negative-pressure respirators, a fit factor that is at least ten times the protection factor for that class of respirators (Table 1 in paragraph (g)(2)(i) of this section) shall be achieved during quantitative fit testing.

(iv) For each employee wearing a tight-fitting, supplied-air respirator or self-contained breathing apparatus, the employer shall perform quantitative fit testing at the time of initial fitting and at least annually thereafter. This shall be accomplished by fit testing an air purifying respirator of identical type facepiece, make, model, and size as the supplied air respirator or self-contained breathing apparatus that is equipped with HEPA filters and tested as a surrogate (substitute) in the negative pressure mode. A fit factor that is at least 10 times the protection factor for that class of respirators (Table 1 in paragraph (g)(2)(i) of this section) shall be achieved during quantitative fit testing. A supplied-air respirator or self-contained breathing apparatus with the same type facepiece, make, model, and size as the air purifying respirator with which the employee passed the quantitative fit test may then be used by that employee up to the protection factor listed in Table 1 in paragraph (g)(2)(i) of this section for that class of respirators.

(v) Fit testing shall be conducted in accordance with Appendix C of this section.

(h) *Emergency situations.* The employer shall develop and implement a written plan for dealing with emergency situations involving substantial releases of airborne cadmium. The plan shall include provisions for the use of appropriate respirators and personal protective equipment. In addition, employees not essential to correcting the emergency situation shall be restricted from the area and normal

operations halted in that area until the emergency is abated.

(i) *Protective work clothing and equipment*—(1) *Provision and use.* If an employee is exposed to airborne cadmium above the PEL or where skin or eye irritation is associated with cadmium exposure at any level, the employer shall provide at no cost to the employee, and assure that the employee uses, appropriate protective work clothing and equipment that prevents contamination of the employee and the employee's garments. Protective work clothing and equipment includes, but is not limited to:

(i) Coveralls or similar full-body work clothing;

(ii) Gloves, head coverings, and boots or foot coverings; and

(iii) Face shields, vented goggles, or other appropriate protective equipment that complies with 29 CFR 1910.133.

(2) *Removal and storage.* (i) The employer shall assure that employees remove all protective clothing and equipment contaminated with cadmium at the completion of the work shift and do so only in change rooms provided in accordance with paragraph (j)(1) of this section.

(ii) The employer shall assure that no employee takes cadmium-contaminated protective clothing or equipment from the workplace, except for employees authorized to do so for purposes of laundering, cleaning, maintaining, or disposing of cadmium-contaminated protective clothing and equipment at an appropriate location or facility away from the workplace.

(iii) The employer shall assure that contaminated protective clothing and equipment, when removed for laundering, cleaning, maintenance, or disposal, is placed and stored in sealed, impermeable bags or other closed, impermeable containers that are designed to prevent dispersion of cadmium dust.

(iv) The employer shall assure that containers of contaminated protective clothing and equipment that are to be taken out of the change rooms or the workplace for laundering, cleaning, maintenance or disposal shall bear labels in accordance with paragraph (m)(2) of this section.

(3) *Cleaning, replacement, and disposal.* (i) The employer shall provide the protective clothing and equipment required by paragraph (i)(1) of this section in a clean and dry condition as often as necessary to maintain its effectiveness, but in any event at least weekly. The employer is responsible for cleaning and laundering the protective clothing and equipment required by this paragraph to maintain its effectiveness and is also responsible for disposing of such clothing and equipment.

(ii) The employer also is responsible for repairing or replacing required protective clothing and equipment as needed to maintain its effectiveness. When rips or tears are detected while an employee is working they shall be immediately mended, or the worksuit shall be immediately replaced.

(iii) The employer shall prohibit the removal of cadmium from protective clothing and equipment by blowing, shaking, or any other means that disperses cadmium into the air.

(iv) The employer shall assure that any laundering of contaminated clothing or cleaning of contaminated equipment in the workplace is done in a manner that prevents the release of airborne cadmium in excess of the permissible exposure limit prescribed in paragraph (c) of this section.

(v) The employer shall inform any person who launders or cleans protective clothing or equipment contaminated with cadmium of the potentially harmful effects of exposure to cadmium, and that the clothing and equipment should be laundered or cleaned in a manner to effectively prevent the release of airborne cadmium in excess of the PEL.

(j) *Hygiene areas and practices.*—(1) *General.* For employees whose airborne exposure to cadmium is above the PEL, the employer shall provide clean change rooms, handwashing facilities, showers, and lunchroom facilities that comply with 29 CFR 1926.51.

(2) *Change rooms.* The employer shall assure that change rooms are equipped with separate storage facilities for street clothes and for protective clothing and equipment, which are designed to prevent dispersion of cadmium and contamination of the employee's street clothes.

(3) *Showers and handwashing facilities.* (i) The employer shall assure that employees whose airborne exposure to cadmium is above the PEL shower during the end of the work shift.

(ii) The employer shall assure that employees who are exposed to cadmium above the PEL wash their hands and faces prior to eating, drinking, smoking, chewing tobacco or gum, or applying cosmetics.

(4) *Lunchroom facilities.* (i) The employer shall assure that the lunchroom facilities are readily accessible to employees, that tables for eating are maintained free of cadmium, and that no employee in a lunchroom facility is exposed at any time to cadmium at or above a concentration of 2.5 $\mu g/m^3$.

(ii) The employer shall assure that employees do not enter lunchroom facilities with protective work clothing or equipment unless surface cadmium has been removed from the clothing and equipment by HEPA vacuuming or some other method that removes cadmium dust without dispersing it.

(k) *Housekeeping.* (1) All surfaces shall be maintained as free as practicable of accumulations of cadmium.

