

DEPARTMENT OF TOXIC SUBSTANCES CONTROL

400 P Street, 4th Floor
P.O. Box 806
Sacramento, CA 95812-0806



28 June 1993

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MCAS EL TORO
SSIC # 5090.3

F. Andrew Piszkin
Southwest Division, Naval Facilities Engineering Command
Department of the Navy
1220 Pacific Highway, Room 18
San Diego, California 92132-5181

Re: Use of California Cancer Potency Factors for Marine Corps Air Station El Toro

Dear Mr. Piszkin,

Mr. Zarnoch of the Department's Region 4 office has asked that the Office of Scientific Affairs respond to your letter of 20 May 1993. Because the chemicals of potential concern at the Air Station have not yet been identified, we are unable to inform you which chemical-specific Cal\EPA cancer potency factors are more stringent than their USEPA counterparts.

Notwithstanding this, we note for your information that Cal\EPA interprets its published cancer potency factors to meet the criteria for designation as potential chemical-specific "applicable or relevant and appropriate" (ARAR) criteria, as defined in the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). We make this interpretation in light of USEPA policies carefully described in the guidance document entitled "CERCLA Compliance with Other Laws Manual" (EPA 540/G-89/006). Thus, any differences between USEPA and Cal/EPA on the technical bases for cancer potency factors are immaterial.

Cancer potency factors published by Cal\EPA are issued according to regulations pursuant to California law, specifically the Safe Drinking Water and Toxic Enforcement Act of 1986 (aka Proposition 65) and the Toxic Air Contaminant Act of 1983. Cal\EPA considers that these cancer potency factors are duly promulgated, having gone through a period of public commentary before publication in Title 22 of the California Code of Regulations. The most current set of cancer potency factors is published in a memorandum dated June 1992 from the Standards and Criteria Work Group, which is comprised of scientists from several programs within Cal\EPA, including the Department of Toxic Substances Control.

We feel it is useful to bring to your attention a recent decision by USEPA Administrator Carol Browner regarding a dispute between the Air Force and Cal\EPA regarding State ARARs. Administrator Browner decided that she had the authority to resolve the dispute, because selection of ARARs bears heavily on selection of the final remedy for CERCLA sites and USEPA has a statutory obligation to approve that final remedy. Administrator Browner stated



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directly that the principal arbiter for interpretation of State ARARs is the State itself. We stress particularly that the Administrator rejected a claim by the Air Force that their interpretation of ARARs should supersede any other.

It is certainly true that neither Cal\EPA nor the Navy has brought to dispute resolution the question of whether Cal\EPA potency factors are ARAR. Cal\EPA feels it is self-evident that its cancer potency factors are at the very least criteria "to be considered" (TBC), as defined in the "CERCLA Compliance with Other Laws Manual". TBC criteria are non-promulgated advisories or guidance issued by Federal or State government that are not legally binding and do not have the status of ARARs. The USEPA guidance manual states on page *xiv*:

"[I]n many circumstances, TBCs will be considered along with ARARs as part of the site risk assessment and may be used in determining the necessary level of cleanup for protection of health or the environment."

The manual further states on page 1-76:

"Chemical specific TBC values such as health advisories and reference doses will be used in the absence of ARARs or where ARARs are not sufficiently protective to develop cleanup goals. In addition, other materials such as guidance or policy documents developed to implement regulations may be considered and used as appropriate, where necessary to ensure protectiveness."

This indicates that Cal\EPA cancer potency factors, whether ARAR or TBC, must be given significant weight in any risk assessment at Marine Corps Air Station El Toro. Therefore, their technical bases relative to other cancer potency factors (such as those of USEPA) are immaterial to any decision on their status as ARAR or TBC.

The various justifications for the Cal\EPA cancer potency factors have undergone extensive scientific review and public scrutiny during the promulgation process. The technical basis for each potency factor can be obtained from the public record. The regulatory package supporting the Cal\EPA potency factor for chromium VI, which is a typical regulatory package, is included for your information. The package contains the legal and regulatory background, toxicological information and risk assessment, public comments, and responses to those comments. Please contact the Office of Scientific Affairs to obtain similar such packages for specific chemicals of particular interest to the Navy.

Regarding resolution of differences between cancer potency factors published by USEPA and Cal\EPA, we urge the Navy and its consultants seek the consensus advice of toxicologists and risk assessors from Cal\EPA and USEPA Region IX. This consensus method is working

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well at many sites and facilities in California, including several interactions with the other uniformed services.

We are pleased to be of assistance to the Navy in this matter. We at the Office of Scientific Affairs look forward to working closely with the Navy on issues of health and environmental risk assessment during the regulation of environmental restoration at bases in California. Please call upon us for any additional inquiries you might have.

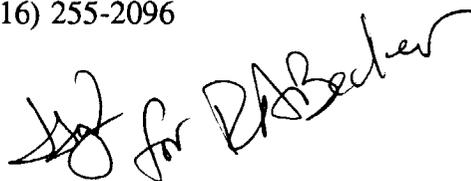
Sincerely yours,



John P. Christopher, Ph.D., D.A.B.T.
Staff Toxicologist
Human and Ecological Risk Section
Office of Scientific Affairs

Telephone: (916) 255-2038
Telefacsimile: (916) 255-2096

Reviewed by: Richard A. Becker, Ph.D., D.A.B.T.
Senior Toxicologist
Chief, Human and Ecological Risk Section



cc: Joe Zarnoch, Region 4 Site Mitigation Branch
Steve Picco, Toxics Legal Office
David Wang, Chief, Base Closure Branch

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bcc: J. Scandura, Chief, Region 4 SMB
Dr. J. Parker, HERS
Dr. D. Stralka, USEPA Region IX

State of California
AIR RESOURCES BOARD

Staff Report: Initial Statement of Reasons
for Proposed Rulemaking

Public Hearing to Consider the Adoption of a Regulatory
Amendment Identifying Hexavalent Chromium as a
Toxic Air Contaminant

Agenda Item No.: 86-1-3
Scheduled for Consideration: January 23, 1986
Release Date: December 9, 1985

(This report has been reviewed by the staffs of the California Air Resources Board and the California Department of Health Services and approved for publication. Approval does not signify that the contents necessarily reflect the views and policies of the Air Resources Board or the Department of Health Services, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.)