(2) All spills and sudden releases of material containing cadmium shall be cleaned up as soon as possible.

(3) Surfaces contaminated with cadmium shall, wherever possible, be cleaned by vacuuming or other methods that minimize the likelihood of cadmium becoming airborne.

(4) HEPA-filtered vacuuming equipment or equally effective filtration methods shall be used for vacuuming. The equipment shall be used and emptied in a manner that minimizes the reentry of cadmium into the workplace.

(5) Shoveling, dry or wet sweeping, and brushing may be used only where vacuuming or other methods that minimize the likelihood of cadmium becoming airborne have been tried and found not to be effective.

(6) Compressed air shall not be used to remove cadmium from any surface unless the compressed air is used in conjunction with a ventilation system designed to capture the dust cloud created by the compressed air.

(7) Waste, scrap, debris, bags, containers, personal protective equipment, and clothing contaminated with cadmium and consigned for disposal shall be collected and disposed of in sealed impermeable bags or other closed, impermeable containers. These bags and containers shall be labeled in accordance with paragraph (m)(2) of this section.

(l) *Medical Surveillance.*—(1) *General.*—(i) *Scope.* (A) Currently exposed—The employer shall institute a medical surveillance program for all employees who are or may be exposed at or above the action level and all employees who perform the following tasks, operations or jobs: Electrical grounding with cadwelding; cutting, brazing, burning, grinding or welding on surfaces that were painted with cadmium-containing paints; electrical work using cadmium-coated conduit; use of cadmium containing paints; cutting and welding cadmium-plated steel; brazing or welding with cadmium alloys; fusing of reinforcing steel by cadmium welding; maintaining or retrofitting cadmium-coated equipment; and, wrecking and demolition where

cadmium is present. A medical surveillance program will not be required if the employer demonstrates that the employee:

(1) Is not currently exposed by the employer to airborne concentrations of cadmium at or above the action level on 30 or more days per year (twelve consecutive months); and,

(2) Is not currently exposed by the employer in those tasks on 30 or more days per year (twelve consecutive months).

(B) Previously exposed—The employer shall also institute a medical surveillance program for all employees who might previously have been exposed to cadmium by the employer prior to the effective date of this standard in tasks specified under paragraph (l)(1)(i)(A) of this section, unless the employer demonstrates that the employee did not in the years prior to the effective date of this section work in those tasks for the employer with exposure to cadmium for an aggregated total of more than 12 months.

(ii) To determine an employee's fitness for using a respirator, the employer shall provide the limited medical examination specified in paragraph (l)(6) of this section.

(iii) The employer shall assure that all medical examinations and procedures required by this section are performed by or under the supervision of a licensed physician, who has read and is familiar with the health effects section of appendix A to this section, the regulatory text of this section, the protocol for sample handling and lab selection in appendix F to this section, and the questionnaire of appendix D to this section.

(iv) The employer shall provide the medical surveillance required by this section, including multiple physician review under paragraph (l)(13) of this section without cost to employees, and at a time and place that is reasonable and convenient to employees.

(v) The employer shall assure that the collecting and handling of biological samples of cadmium in urine (CdU), cadmium in blood (CdB), and beta-2 microglobulin in urine (β_2-M) taken from employees under this section is done in a manner that assures their reliability and that analysis of biological samples of cadmium in urine (CdU), cadmium in blood (CdB), and beta-2 microglobulin in urine (β_2-M) taken from employees under this section is performed in laboratories with demonstrated proficiency to perform the particular analysis. (See appendix F to this section.)

(2) *Initial Examination.* (i) For employees covered by medical surveillance under paragraph (l)(1)(i) of this section, the employer shall provide an initial medical examination. The examination shall be provided to those employees within 30 days after initial assignment to a job with exposure to cadmium or no later than 90 days after the effective date of this section, whichever date is later.

(ii) The initial medical examination shall include:

(A) A detailed medical and work history, with emphasis on: Past, present, and anticipated future exposure to cadmium; any history of renal, cardiovascular, respiratory, hematopoietic, reproductive, and/or musculo-skeletal system dysfunction; current usage of medication with potential nephrotoxic side-effects; and smoking history and current status; and

(B) Biological monitoring that includes the following tests:

(1) Cadmium in urine (CdU), standardized to grams of creatinine (g/Cr);

(2) Beta-2 microglobulin in urine (β_2-M), standardized to grams of creatinine (g/Cr), with pH specified, as described in Appendix F to this section; and

(3) Cadmium in blood (CdB), standardized to liters of whole blood (lwb).

(iii) Recent Examination: An initial examination is not required to be provided if adequate records show that the employee has been examined in accordance with the requirements of paragraph (l)(2)(ii) of this section within the past 12 months. In that case, such records shall be maintained as part of the employee's medical record and the prior exam shall be treated as if it were an initial examination for the purposes of paragraphs (l)(3) and (4) of this section.

(3) *Actions triggered by initial biological monitoring.* (i) If the results of the biological monitoring tests in the initial examination show the employee's CdU level to be at or below 3μg/g Cr, β_2-M level to be at or below 300μg/g Cr and CdB level to be at or below 5μg/lwb, then:

(A) For employees who are subject to medical surveillance under paragraphs (l)(1)(i)(A) of this section because of current or anticipated exposure to cadmium, the employer shall provide the minimum level of periodic medical surveillance in accordance with the requirements in paragraph (l)(4)(i) of this section; and

(B) For employees who are subject to medical surveillance under paragraph (l)(1)(i)(B) of this section because of prior but not current exposure, the employer shall provide biological monitoring for CdU, B_2-M, and CdB within one year after the initial biological monitoring and then the employer shall comply with the requirements of paragraph (l)(4)(vi) of this section.

(ii) For all employees who are subject to medical surveillance under paragraph (l)(1)(i) of this section, if the results of the initial biological monitoring tests show the level of CdU to exceed 3 μg/g Cr, the level of β_2-M to be in excess of 300 μg/g Cr, or the level of CdB to be in excess of 5 μg/lwb, the employer shall:

(A) Within two weeks after receipt of biological monitoring results, reassess the employee's occupational exposure to cadmium as follows:

(1) Reassess the employee's work practices and personal hygiene;

(2) Reevaluate the employee's respirator use, if any, and the respirator program;

(3) Review the hygiene facilities;

(4) Reevaluate the maintenance and effectiveness of the relevant engineering controls;

(5) Assess the employee's smoking history and status;

(B) Within 30 days after the exposure reassessment, specified in paragraph (l)(3)(ii)(A) of this section, take reasonable steps to correct any deficiencies found in the reassessment that may be responsible for the employee's excess exposure to cadmium; and,

(C) Within 90 days after receipt of biological monitoring results, provide a full medical examination to the employee in accordance with the requirements of paragraph (l)(4)(ii) of this section. After completing the medical examination, the examining physician shall determine in a written medical opinion whether to medically remove the employee. If the physician determines that medical removal is not necessary, then until the employee's CdU level falls to or below 3 μg/g Cr, β_2-M level falls to or below 300 μg/g Cr and CdB level falls to or below 5 μg/lwb, the employer shall:

(*1*) Provide biological monitoring in accordance with paragraph (l)(2)(ii)(B) of this section on a semiannual basis; and

(*2*) Provide annual medical examinations in accordance with paragraph (l)(4)(ii) of this section.

(iii) For all employees who are subject to medical surveillance under paragraph (l)(1)(i) of this section, if the results of the initial biological monitoring tests show the level of CdU to be in excess of 15 μg/g Cr, or the level of CdB to be in excess of 15 μg/lwb, or the level of β_2-M to be in excess of 1,500 μg/g Cr, the employer shall comply with the

requirements of paragraphs (l)(3)(ii)(A)–(B) of this section. Within 90 days after receipt of biological monitoring results, the employer shall provide a full medical examination to the employee in accordance with the requirements of paragraph (l)(4)(ii) of this section. After completing the medical examination, the examining physician shall determine in a written medical opinion whether to medically remove the employee. However, if the initial biological monitoring results and the biological monitoring results obtained during the medical examination both show that: CdU exceeds 15 μg/g Cr; or CdB exceeds 15 μg/lwb; or β_2-M exceeds 1500 μg/g Cr, and in addition CdU exceeds 3 μg/g Cr or CdB exceeds 5 μg/liter of whole blood, then the physician shall medically remove the employee from exposure to cadmium at or above the action level. If the second set of biological monitoring results obtained during the medical examination does not show that a mandatory removal trigger level has been exceeded, then the employee is not required to be removed by the mandatory provisions of this paragraph. If the employee is not required to be removed by the mandatory provisions of this paragraph or by the physician's determination, then until the employee's CdU level falls to or below 3 μg/g Cr, β_2-M level falls to or below 300 μg/g Cr and CdB level falls to or below 5 μg/lwb, the employer shall:

(A) Periodically reassess the employee's occupational exposure to cadmium;

(B) Provide biological monitoring in accordance with paragraph (l)(2)(ii)(B) of this section on a quarterly basis; and

(C) Provide semiannual medical examinations in accordance with paragraph (l)(4)(ii) of this section.

(iv) For all employees to whom medical surveillance is provided, beginning on January 1, 1999, and in lieu of paragraph (l)(3)(iii) of this section, whenever the results of initial biological monitoring tests show the employee's CdU level to be in excess of 7 μg/g Cr, or β_2-M level to be in excess of 750 μg/g Cr, or CdB level to be in excess of 10 μg/lwb, the employer shall comply with the requirements of paragraphs (l)(3)(ii)(A)–(B) of this section. Within 90 days after receipt of biological monitoring results, the employer shall provide a full medical examination to the employee in accordance with the requirements of paragraph (l)(4)(ii) of this section. After completing the medical examination, the examining physician shall determine in a written medical opinion whether to medically remove the employee. However, if the initial biological monitoring results and the biological monitoring results obtained during the medical examination both show that: CdU exceeds 7 μg/g Cr; or CdB exceeds 10 μg/lwb; or β_2-M exceeds 750 μg/g Cr, and in addition CdU exceeds 3 μg/g Cr or CdB exceeds 5 μg/liter of whole blood, then the physician shall medically remove the employee from exposure to cadmium at or above the action level. If the second set of biological monitoring results obtained during the medical examination does not show that a mandatory removal trigger level has been exceeded, then the employee is not required to be removed by the mandatory provisions of this paragraph. If the employee is not required to be removed by the mandatory provisions of this paragraph or by the physician's determination, then until the employee's CdU level falls to or below 3 μg/g Cr, β_2-M level falls to or below 300 μg/g Cr and CdB level falls to or below 5 μg/lwb, the employer shall:

(A) Periodically reassess the employee's occupational exposure to cadmium;

(B) Provide biological monitoring in accordance with paragraph (l)(2)(ii)(B) of this section on a quarterly basis; and

(C) Provide semiannual medical examinations in accordance with paragraph (l)(4)(ii) of this section.

(4) *Periodic medical surveillance.* (i) For each employee who is covered by medical surveillance under paragraph (l)(1)(i)(A) of this section because of current or anticipated exposure to cadmium, the employer shall provide at least the minimum level of periodic medical surveillance, which consists of periodic medical examinations and periodic biological monitoring. A periodic medical examination shall be provided within one year after the initial examination required by paragraph (l)(2) of this section and thereafter at least biennially. Biological sampling shall be provided at least annually either as part of a periodic medical examination or separately as periodic biological monitoring.