OVERVIEW AND RECOMMENDATION

I. INTRODUCTION

The Air Resources Board ("ARB" or "Board") identified toxic air contaminants and develops regulations for the control of their emissions according to the requirements of state law. A toxic air contaminant (TAC) is an air pollutant that the Board or the Department of Food and Agriculture* finds "may cause or contribute to an increase in mortality or an increase in serious illness, or which may pose a present or potential hazard to human health."** This report recommends that the Board find hexavalent chromium chromium(VI) to be a toxic air contaminant.

Section II of this Overview to the report presents the regulatory background and reviews the procedures by which the Board considers substances for the TAC designation. The Overview also summarizes the technical and toxicological information that supports the staff's recommendation. Section IIIA is a summary of Part A, which presents data on the uses of chromium, its emissions, and the public's exposure to chromium via the ambient air. Section IIIB summarizes the Department of Health Services' (DHS) analysis in Part B of the health effects of chromium. Section IV of this Overview discusses potential environmental effects of the recommended action, and Section V contains the staff's recommendation to the Board.

II. REGULATORY BACKGROUND AND PROCEDURES

Health and Safety Code (HSC) Section 39650 et seq. and Food and Agriculture Section 14021 et seq. set forth the procedure for identifying

* See Section II.

** Health and Safety Code Section 39655; all statutory references are to the Health and Safety Code, except as otherwise stated.

and controlling toxic air contaminants in California. (These provisions were enacted in September 1983 as Assembly Bill 1807; Stats 1983 ch 1047.) The Department of Food and Agriculture is responsible for identifying and controlling TACs in their pesticial uses. The ARB has authority over TACs in all their other uses.

HSC Section 39650 sets forth the Legislature's findings about substances which may be TACs. The Legislature has declared:

"That public health, safety, and welfare may be endangered by the emission into the ambient air of substances which are determined to be carcinogenic, teratogenic, mutagenic, or otherwise toxic or injurious to humans" (HSC Section 39650(a).)

The findings also include directives on the consideration of scientific evidence and the basis for regulatory action. With respect to the control of TACs, the Legislature has declared:

"That it is the public policy of this state that emissions of toxic air contaminants should be controlled to levels which prevent harm to the public health," (HSC Section 39650(b).)

The Legislature has further declared:

"That, while absolute and undisputed scientific evidence may not be available to determine the exact nature and extent of risk from toxic air contaminants, it is necessary to take action to protect public health," (HSC Section 39650(e).)

In the evaluation of substances, the Legislature has declared that the best available scientific evidence, gathered from both public agencies and private sources including industry, should be used. The Legislature has also determined that this information should be reviewed by a scientific review panel, created pursuant to HSC Section 39670, and by the public.

The Board's determination of whether or not a substance is a toxic air contaminant includes several steps specified in the HSC. First, we request the DHS to evaluate the health effects of a substance (HSC Section 39660). The evaluation includes a comprehensive review of all available scientific data. Upon receipt of a report on health effects from DHS and in consideration of their recommendations, we prepare and submit a report to the Scientific Review Panel (SRP) for its review (HSC Section 39661(a)). The report consists of the DHS report (Part B), material prepared by the ARB staff on the use, emissions and ambient concentrations of the substance (Part A), and public comments on the draft Report and responses (Part C). It serves as the basis for future regulatory action by the Board. The report is also made available to the public, which may submit comments on the report to the SRP (HSC Section 39661(b)).

After receiving the SRP's written findings on the report, the Board issues a public hearing notice and a proposed regulation which includes a proposed determination as to whether or not the substance is a toxic air contaminant (HSC Section 39662(a)). If, after a public hearing and other procedures to comply with Government Code Section 11340 et seq., the Board determines that a substance is a toxic air contaminant, its findings must be set forth in a regulation (Section 39662). The HSC also sets forth procedures for developing and adopting control measures for substances identified as TACs (Sections 39665-39667); such measures are not proposed during this proceeding.

III. EVALUATION OF CHROMIUM

Consistent with the provisions of state law, the ARB and the DHS prioritize candidate substances for evaluation and regulation as "toxic air contaminants" pursuant to HSC Section 39660(f). Briefly, the selection of a substance for the Board's evaluation and consideration as a toxic air contaminant is to be based on the risk to the public from exposure to the substance, amount or potential amount of emissions from use of the substance,

manner of usage in California, atmospheric persistence, and concentration in the ambient air. After consulting with the Department of Health Services (DHS), chromium and its compounds were among candidate substances selected for consideration as a TAC.

Chromium was chosen for evaluation because it was identified by the International Agency for Research on Cancer (IARC) as a human and animal carcinogen, because chromium was found to be emitted from many sources throughout the state (both directly from processes using chromium or chromium compounds, and as a product of the combustion of coal, oil, and other chromium-containing fuels), and because its presence in the atmosphere was documented.

A. EMISSIONS, PERSISTENCE IN THE ATMOSPHERE, AND AMBIENT CONCENTRATIONS OF CHROMIUM

Data in the revised Part A are summarized in Table I.

Industrial sources of chromium may emit chromium in the hexavalent state (chromium(VI)) or the trivalent state (chromium(III)), or a mixture of the two. Chrome plating and the use of hexavalent chromium as a corrosion inhibitor in cooling towers accounted for most of the known hexavalent chromium emissions in California. Refractory (firebrick) production is a source of trivalent chromium emissions.

Combustion of oil, coal, municipal waste, and sewage sludge is a source of chromium emissions. Because historical data for these source categories refer to total chromium, rather than to one form or the other, the oxidation state of chromium emitted from these sources is not known. Available information suggests that combustion-related emissions are trivalent chromium.

Total chromium has been measured in the air at sites in many populated areas of California. Estimates of population exposure to total and hexavalent chromium are summarized in Table 1. Limited preliminary data on ambient concentrations of hexavalent chromium indicate that hexavalent chromium comprised between 3 and 8 percent of ambient total chromium. Efforts are under way to validate the analytical method and to gather more data on ambient concentrations.

Evaluation of concentrations of chromium near sources of chromium(VI) suggest that significant population exposure may occur close to sources.

The atmospheric persistence of chromium(VI) is not known. It has been suggested that chromium(VI) reacts in the atmosphere with available organic matter; however, there is no information available on the atmospheric reactions of chromium(VI) or chromium(III). Chromium is removed from the atmosphere by physical deposition processes. Measurements have shown that most chromium deposition occurs through wet deposition.