(ii) The periodic medical examination shall include:

(A) A detailed medical and work history, or update thereof, with emphasis on: Past, present and anticipated future exposure to cadmium; smoking history and current status; reproductive history; current use of medications with potential nephrotoxic side-effects; any history of renal, cardiovascular, respiratory, hematopoietic, and/or musculo-skeletal system dysfunction; and as part of the medical and work history, for employees who wear respirators, questions 3–11 and 25–32 in appendix D to this section;

(B) A complete physical examination with emphasis on: blood pressure, the respiratory system, and the urinary system;

(C) A 14 inch by 17 inch, or a reasonably standard sized posterior-anterior chest X-ray (after the initial X-ray, the frequency of chest X-rays is to be determined by the examining physician);

(D) Pulmonary function tests, including forced vital capacity (FVC) and forced expiratory volume at 1 second (FEV1);

(E) Biological monitoring, as required in paragraph (l)(2)(ii)(B) of this section;

(F) Blood analysis, in addition to the analysis required under paragraph (l)(2)(ii)(B) of this section, including blood urea nitrogen, complete blood count, and serum creatinine;

(G) Urinalysis, in addition to the analysis required under paragraph (l)(2)(ii)(B) of this section, including the determination of albumin, glucose, and total and low molecular weight proteins;

(H) For males over 40 years old, prostate palpation, or other at least as effective diagnostic test(s), and;

(I) Any additional tests or procedures deemed appropriate by the examining physician.

(iii) Periodic biological monitoring shall be provided in accordance with paragraph (l)(2)(ii)(B) of this section.

(iv) If the results of periodic biological monitoring or the results of biological monitoring performed as part of the periodic medical examination show the level of the employee's CdU, β_2–M, or CdB to be in excess of the levels specified in paragraphs (l)(3)(iii) of this section; or, beginning on January 1, 1999, in excess of the levels specified in paragraph (l)(3)(iv), the employer shall take the appropriate actions specified in paragraphs (l)(3)(iii)–(iv) of this section, respectively.

(v) For previously exposed employees under paragraph (l)(1)(i)(B) of this section:

(A) If the employee's levels of CdU did not exceed 3 μg/g Cr, CdB did not exceed 5 μg/lwb, and β_2–M did not exceed 300 μg/g Cr in the initial biological monitoring tests, and if the results of the followup biological monitoring required by paragraph (l)(3)(i)(B) of this section within one year after the initial examination confirm the previous results, the employer may discontinue all periodic medical surveillance for that employee.

(B) If the initial biological monitoring results for CdU, CdB, or β_2–M were in excess of the levels specified in

paragraph (l)(3)(i) of this section, but subsequent biological monitoring results required by paragraph (l)(3)(ii)–(iv) of this section show that the employee's CdU levels no longer exceed 3 μg/g Cr, CdB levels no longer exceed 5 μg/l wb, and β_2–M levels no longer exceed 300 μg/g Cr, the employer shall provide biological monitoring for CdU, CdB, and β_2–M within one year after these most recent biological monitoring results. If the results of the followup biological monitoring within one year, specified in this paragraph, confirm the previous results, the employer may discontinue all periodic medical surveillance for that employee.

(C) However, if the results of the follow-up tests specified in paragraph (l)(4)(v)(A) or (B) of this section indicate that the level of the employee's CdU, β_2–M, or CdB exceeds these same levels, the employer is required to provide annual medical examinations in accordance with the provisions of paragraph (l)(4)(ii) of this section until the results of biological monitoring are consistently below these levels or the examining physician determines in a written medical opinion that further medical surveillance is not required to protect the employee's health.

(vi) A routine, biennial medical examination is not required to be provided in accordance with paragraphs (l)(3)(i) and (l)(4) of this section if adequate medical records show that the employee has been examined in accordance with the requirements of paragraph (l)(4)(ii) of this section within the past 12 months. In that case, such records shall be maintained by the employer as part of the employee's medical record, and the next routine, periodic medical examination shall be made available to the employee within two years of the previous examination.

(5) *Actions triggered by medical examinations.* (i) If the results of a medical examination carried out in accordance with this section indicate any laboratory or clinical finding consistent with cadmium toxicity that does not require employer action under paragraphs (l)(2), (3) or (4) of this section, the employer shall take the following steps and continue to take them until the physician determines that they are no longer necessary.

(A) Periodically reassess: The employee's work practices and personal hygiene; the employee's respirator use, if any; the employee's smoking history and status; the respiratory protection program; the hygiene facilities; the maintenance and effectiveness of the relevant engineering controls; and take all reasonable steps to correct the deficiencies found in the reassessment that may be responsible for the employee's excess exposure to cadmium.

(B) Provide semi-annual medical reexaminations to evaluate the abnormal clinical sign(s) of cadmium toxicity until the results are normal or the employee is medically removed; and

(C) Where the results of tests for total proteins in urine are abnormal, provide a more detailed medical evaluation of the toxic effects of cadmium on the employee's renal system.

(6) *Examination for respirator use.* (i) To determine an employee's fitness for respirator use, the employer shall provide a medical examination that includes the elements specified in paragraph (l)(6)(i)(A)–(D) of this section. This examination shall be provided prior to the employee's being assigned to a job that requires the use of a respirator or no later than 90 days after this section goes into effect, whichever date is later, to any employee without a medical examination within the preceding 12 months that satisfies the requirements of this paragraph.

(A) A detailed medical and work history, or update thereof, with emphasis on: past exposure to cadmium; smoking history and current status; any history of renal, cardiovascular, respiratory, hematopoietic, and/or musculo-skeletal system dysfunction; a description of the job for which the respirator is required; and questions 3–11 and 25–32 in appendix D;

(B) A blood pressure test;

(C) Biological monitoring of the employee's levels of CdU, CdB and β_2–M in accordance with the requirements of paragraph (l)(2)(ii)(B) of this section, unless such results already have been obtained within the twelve months; and

(D) Any other test or precedure that the examining physician deems appropriate.

(ii) After reviewing all the information obtained from the medical examination required in paragraph (l)(6)(i) of this section, the physician shall determine whether the employee is fit to wear a respirator.

(iii) Whenever an employee has exhibited difficulty in breathing during a respirator fit test or during use of a respirator, the employer, as soon as possible, shall provide the employee with a periodic medical examination in accordance with paragraph (l)(4)(ii) of this section to determine the employee's fitness to wear a respirator.

(iv) Where the results of the examination required under paragraph (l)(6)(i) or (ii) of this section are abnormal, medical limitation or prohibition of respirator use shall be considered. If the employee is allowed to wear a respirator, the employee's ability to continue to do so shall be periodically evaluated by a physician.

(7) *Emergency Examinations.* (i) In addition to the medical surveillance required in paragraphs (l)(2)–(6) of this section, the employer shall provide a medical examination as soon as possible to any employee who may have been acutely exposed to cadmium because of an emergency.

(ii) The examination shall include the requirements of paragraph (l)(4)(ii), of this section, with emphasis on the respiratory system, other organ systems considered appropriate by the examining physician, and symptoms of acute overexposure, as identified in paragraphs II(B)(1)–(2) and IV of appendix A of this section.

(8) *Termination of employment examination.* (i) At termination of employment, the employer shall provide a medical examination in accordance with paragraph (l)(4)(ii) of this section, including a chest X-ray where necessary, to any employee to whom at any prior time the employer was required to provide medical surveillance under paragraph (l)(1)(i) or (l)(7) of this section. However, if the last examination satisfied the requirements of paragraph (l)(4)(ii) of this section and was less than six months prior to the date of termination, no further examination is required unless otherwise specified in paragraph (l)(3) or (l)(5) of this section;

(ii) In addition, if the employer has discontinued all periodic medical surveillance under paragraph (l)(4)(vi) of this section, no termination of employment medical examination is required.

(9) *Information provided to the physician.* The employer shall provide the following information to the examining physician:

(i) A copy of this standard and appendices;

(ii) A description of the affected employee's former, current, and anticipated duties as they relate to the employee's occupational exposure to cadmium;

(iii) The employee's former, current, and anticipated future levels of occupational exposure to cadmium;

(iv) A description of any personal protective equipment, including respirators, used or to be used by the employee, including when and for how long the employee has used that equipment; and

(v) relevant results of previous biological monitoring and medical examinations.

(10) *Physician's written medical opinion.* (i) The employer shall promptly obtain a written, signed medical opinion from the examining physician for each medical examination performed on each employee. This written opinion shall contain:

(A) The physician's diagnosis for the employee;

(B) The physician's opinion as to whether the employee has any detected medical condition(s) that would place the employee at increased risk of material impairment to health from further exposure to cadmium, including any indications of potential cadmium toxicity;

(C) The results of any biological or other testing or related evaluations that directly assess the employee's absorption of cadmium;

(D) Any recommended removal from, or limitation on the activities or duties of the employee or on the employee's use of personal protective equipment, such as respirators;

(E) A statement that the physician has clearly and carefully explained to the employee the results of the medical examination, including all biological monitoring results and any medical conditions related to cadmium exposure that require further evaluation or treatment, and any limitation on the employee's diet or use of medications.

(ii) The employer shall promptly obtain a copy of the results of any biological monitoring provided by an employer to an employee independently of a medical examination under paragraphs (l)(2) and (l)(4) of this section, and, in lieu of a written medical opinion, an explanation sheet explaining those results.

(iii) The employer shall instruct the physician not to reveal orally or in the written medical opinion given to the employer specific findings or diagnoses unrelated to occupational exposure to cadmium.

(11) *Medical Removal Protection (MRP).* (i) General.

(A) The employer shall temporarily remove an employee from work where there is excess exposure to cadmium on each occasion that medical removal is required under paragraphs (l)(3), (l)(4), or (l)(6) of this section and on each occasion that a physician determines in a written medical opinion that the employee should be removed from such exposure. The physician's determination may be based on biological monitoring results, inability to wear a respirator, evidence of illness, other signs or symptoms of cadmium-related dysfunction or disease, or any other reason deemed medically sufficient by the physician.

(B) The employer shall medically remove an employee in accordance with paragraph (l)(11) of this section regardless of whether at the time of removal a job is available into which the removed employee may be transferred.

(C) Whenever an employee is medically removed under paragraph (l)(11) of this section, the employer shall transfer the removed employee to a job where the exposure to cadmium is within the permissible levels specified in that paragraph as soon as one becomes available.

(D) For any employee who is medically removed under the provisions of paragraph (l)(11)(i) of this section, the employer shall provide follow-up medical examinations semi-annually until, in a written medical opinion, the examining physician determines that either the employee may be returned to his/her former job status or the employee must be permanently removed from excess cadmium exposure.

(E) The employer may not return an employee who has been medically removed for any reason to his/her former job status until a physician determines in a written medical opinion that continued medical removal is no longer necessary to protect the employee's health.

(ii) Where an employee is found unfit to wear a respirator under paragraph (l)(6)(ii) of this section, the employer shall remove the employee from work where exposure to cadmium is above the PEL.

(iii) Where removal is based upon any reason other than the employee's inability to wear a respirator, the employer shall remove the employee from work where exposure to cadmium is at or above the action level.