The draft of Part A was released for public review and comment. Comments and our responses are presented in Part C.

B. HEALTH EFFECTS AND RISK ASSESSMENT

Pursuant to Health and Safety Code Section 39660, we requested that the Department of Health Services conduct a health effects evaluation of chromium. The DHS evaluation was conducted in accordance with the provisions of that section, which requires that the DHS consider all available scientific data, including, but not limited to, relevant data provided by the ARB, the Department of Industrial Relations, international and federal health agencies, private industry, academic researchers, and public health and environmental

TABLE I
SUMMARY OF DATA IN PART A

Emissions

	<u>Inventory Year</u>	<u>Chromium Measured</u>	<u>Estimated Statewide Emissions, tons</u>
Stationary Sources			
Chrome plating	1983	Hexavalent	0.77-16.
Cooling towers	1979/81	Hexavalent	0.23-9.2
Oil combuston	1983	Total	13.2-28.1
Coal combustion	1981	Total	0.02
Cement production	1981	Total	0.9
Waste incineration	1981	Total	0.02-0.16
Refractory Production	1984	Hexavalent	< 0.01

Fate in the atmpshere: The half-life and reactions of chromium(VI) are unknown; chromium particulate is removed from the atmosphere through physical processes, mainly by wet deposition.

Ambient Concentrations

Location (year)	<u>Form</u>	<u>Concentration nanogram/cubic meter (ng/m³)</u>
San Francisco Bay Area Air Basin (partial)(1977)	Total chromium, annual average	10.8
South Coast Air Basin (1977)	Total chromium, annual average	16.9
Fresno Area (1977)	Total chromium, annual average	12.3
San Diego Area (1977)	Total chromium, annual average	11.7
San Jose Area (1977)	Total chromium, annual average	14.3
El Monte (1985) ¹	Total chromium (average of four samples)	13.2
El Monte (1985) ¹	Hexavalent chromium (average of four samples)	0.5

¹Samples taken during the last week of August, 1985

organizations. To facilitate the identification of all available data, we sent, prior to formally requesting the DHS evaluation, a letter to potential sources of chromium compounds in California and other interested members of the public requesting that they submit any information they considered pertinent to the DHS evaluation. We also conducted a reference search on the health effects of chromium and its compounds using the MEDLARS II and DIALOG Information Services and included a bibliography from that search in our request for information. The data compiled in the search were also provided to the DHS.

The DHS' draft report (Part B) was released to the public for comment. The comments received and responses are included in Part C. A revised Part B is presented to the Scientific Review Panel for review.

In meeting the requirements of Section 39666 for DHS' evaluation, the DHS addresses these issues in Part B: 1) Is chromium or its compounds, or both, a human and/or animal carcinogen? 2) Does chromium have a carcinogenic threshold? 3) Are health effects other than cancer expected to occur at current ambient levels?, and 4) What is the range of added lifetime cancer risk for populations continuously exposed to the ambient concentrations of chromium measured in California? In response to these issues, the DHS concludes that: 1) hexavalent chromium is a human and animal carcinogen and insufficient information exists to decide whether chromium(III) is a potential human carcinogen; 2) hexavalent chromium should be treated as a substance without a carcinogenic threshold; 3) health effects other than cancer are not expected to occur at current ambient levels with the possible exception of adverse reproductive effects, where experimental data are inadequate to assess potential human reproductive risks; and, 4) the theoretical added

lifetime cancer risk from a continuous 70-year exposure to atmospheric hexavalent chromium (chromiumVI) exposure ranges from 12 to 146 cases per million people per nanogram per cubic meter (ng/m³).

The DHS has found in its report that: 1) many epidemiologic studies show a strong high association between hexavalent chromium exposure in the work place and respiratory cancer; and 2) all short-term assays reported show that hexavalent chromium compounds possess genotoxic capabilities, while tests of chromium(III) compounds are generally negative or generate positive results at much higher doses than those used in chromium(VI) tests. The DHS agrees with the findings of IARC that there is sufficient evidence to demonstrate the carcinogenicity of chromium in both animals and humans. The DHS believes there are inadequate data available at this time to confirm or refute the carcinogenic potential of trivalent chromium.

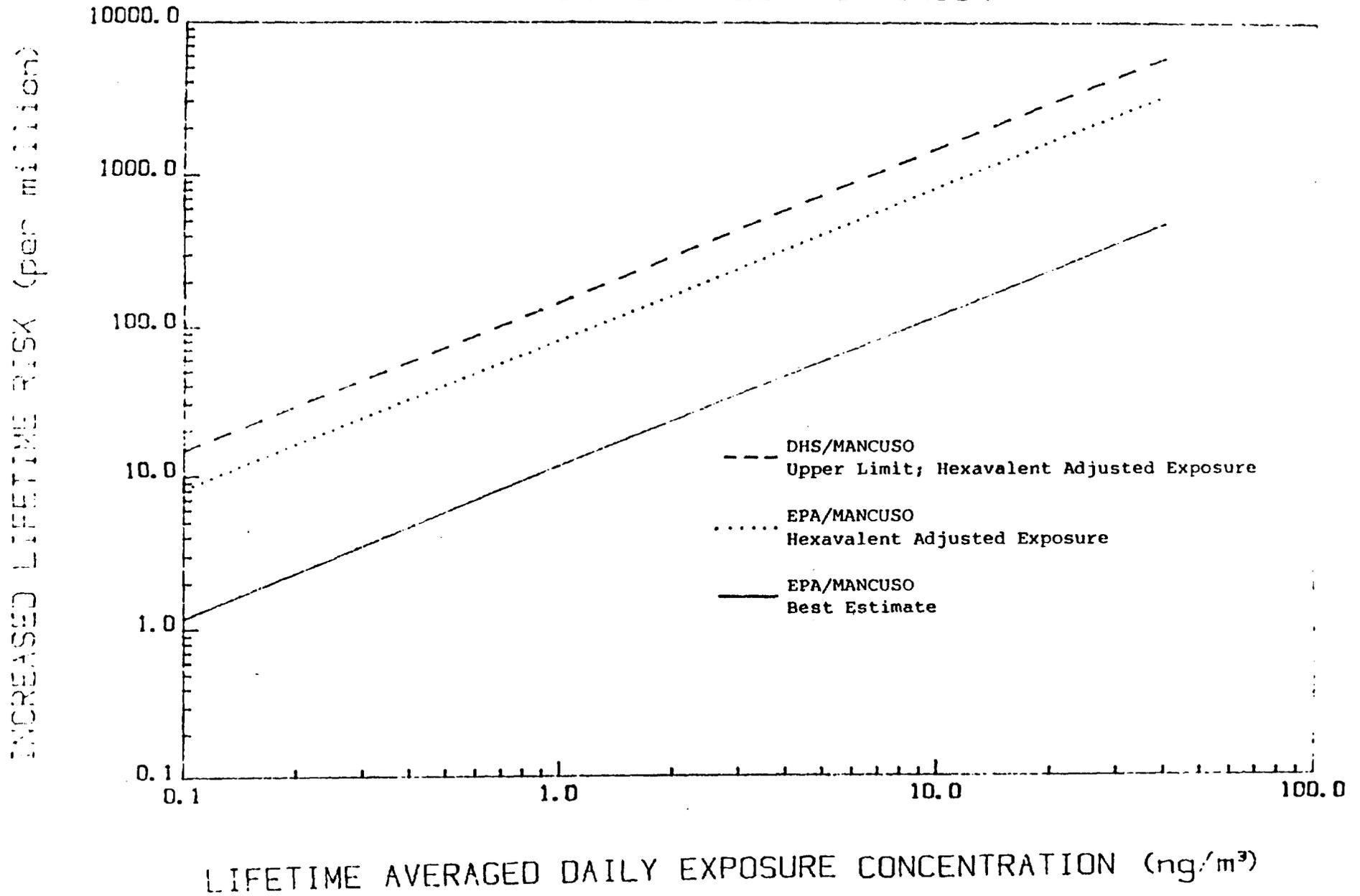
To determine that a substance has a carcinogenic threshold, the DHS requires strong positive evidence that the substance acts only through mechanisms which ought to have a threshold. The DHS found that no positive evidence exists for this position with respect to chromium.