(iv) Except as specified in paragraph (l)(11)(v) of this section, no employee who was removed because his/her level of CdU, CdB and/or β_2–M exceeded the trigger levels in paragraph (l)(3) or (l)(4) of this section may be returned to work with exposure to cadmium at or above the action level until the employee's levels of CdU fall to or below 3 μg/g Cr, CdB fall to or below 5 μg/lwb, and β_2–M fall to or below 300 μg/g Cr.

(v) However, when in the examining physician's opinion continued exposure to cadmium will not pose an increased risk to the employee's health and there are special circumstances that make continued medical removal an inappropriate remedy, the physician shall fully discuss these matters with the employee, and then in a written determination may return a worker to his/her former job status despite what would otherwise be unacceptably high biological monitoring results. Thereafter and until such time as the employee's biological monitoring results have decreased to levels where he/she could have been returned to his/her former job status, the returned employee shall continue medical surveillance as if he/she were still on medical removal. Until such time, the employee is no longer subject to mandatory medical removal. Subsequent questions regarding the employee's medical removal shall be decided solely by a final medical determination.

(vi) Where an employer, although not required by this section to do so, removes an employee from exposure to cadmium or otherwise places limitations on an employee due to the effects of cadmium exposure on the employee's medical condition, the employer shall provide the same medical removal protection benefits to that employee under paragraph (l)(12) of this section as would have been provided had the removal been required under paragraph (l)(11) of this section.

(12) *Medical removal protection benefits.* (i) The employer shall provide medical removal protection benefits to an employee for up to a maximum of 18 months each time, and while the employee is temporarily medically removed under paragraph (l)(11) of this section.

(ii) For purposes of this section, the requirement that the employer provide medical removal protection benefits means that the employer shall maintain the total normal earnings, seniority, and all other employee rights and benefits of the removed employee, including the employee's right to his/her former job status, as if the employee had not been removed from the employee's job or otherwise medically limited.

(iii) Where, after 18 months on medical removal because of elevated biological monitoring results, the employee's monitoring results have not declined to a low enough level to permit the employee to be returned to his/her former job status:

(A) The employer shall make available to the employee a medical examination pursuant to this section in order to obtain a final medical determination as to whether the employee may be returned to his/her former job status or must be permanently removed from excess cadmium exposure; and

(B) The employer shall assure that the final medical determination indicates whether the employee may be returned to his/her former job status and what steps, if any, should be taken to protect the employee's health;

(iv) The employer may condition the provision of medical removal protection benefits upon the employee's participation in medical surveillance provided in accordance with this section.

(13) *Multiple physician review.* (i) If the employer selects the initial physician to conduct any medical examination or consultation provided to an employee under this section, the employee may designate a second physician to:

(A) Review any findings, determinations, or recommendations of the initial physician; and

(B) Conduct such examinations, consultations, and laboratory tests as the second physician deems necessary to facilitate this review.

(ii) The employer shall promptly notify an employee of the right to seek a second medical opinion after each occasion that an initial physician provided by the employer conducts a medical examination or consultation pursuant to this section. The employer may condition its participation in, and payment for, multiple physician review upon the employee doing the following within fifteen (15) days after receipt of this notice, or receipt of the initial physician's written opinion, whichever is later:

(A) Informing the employer that he or she intends to seek a medical opinion; and

(B) Initiating steps to make an appointment with a second physician.

(iii) If the findings, determinations, or recommendations of the second physician differ from those of the initial physician, then the employer and the employee shall assure that efforts are made for the two physicians to resolve any disagreement.

(iv) If the two physicians have been unable to quickly resolve their disagreement, then the employer and the employee, through their respective physicians, shall designate a third physician to:

(A) Review any findings, determinations, or recommendations of the other two physicians; and

(B) Conduct such examinations, consultations, laboratory tests, and discussions with the other two physicians as the third physician deems necessary to resolve the disagreement among them.

(v) The employer shall act consistently with the findings, determinations, and recommendations of the third physician, unless the employer and the employee reach an agreement that is consistent with the recommendations of at least one of the other two physicians.

(14) *Alternate physician determination.* The employer and an employee or designated employee representative may agree upon the use of any alternate form of physician determination in lieu of the multiple physician review provided by paragraph (l)(13) of this section, so long as the alternative is expeditious and at least as protective of the employee.

(15) *Information the employer must provide the employee.* (i) The employer shall provide a copy of the physician's written medical opinion to the examined employee within five working days after receipt thereof.

(ii) The employer shall provide the employee with a copy of the employee's biological monitoring results and an explanation sheet explaining the results within five working days after receipt thereof.

(iii) Within 30 days after a request by an employee, the employer shall provide the employee with the information the employer is required to provide the examining physician under paragraph (l)(9) of this section.

(16) *Reporting.* In addition to other medical events that are required to be reported on the OSHA Form No. 200, the employer shall report any abnormal condition or disorder caused by occupational exposure to cadmium associated with employment as specified in Chapter (V)(E) of the *Reporting Guidelines for Occupational Injuries and Illnesses.*

(m) *Communication of cadmium hazards to employees*—(1) *General.* In communications concerning cadmium hazards, employers shall comply with the requirements of OSHA's Hazard Communication Standard for the construction industry, 29 CFR 1926.59, including but not limited to the requirements concerning warning signs and labels, material safety data sheets (MSDS), and employee information and training. In addition, employers shall comply with the following requirements:

(2) *Warning signs.* (i) Warning signs shall be provided and displayed in regulated areas. In addition, warning signs shall be posted at all approaches to regulated areas so that an employee may read the signs and take necessary protective steps before entering the area.