The staff of DHS recommends adopting the risk assessment performed by the Environmental Protection Agency (EPA), in which a linear nonthreshold model was applied to the epidemiologic study (Mancuso, 1975) judged to be most methodologically sound and to contain the best exposure data to derive dose-response curves for hexavalent chromium. Data from animal studies were judged to be inadequate for quantitative risk assessment by the staff of DHS.

Making certain assumptions, the DHS described dose-response curves for hexavalent chromium. Based on the results derived from application of the

CANCER RISK FROM HEXAVALENT CHROMIUM

Figure A



linear nonthreshold model and the Mancuso data, the staff of DHS recommends that the Air Resources Board consider the increased lifetime carcinogenic risk from a continuous lifetime exposure to hexavalent chromium as falling in the range of 12 to 146 cancer cases per nanogram hexavalent chromium per cubic meter of air per million people exposed (12-146 cancers/ng/m³/million). This range is illustrated in Figure A, where the solid line represents the curve based on the EPA assessment using total chromium as the exposure, the dotted line is based on the EPA assessment adjusting for the hexavalent chromium fraction of the exposure, and the dashed line was generated by taking the upper limit of the 95% confidence interval for carcinogenic risk due to chromium and adjusting for the hexavalent fraction of the workplace exposure. There are not, however, sufficient data from this or other epidemiologic studies to estimate the risk of specific hexavalent compounds for airborne exposures.

There is very limited information on levels of ambient hexavalent chromium in California. Preliminary data on ambient concentrations of hexavalent and total chromium at a site in the South Coast Air Basin during August 1985 indicate that 3 to 8 percent of total ambient chromium is in the hexavalent state. Although it is not known whether this ratio is representative of other sites, it is the best information available at this time.

There is a need to better characterize the concentration of chromium(VI) in the ambient air of California; we are working with the air pollution control districts and air quality management districts to gather such data. We are also carrying out emission testing of chromium sources to determine the oxidation state and magnitude of chromium emissions. Such information will be an important part of any control effort for hexavalent chromium.

III. ENVIRONMENTAL IMPACTS

The identification of hexavalent chromium as a toxic air contaminant is not in itself expected to result in any environmental effects. The identification of hexavalent chromium as a toxic air contaminant by the Board may require that the Board and air pollution control districts adopt toxic control measures in accordance with the provisions of state law. Any such toxic control measures may result in reduced emissions of hexavalent chromium to the atmosphere, resulting in reduced ambient concentrations, concurrently reducing the health risk due to hexavalent chromium. Therefore, the identification of hexavalent chromium as a toxic air contaminant may ultimately result in environmental benefits. Environmental impacts identified with respect to specific control measures will be included in the consideration of such control measures pursuant to Health and Safety Code Sections 39665 and 39666.

IV. RECOMMENDATION

Because hexavalent chromium is a known human and animal carcinogen, and is known to be emitted in California, the ARB staff recommends the listing of hexavalent chromium as a toxic air contaminant. In making this recommendation, we note that there is not sufficient available scientific evidence to support the identification of an exposure level below which carcinogenic effects would not occur.

NOV 25 1985

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DAVID PIERPONT GARDNER
President of the University

UNIVERSITY HOUSE
DAVIS, CALIFORNIA 95616

EMIL M. MRAK
Chancellor Emeritus

November 21, 1985

Mr. James D. Boyd, Executive Officer
State Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Dear Mr. Boyd:

The Scientific Review Panel on Toxic Air Contaminants has reviewed the Report to the Scientific Review Panel on Chromium, and has formulated its findings regarding the report. With this letter, I am formally submitting the Scientific Review Panel's written findings to the Air Resources Board.

Kindest personal regards,

A handwritten signature in black ink, appearing to read "Emil M. Mrak".

Emil M. Mrak

Enclosure

cc: Scientific Review Panel
Dr. John Holmes
Mr. Richard Bode

Findings of the Scientific Review Panel

Regarding the Report on Chromium

In accordance with the provisions of the Health and Safety Code Section 39661, the Scientific Review Panel (SRP) has reviewed the September 1985 Report to the Scientific Review Panel on Chromium, and has reviewed the public comments received regarding this report. The SRP finds the Report on Chromium to be adequate and sufficient.