(ii) Warning signs required by paragraph (m)(2)(i) of this section shall bear the following information:

Danger, Cadmium, Cancer Hazard, Can Cause Lung and Kidney Disease, Authorized Personnel Only, Respirators Required in This Area

(iii) The employer shall assure that signs required by this paragraph are illuminated, cleaned, and maintained as necessary so that the legend is readily visible.

(3) *Warning labels.* (i) Shipping and storage containers containing cadmium, cadmium compounds, or cadmium contaminated clothing, equipment, waste, scrap, or debris shall bear appropriate warning labels, as specified in paragraph (m)(3)(ii) of this section.

(ii) The warning labels shall shall include at least the following information:

Danger, Contains Cadmium, Cancer Hazard, Avoid Creating Dust, Can Cause Lung and Kidney Disease

(iii) Where feasible, installed cadmium products shall have a visible label or other indication that cadmium is present.

(4) *Employee information and training.* (i) The employer shall institute a training program for all employees who are potentially exposed to cadmium, assure employee participation in the program, and maintain a record of the contents of such program.

(ii) Training shall be provided prior to or at the time of initial assignment to a job involving potential exposure to cadmium and at least annually thereafter.

(iii) The employer shall make the training program understandable to the employee and shall assure that each employee is informed of the following:

(A) The health hazards associated with cadmium exposure, with special attention to the information incorporated in appendix A to this section;

(B) The quantity, location, manner of use, release, and storage of cadmium in the workplace and the specific nature of operations that could result in exposure to cadmium, especially exposures above the PEL;

(C) The engineering controls and work practices associated with the employee's job assignment;

(D) The measures employees can take to protect themselves from exposure to cadmium, including modification of such habits as smoking and personal hygiene, and specific procedures the employer has implemented to protect employees from exposure to cadmium such as appropriate work practices, emergency procedures, and the provision of personal protective equipment;

(E) The purpose, proper selection, fitting, proper use, and limitations of respirators and protective clothing;

(F) The purpose and a description of the medical surveillance program required by paragraph (l) of this section;

(G) The contents of this section and its appendices, and,

(H) The employee's rights of access to records under § 1910.20(g)(1) and (2).

(iv) Additional access to information and training program and materials.

(A) The employer shall make a copy of this section and its appendices readily available to all affected employees and shall provide a copy without cost if requested.

(B) Upon request, the employer shall provide to the Assistant Secretary or the Director all materials relating to the employee information and the training program.

(5) *Multi-employer workplace.* In a multi-employer workplace, an employer who produces, uses, or stores cadmium in a manner that may expose employees of other employers to cadmium shall notify those employers of the potential hazard in accordance with paragraph (e) of the hazard communication standard for construction, 29 CFR 1926.59.

(n) *Recordkeeping*—(1) *Exposure monitoring.* (i) The employer shall establish and keep an accurate record of all air monitoring for cadmium in the workplace.

(ii) This record shall include at least the following information:

(A) The monitoring date, shift, duration, air volume, and results in terms of an 8-hour TWA of each sample taken, and if cadmium is not detected, the detection level;

(B) The name, social security number, and job classification of all employees monitored and of all other employees whose exposures the monitoring result is intended to represent, including, where applicable, a description of how it was determined that the employee's monitoring result could be taken to represent other employee's exposures;

(C) A description of the sampling and analytical methods used and evidence of their accuracy;

(D) The type of respiratory protective device, if any, worn by the monitored employee and by any other employee whose exposure the monitoring result is intended to represent;

(E) A notation of any other conditions that might have affected the monitoring results.

(F) Any exposure monitoring or objective data that were used and the levels.

(iii) The employer shall maintain this record for at least thirty (30) years, in accordance with 29 CFR 1910.20.

(iv) The employer shall also provide a copy of the results of an employee's air monitoring prescribed in paragraph (d) of this section to an industry trade association and to the employee's union, if any, or, if either of such associations or unions do not exist, to another comparable organization that is competent to maintain such records and is reasonably accessible to employers and employees in the industry.

(2) *Objective data for exemption from requirement for initial monitoring.* (i) For purposes of this section, objective data are information demonstrating that a particular product or material containing cadmium or a specific process, operation, or activity involving cadmium cannot release dust or fumes in concentrations at or above the action level even under the worst-case release conditions. Objective data can be obtained from an industry-wide study or from laboratory product test results from manufacturers of cadmium-containing products or materials. The data the employer uses from an industry-wide survey must be obtained under workplace conditions closely resembling the processes, types of material, control methods, work practices and environmental conditions in the employer's current operations.

(ii) The employer shall maintain the record for at least 30 years of the objective data relied upon.

(3) *Medical surveillance.* (i) The employer shall establish and maintain an accurate record for each employee covered by medical surveillance under paragraph (l)(1)(i) of this section.

(ii) The record shall include at least the following information about the employee:

(A) Name, social security number, and description of duties;

(B) A copy of the physician's written opinions and of the explanation sheets for biological monitoring results;

(C) A copy of the medical history, and the results of any physical examination and all test results that are required to be provided by this section, including biological tests, X-rays, pulmonary function tests, etc., or that have been obtained to further evaluate any condition that might be related to cadmium exposure;

(D) The employee's medical symptoms that might be related to exposure to cadmium; and

(E) A copy of the information provided to the physician as required by paragraph (l)(9) of this section.

(iii) The employer shall assure that this record is maintained for the duration of employment plus thirty (30) years, in accordance with 29 CFR 1910.20.

(iv) At the employee's request, the employer shall promptly provide a copy of the employee's medical record, or update as appropriate, to a medical doctor or a union specified by the employee.