Specifically, the SRP finds each of the following propositions to be prudent interpretations of the available evidence:

1. In epidemiologic studies, where the oxidation state of chromium was unknown (either in the hexavalent [Cr(VI)] or trivalent [Cr(III)] state, chromium was shown to be a human carcinogen.
2. In other studies conducted in laboratory animals, chromium in the hexavalent state [Cr(VI)] was shown to be carcinogenic. Accordingly, the SRP finds that hexavalent chromium [Cr(VI)] should be considered a potential carcinogen in humans.
3. An exposure level below which no significant adverse health effects are anticipated could not be identified. Based on our knowledge of the pharmacokinetics, metabolism, and mode of action of chemical carcinogens like chromium, there is no scientific basis for determining an exposure level below which carcinogenic effects would not have some probability of occurring.
4. Adverse health effects other than cancer are not anticipated at current ambient chromium exposure levels.

For these reasons, we agree that hexavalent chromium [Cr(VI)] should be listed by the Air Resources Board as a toxic air contaminant, but we are unable to recommend an exposure level below which carcinogenic effects would not have some probability of occurring.

COMMENTS

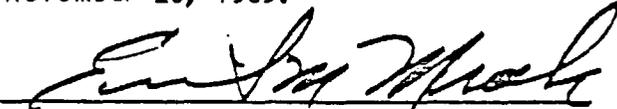
Using extrapolation procedures recommended by the EPA and Interagency advisory groups, DHS has estimated that the added lifetime cancer risk from a 70-year exposure to 1 nanogram per cubic meter (ng/m³) of atmospheric hexavalent chromium ranges from .12 to 146 cases per million people exposed. The SRP concurs with DHS's evaluation, but wishes to clarify several points:

1. The range of risk presented (.12 to 146 cases) was derived using conservative estimation procedures.
2. Chromium may exist in several chemical states, predominately at the trivalent [Cr(III)] and hexavalent [Cr(VI)] states. The health effects impact of these states are not equal. Hexavalent chromium [Cr(VI)] has been shown in animal tests to be carcinogenic. On the other hand, there are inadequate data to indicate any association between trivalent chromium [Cr(III)] exposure and cancer induction in animal tests. However, trivalent chromium [Cr(III)] is an essen-

tial element. Chromium, as a mixture of oxidation states, has been shown to be a human carcinogen.

3. Whereas there is uncertainty associated with the absolute value of the risk estimated, the range of 12 to 146 cases is useful in comparing risk from exposure to chromium to other environmental carcinogens in ambient air.

I certify that the above is a true and correct copy of the findings adopted by the Scientific Review Panel on November 20, 1985.



Dr. Emil M. Mrak, Chairman
Scientific Review Panel

Date

11/21/85

STATE OF CALIFORNIA
AIR RESOURCES BOARD

TECHNICAL SUPPORT DOCUMENT

PUBLIC HEARING TO CONSIDER THE ADOPTION OF A REGULATORY
AMENDMENT IDENTIFYING HEXAVALENT CHROMIUM AS A
TOXIC AIR CONTAMINANT

Agenda Item No.: 86-
Scheduled for consideration: January 24, 1986
Release Date: December 9, 1985

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- Part B Health Effects of Chromium
- Part C Public Comments and Responses

PART A - A REVIEW OF CHROMIUM USES,
EMISSIONS, AND PUBLIC EXPOSURE

Prepared by the Staff of the Air Resources Board

November 1985

(This report has been reviewed by the staffs of the California Air Resources Board and the California Department of Health Services and approved for publication. Approval does not signify that the contents necessarily reflect the views and policies of the Air Resources Board or the Department of Health Services, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.)

Part A - A Review of Chromium Uses,
Emissions, and Public Exposure

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I. USAGE AND EMISSIONS

A. PRODUCTION AND USAGE

Chromium occurs in nature primarily as chromite (chrome iron ore). This mineral is best represented as $(\text{Fe,Mg})\text{O}(\text{Cr,Fe,Al})_2\text{O}_3$.^{1/} Chromite ore is not mined commercially in the United States; countries in Africa and Europe are the main sources of United States imports^{2/}. The ore is used to produce chromium metal and alloys, refractory materials, and chromium chemicals.

The metallurgical industry used 49 percent of the chromite ore consumed in the United States in 1982, mostly in the production of stainless steels.^{2/}

There are no primary steel production facilities currently operating in California. However, there are a number of melting and recasting facilities; hence, chromium use in the California steel industry would be limited to that present in scrap metal or feedstock.

Production of refractory brick accounted nationally in 1982 for 15 percent of the chromite ore consumption.^{2/} Kaiser Refractories is the major facility in California manufacturing chromium containing refractory products.^{3/} Production furnaces in the cement, glass, and nonferrous metal industries use chromium-containing refractory materials.

The chemical industry used 36 percent of the chromite ore consumed in the United States in 1982 in the manufacture of various chromium chemicals.^{2/} These chemicals find diverse use in metal finishing and plating, in leather tanning, in wood preserving and textile finishing, and as corrosion inhibitors in water treatment.

There are no plants in California which produce chromic acid, sodium chromate, or sodium dichromate chemicals, which are used to make a wide range

of other chromium chemicals. These or other chromium chemicals are used in the State in metal finishing and plating, in the manufacture of certain green container glass, and in formulation of corrosion inhibitors for water treatment. Nationwide use of sodium dichromate in 1982 was 150,000 tons, of which 42,000 tons (28%) was used to produce chromic acid^{4/} for metal plating. The largest supplier of chromic acid in the United States estimated that 1,500 tons of chromic acid were sold in California in 1984 for chrome plating usage.^{18/} It has been estimated that there are 9,750 chromium plating shops in the United States.^{5/} It has been estimated that between 1,500 and 1,800 electroplaters operate in California.^{6/} An ARB survey of chrome platers in Northern California which are known to discharge to publicly-owned treatment works accounted for 150 facilities. There are 168 chrome platers listed in the South Coast Air Quality Management District inventory of potentially toxic compound emissions.^{7/} Based on this information, it is estimated that about 400 chrome platers operate in California.

Chromium pigments are used in inks, plastics, industrial coatings, some truck original equipment manufacture finishes, and traffic paints. One industry estimate of chromium pigment usage in California in 1983 was 2,500 tons.^{8/} Calculation of California chromium pigment consumption as a fraction of the 1982 national total^{9/} yields an estimate of 3,600 tons. Formulators of chromium paint pigments have been identified in Southern California. In the 1983 South Coast AQMD emission inventory of potentially toxic/hazardous air contaminants^{7/}, approximately 90 tons of chromium pigments were reported used in the formulation of paints and coatings in the South Coast air basin.

There are six container glass manufacturers in California that use chromium compounds as colorants to produce green glass. Trivalent chromium (as iron chromite) or hexavalent chromium (as sodium or potassium dichromate) may be used as colorants in green glass formulations.^{10/}

Also, chromium(VI) compounds are used in cooling towers as corrosion inhibitors by some industrial and commercial facilities.

Five facilities listed in the ARB's emissions data system (EDS) use chromium in wood preservation or fire retardant formulations, and sixteen other wood products facilities appear in the EDS which may also be users of chromium compounds.^{11/}

B. CURRENT AND PROJECTED STATIONARY AND MOBILE SOURCE EMISSIONS

Chromium emissions in California were estimated using data from local air pollution control districts, the Air Resources Board (ARB), the Environmental Protection Agency (EPA), and industry.

Stationary sources contribute most of the known chromium emissions which occur in California. Chromium is emitted both directly in the use and production of chromium compounds, and secondarily (or inadvertently) through the combustion of chromium-containing fuels, or as a result of other processes.

Direct sources of hexavalent chromium emissions in California include chromium plating facilities, cooling towers using hexavalent chromium-containing water treatments, and green glass plants which use chromium(VI) colorants. Steel recasting and melting facilities, and refractory (fire-brick) plants are direct sources of chromium(III). Secondary sources of chromium emissions include combustion of coal and oil, cement production,

sewage sludge and other waste incineration, and wear from furnaces with chromite refractory; available evidence suggests that chromium emitted from secondary sources is principally in the trivalent state.

Motor vehicles may contribute to chromium emissions in California. Limited information available on trace metal emissions from diesel-fueled passenger cars indicates that these cars may be a source of chromium.^{12,13/}

Table I-1 summarizes estimates of chromium emissions in California. Some emission sources of chromium are not listed, because insufficient data are available at this time to make emission estimates.

Table I-1
Estimated Chromium Emissions in California

Source	Chromium Measured	Source Type	Emissions (tons/year)	Inventory Year	Refs.
Chromium plating	Hexavalent	Point	0.77-16	1983	7,17
Cooling towers	Hexavalent	Point	0.23-9.2	1979, 1981	5,35
Oil combustion	Total	Point			
Residual oil			5.1-20	1983	22,39
Distillate oil			7.2	1983	22,39
Waste Oil			0.91	1983	23,24,25
Refractory Production	Hexavalent	Point	< 0.01	1984	36
Cement Production	Total	Point	0.9	1981	26,27
Coal combustion	Total	Point	0.02	1981	26,37
Waste Incineration	Total	Point	0.02-0.16	1981	28,29,30, 31,32

Stationary Source Total 15-54

1. Stationary Emission Sources

Chrome plating is one of the largest known sources of chromium(VI) emissions in the State. Both hard chrome (used to provide a durable coating), and decorative chrome electroplating operations are conducted in baths containing chromic acid. During the plating process, bubbles of gas are emitted through the surface of the bath; these bubbles carry entrained chromium(VI) into the air, which is usually vented to the atmosphere. Estimated emission factors from these uncontrolled operations range from 1.5×10^{-4} to 6.2×10^{-2} pounds per hour per square foot of bath surface.^{14,15,16/} Higher estimates, of up to 6.5 pounds per hour per square foot, have been obtained for large bath hard chrome operations.^{16/} A recent well documented report on plating operations at the Long Beach Naval Shipyard^{17/} yielded an emission factor of 6.4×10^{-4} pounds per hour per square foot of bath surface for uncontrolled hard chrome plating. Although there is considerable evidence for variability, two studies^{16,17/} indicate that the emission factor for decorative chrome plating is about 40 percent as much as for hard chrome plating.

Surveys have indicated that approximately 400 chrome platers operate in California. Roughly three-fourths of national chromic acid use for chrome plating is for hard chrome, while one-fourth is for decorative^{18/}, based on one industry estimate. California usage patterns are similar, according to an industry association estimate.

This information, in conjunction with the emission factor derived from the Long Beach Naval Shipyard report, and certain assumptions (see Appendix C) yields a emissions estimate of 0.77-15.6 tons of chromium(VI) per year for

chrome plating in California. This estimate reflects the fact that both hard and decorative chrome plating are done in California. The lower value represents a theoretical minimum emission estimate, based on technically achievable control (92% removal efficiency by wet scrubber) of emissions from all platers statewide. The higher value assumes that no emissions controls are used.

Although there are no air pollution control regulations which pertain specifically to chromium(VI) emissions from chrome plating operations, emission controls have been required on some chrome plating operations. These controls are usually required on the basis of nuisance law, to control chromic acid mist emissions causing property damages or nuisance. The extent to which emission controls are required, and the efficiency of any such controls, are not well known.

Insufficient evidence is available to determine whether green container glass manufacture is a source of chromium(VI) emissions. Iron chromite, or sodium dichromate, or both, have been used as colorants in green glass manufacture.^{10/} ARB tests indicate that a large green container glass manufacturer which used chromium(VI) colorants emitted 2.5 tons a year of chromium, mostly in the hexavalent form^{19/}; a recent change in the type of chromium colorant [to chromium(III)] used by this manufacturer may result in reduced hexavalent chromium emissions. Another test of this source has been conducted to measure chromium(VI) emissions subsequent to the change in formulation; results are not available at this time. Five other green glass manufacturing facilities, generally with smaller production commitments to produce green container glass, are located in California. Industry sources

indicate that only chromium(III) colorants are presently used in the California green-container glass industry.

Although an EPA-sponsored study reported chromium emissions (0.22 percent of particle emissions) from clear soda-lime glass melting furnaces to which no chromium colorants were added, a recent ARB test of a flint container glass manufacturer showed much lower (0.001 percent of particle emissions) chromium(VI) emissions. These emissions may be due to chromium loss from the chromium-containing firebrick lining of the glass furnace.^{20,21/} Additional tests are planned to measure chromium(VI) emissions from clear glass plants. Until additional data are available on chromium(VI) emissions from green-glass manufacturers which use chromium(III) colorants, and from clear glass manufacturers, it is not possible to develop a representative emission estimate for these source categories.