(4) *Training.* The employer shall certify that employees have been trained by preparing a certification record which includes the identity of the person trained, the signature of the employer or the person who conducted the training, and the date the training was completed. The certification records shall be prepared at the completion of training and shall be maintained on file for one (1) year beyond the date of training of that employee.

(5) *Availability.* (i) Except as otherwise provided for in this section, access to all records required to be maintained by paragraphs (n)(1)–(4) of this section shall be in accordance with the provisions of 29 CFR 1910.20.

(ii) Within 15 days after a request, the employer shall make an employee's medical records required to be kept by paragraph (n)(3) of this section available for examination and copying to the subject employee, to designated representatives, to anyone having the specific written consent of the subject employee, and after the employee's death or incapacitation, to the employee's family members.

(6) *Transfer of records.* Whenever an employer ceases to do business and there is no successor employer or designated organization to receive and retain records for the prescribed period, the employer shall comply with the requirements concerning transfer of records set forth in 29 CFR 1910.20 (h).

(o) *Observation of monitoring.*—(1) *Employee observation.* The employer shall provide affected employees or their designated representatives an opportunity to observe any monitoring of employee exposure to cadmium.

(2) *Observation procedures.* When observation of monitoring requires entry into an area where the use of protective clothing or equipment is required, the employer shall provide the observer with that clothing and equipment and shall assure that the observer uses such clothing and equipment and complies with all other applicable safety and health procedures.

(p) *Dates.*—(1) *Effective date.* This section shall become effective on December 14, 1992.

(2) *Start-up dates.* All obligations of this section commence on the effective date except as follows:

(i) *Exposure monitoring.* Except for small businesses (nineteen (19) or fewer employees), initial monitoring required by paragraph (d)(2) of this section shall be completed as soon as possible and in any event no later than 60 days after the effective date of this standard. For small businesses, initial monitoring required by paragraph (d)(2) of this section shall

be completed as soon as possible and in any event no later than 120 days after the effective date of this standard.

(ii) *The permissible exposure limit (PEL).* Except for small businesses, as defined under paragraph (p)(2)(i) of this section, the employer shall comply with the PEL established by paragraph (c) of this section as soon as possible and in any event no later than 90 days after the effective date of this section. For small businesses, the employer shall comply with the PEL established by paragraph (c) of this section as soon as possible and in any event no later than 150 days after the effective date of this section.

(iii) *Regulated areas.* Except for small businesses, as defined under paragraph (p)(2)(i) of this section, regulated areas required to be established by paragraph (e) of this section shall be set up as soon as possible after the results of exposure monitoring are known and in any event no later than 90 days after the effective date of this section. For small businesses, regulated areas required to be established by paragraph (e) of this section shall be set up as soon as possible after the results of exposure monitoring are known and in any event no later than 150 days after the effective date of this section.

(iv) *Respiratory protection.* Except for small businesses, as defined under paragraph (p)(2)(i) of this section, respiratory protection required by paragraph (g) of this section shall be provided as soon as possible and in any event no later than 90 days after the effective date of this section. For small businesses, respiratory protection required by paragraph (g) of this section shall be provided as soon as possible and in any event no later than 150 days after the effective date of this section.

(v) *Compliance program.* Except for small businesses, as defined under paragraph (p)(2)(i) of this section, written compliance programs required by paragraph (f)(2) of this section shall be completed and available as soon as possible and in any event no later than 90 days after the effective date of this section. For small businesses, written compliance programs required by paragraph (f)(2) of this section shall be completed and available as soon as possible and in any event no later than 180 days after the effective date of this section.

(vi) *Methods of compliance.* Except for small businesses, as defined under paragraph (p)(2)(i) of this section, the engineering controls required by paragraph (f)(1) of this section shall be implemented as soon as possible and in any event no later than 120 days after the effective date of this section. For small businesses, the engineering controls required by paragraph (f)(1) of this section shall be implemented as soon as possible and in any event no later than 240 days after the effective date of this section. Work practice controls shall be implemented as soon as possible. Work practice controls that are directly related to engineering controls to be implemented shall be implemented as soon as possible after such engineering controls are implemented.

(vii) *Hygiene and lunchroom facilities.* Except for small businesses, as defined under paragraph (p)(2)(i) of this section, handwashing facilities, showers, change rooms and eating facilities required by paragraph (j) of this section, whether permanent or temporary, shall be provided as soon as possible and in any event no later than 60 days after the effective date of this section. For small businesses, handwashing facilities, showers, change rooms and eating facilities required by paragraph (j) of this section, whether permanent or temporary, shall be provided as soon as possible and in any event no later than 120 days after the effective date of this section.

(viii) *Employee information and training.* Except for small businesses, as defined under paragraph (p)(2)(i) of this section, employee information and training required by paragraph (m)(4) of this section shall be provided as soon as possible and in any event no later than 90 days after the effective date of this standard. For small businesses, employee information and training required by paragraph (m)(4) of this section shall be provided as soon as possible and in any event no later than 180 days after the effective date of this standard.

(ix) *Medical surveillance.* Except for small businesses, as defined under paragraph (p)(2)(i) of this section, initial medical examinations required by paragraph (l) of this section shall be provided as soon as possible and in any event no later than 90 days after the effective date of this standard. For small businesses, initial medical examinations required by paragraph (l) of this section shall be provided as soon as possible and in any event no later than 180 days after the effective date of this standard.

(q) *Appendices.* (1) Appendix C to this section is incorporated as part of this section, and compliance with its contents is mandatory.

(2) Except where portions of appendices A, B, D, E, and F to this section are expressly incorporated in requirements of this section, these appendices are purely informational and are not intended to create any additional obligations not otherwise imposed or to detract from any existing obligations.

[FR Doc. 92-21298 Filed 9-11-92; 8:45 am]
BILLING CODE 4510-26-M