Oil combustion is estimated to be responsible for 13.2-28.1 tons per year of chromium emissions. Chromium occurs naturally as a trace component of most oils, and the concentrations of chromium found in residual and distillate oils have been measured.^{22,23/} Also, chromium is found in waste oil as a contaminant.^{25/} When these oils are burned, chromium is emitted. Available information suggests that the chromium is emitted in the trivalent state.

Emissions of chromium from refractory production have been shown to be in the trivalent state.^{36/} An estimate of maximum chromium(VI) emissions from this source type is based on the detection limit for chromium(VI) for the test method used; no chromium(VI) was detected in the source test on which the estimate was based.

Chromium emissions from cement production have been estimated based on the chromium content of emitted particulate matter. The chromium content in emitted particulate matter has been estimated at 0.03 percent (weight).^{26/} Emissions of chromium from the combustion of chromium-containing fuels in cement production have been included in statewide fuel combustion estimates. There are 13 cement plants in California with a total of 43 kilns. The statewide annual production of clinker was about 8 million pounds in 1980.^{27/}

Sewage sludge and municipal waste incinerators are known sources of chromium emissions.^{30,31/} Chromium present in the sludge or refuse is emitted when the fuel is burned. There are 11 facilities in California listed in the ARB's emission data system (EDS) which incinerate sewage sludge or municipal waste.^{32/} Emissions of chromium from these sources are estimated to total 0.02 to 0.16 ton per year.

C. NATURAL OCCURRENCE

Chromium(III) is a component of most soils. In areas of serpentine and peridotite rocks, chromite (chrome ore) is the predominant chromium mineral. Deposits of 5-10 percent chromite have been found in beach sands and stream placers in several California counties.^{33/} Also, chromium has been found in non-serpentine areas in the state at concentrations ranging from a trace to 500 ppm.^{34/}

Soil chromium is generally in an insoluble, biologically unavailable form, mainly as the weathered form of the parent chromite or as the chromium (III) oxide hydrate. Weathering and wind action can transport soil chromium to the atmosphere; generally, such mechanical weathering processes generate

particles greater than 10 um diameter, which have significant settling velocities. The extent to which natural sources of chromium contribute to measured ambient chromium levels in California is not known. Ambient chromium derived from soil is expected to exist as chromium(III).^{38/}

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II. PERSISTENCE IN THE ATMOSPHERE

A. PHYSICAL AND CHEMICAL PROPERTIES

Chromium (Cr) is a hard, colorless, and lustrous metal, with a melting point above 1800°C. It is extremely resistant to corrosive agents. Selected physical properties are presented in Table II-1. Chromium metal is not found in nature, but is produced principally from the mineral chromite. Chromite contains chromium in the +3 oxidation state, or Cr(III). Chromium combines with various other elements to give compounds, the most common of which contain either Cr(III), which is trivalent chromium (the +3 oxidation state) or Cr(VI), which is hexavalent chromium (the +6 oxidation state).^{1/}

Thousands of Cr(III) compounds exist, exhibiting a wide range of colors, structures, and chemical properties.^{2/} Cr(VI) compounds are produced industrially by heating Cr(III) compounds in the presence of mineral bases (such as soda ash) and atmospheric oxygen. Most Cr(VI) compounds contain oxygen, and are highly soluble in water. Cr(VI) solutions are powerful oxidizing agents under acidic conditions, but much less oxidizing under basic conditions. Depending on the concentration and acidity, Cr(VI) can exist as either chromate ion $(\text{CrO}_4)^{=}$, or as dichromate ion $(\text{Cr}_2\text{O}_7)^{=}$. Because dilute chromate solutions passivate metal surfaces, they are widely used to inhibit corrosion in recirculating water systems such as cooling towers.

Table II-1
Physical Properties of Chromium^{1/}

Property	Value
atomic weight	51.996
isotopes, %	
50	4.31
52	83.76
53	9.55
54	2.38
crystal structure	body centered cube
density at 20°C, g/cm ³	7.19
melting point, °C	1875
boiling point, °C	2680
vapor pressure, 130 Pa ^{a/} , °C	1610
heat of fusion, kJ/mol ^{b/}	13.4-14.6
latent heat of vaporization at bp, kJ/mol ^{b/}	320.6
specific heat at 25°C, kJ/(mol-K) ^{b/}	23.9 (0.46 kJ/kg-K)
linear coefficient of thermal expansion at 20°C	6.2 x 10 ⁻⁶
thermal conductivity at 20°C, W/(m-K)	91
electrical resistivity at 20°C, microhm-m	0.129
specific magnetic susceptibility at 20°C	3.6 x 10 ⁻⁶
total emissivity at 100°C nonoxidizing atm	0.08
reflectivity, R	
lambda, nm	300 500 1000 4000
%	67 70 63 88
refractive index	
alpha	1.64-3.28
lambda	2,570-6,080
standard electrode potential, valence 0 to 3+, V	0.71
ionization potential, V	
1st	6.74
2nd	16.6
half-life of ⁵¹ Cr isotope, days	27.8
thermal neutron scattering cross section, m ²	6.1 x 10 ⁻²⁸
elastic modulus, GPa ^{c/}	250
compressibility ^{a,d/} at 10-60 TPa	70 x 10 ⁻³

^{a/} To convert Pa to mm Hg, multiply by 0.0075.

^{b/} To convert J to cal, divide by 4.184.

^{c/} To convert GPa to psi, multiply by 145,000.

^{d/} 99% Cr; to convert TPa to megabars, multiply by 10.

B. FORMATION AND FATE IN THE ATMOSPHERE

There is very little information available on the reactivity of chromium compounds in the atmosphere.

Atmospheric reactions of chromium compounds have not been characterized. The persistence of chromium(VI) in the atmosphere has not been determined. It has been postulated that chromium metal and chromium (III) would be stable in the atmosphere, based on their low reactivity.^{3/} The assertion has been made that chromium(VI) would eventually react with dust or other pollutants to form chromium (III).^{4/} The rate at which chromium (VI) reacts in the atmosphere may depend on the presence and nature of oxidizable species, relative humidity, or the pH of atmospheric water, or a combination of these factors.

Physical removal of chromium from the atmosphere occurs both by atmospheric fallout (dry deposition) and by washout and rainout (wet deposition). Measurements have shown that most chromium deposition occurs through wet deposition.^{3/} Chromium particles of less than 5 um (aerodynamic equivalent) diameter may remain airborne for extended periods of time, allowing long distance transport by wind currents.^{5,6/} Because of this, meteorological conditions can play a significant role in the dispersion of chromium emitted from some sources.

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III. AMBIENT CONCENTRATIONS IN THE COMMUNITY

A. AMBIENT AIR DATA

Chromium databases compiled by both the Environmental Protection Agency (EPA) and the California Air Resources Board (ARB) were used in this analysis. The EPA data are included in the National Aerometric Data Bank and contain total chromium concentrations sampled from 1960 through 1968 and from 1977 through 1981 throughout California by various public agencies (federal, state, and local). All data were collected using high-volume samplers and were subsequently analyzed for chromium. The accuracy of data contained in the EPA database is not documented.

However, certain procedures have been undertaken to ensure reliable data. Although the chromium data were originally sampled and analyzed by a number of different agencies, the agencies presumably applied acceptable quality assurance practices during the collection and analysis phases. Additionally, after the data were received by EPA, edit and validation checks were used to further screen the data before they were included in the NADB. The purpose of the checks is to assure the accuracy and completeness of data contained in the NADB system (EPA, 1976).

Although data are available for 1960 through 1981, data from only the five most recent years (1977-1981) were used in our analysis. These data as reported in the NADB comprise total chromium concentrations greater than zero as well as values equal to zero, for a single analysis method. It should be noted that a concentration reported as zero does not necessarily indicate the absence of chromium but rather that the chromium concentration sampled was

below the limit of the analytical techniques. For the work presented in this section, zero values were replaced with a concentration equal to one-half the lowest non-zero concentration measured during the particular year of concern.

In addition to total chromium data, the EPA NADB database contains corresponding measurements of total suspended particulate matter. The Statistical Analysis System (SAS) software package was used to determine what, if any, relationship exists between chromium and total suspended particulate matter (TSP) (SAS, 1982). This analysis was used to determine whether total chromium concentrations could be predicted using TSP concentrations. Data collected at twenty sites from January 1977 through December 1981 were analyzed. No site had complete data for the entire period.

The ratio of mean chromium to mean TSP, the corresponding standard deviation, the coefficient of variation (SD/Mean), and the correlation coefficient between chromium and TSP were evaluated for each site included in the analysis. The results show a wide range of individual mean ratios, and large standard deviations around the mean ratios. No spatial or temporal patterns were apparent in the results. Correlation coefficients between chromium and TSP are relatively low (less than 0.64), indicating no significant relationship between the two variables. Based on these results, no usable relationship was found.

In addition to the statistics already discussed, peak-to-mean ratios for total chromium were also calculated to give general insights as to the nature of chromium emissions. These results are given in Table III-1. A small peak-to-mean ratio (less than 4.0) indicates relatively constant chromium concentrations and therefore, a relatively constant and homogeneous source

TABLE III-1

PEAK-TO-MEAN RATIOS FOR CHROMIUM -- 1977-1981
(units are ng/m³)

<u>Site Name</u>	<u>EPA Site Number</u>	<u>Peak Chromium</u>	<u>Mean Chromium</u>	<u>Peak: Mean Ratio</u>	<u>n</u>
Anaheim-Harbor	0230001	28.3	7.1	3.99	106
Bakersfield	0520003	22.5	9.4	2.39	28
Berkeley-Berkeley Wy	0740001	72.9	7.5	9.72	61
Burbank-W. Palm	0900002	23.6	10.5	2.25	30
Fresno-S. Cedar	2800002	32.4	9.5	3.41	58
Long Beach-Pine	4100001	41.0	17.9	2.29	27
Los Angeles-S. San Pedro	4180001	66.6	15.5	4.30	93
Los Angeles-Downtown	4180103	35.2	17.3	2.03	25
Oakland-Fifth St	5300001	60.3	19.0	3.17	29
Ontario-Airport	5380001	50.5	15.6	3.24	137
Oxnard	5560001	15.0	6.0	2.50	26
Pasadena	5760002	32.8	13.5	2.43	29
San Bernardino-W. 3rd	6680001	280.8	23.6	11.90	99
San Diego-Island	6800004	40.8	9.1	4.48	94
San Francisco-Grove	6860001	14.8	5.8	2.55	30
San Francisco	6860004	21.8	9.3	2.34	23
San Jose-N. 4th	6980004	36.3	12.2	2.98	99
Santa Ana-Ross	7180001	24.4	9.1	2.68	64
Torrance-Carson	8260001	315.3	30.5	10.34	29

area. A large peak-to-mean ratio (greater than or equal to 4.0) is indicative of variable chromium concentrations and either intermittent or heterogeneous emission sources.

Peak-to-mean ratios calculated for EPA data are generally low. Ratios less than 4.0 were calculated for fifteen of the twenty sites; conversely, ratios equal to or greater than 4.0 were calculated for one-fourth of the sites. The sites with the highest peak-to-mean ratios, San Bernardino-West 3rd and Torrance-Carson, also showed the highest peak concentrations and the highest mean concentrations. Results of the peak-to-mean analysis suggest that while chromium concentrations surrounding the majority of sites analyzed reflect homogeneous source areas, twenty-five percent of the sites analyzed are impacted by spatially non-uniform or intermittent sources.

The second chromium database, the ARB database, was collected from December 1982 through June 1984 using dichotomous (di-chot) samplers. The dichot samplers collect only those particles which are less than or equal to ten microns aerodynamic diameter. Particles are further subdivided into a coarse (2.5 microns to 10.0 microns diameter) and a fine (less than 2.5 microns diameter) fraction. All di-chot data used in this analysis reflect use of a percentage factor to correct for error in the sampling apparatus. Because of the nature of the dichotomous sampling apparatus, most of the fine fraction particles (approximately ninety percent) are captured in the fine fraction; however, a small percentage (approximately ten percent), are deposited in the coarse fraction. Consequently, fine and coarse fraction concentrations must be adjusted to reflect this sampling error. The accuracy of the di-chot data is approximately +50 percent.

Chromium data from the di-chot samplers (PM_{10} chromium) are summarized in Table III-2. Averages of total chromium range from 1.6 ng/m^3 to 11.4 ng/m^3 with most values in the 3 to 4 ng/m^3 range. The coarse fraction generally contained about twice as much PM_{10} chromium as the fine fraction. Long Beach showed the highest peak and the highest mean concentrations.

In addition to total chromium, the database contains corresponding measurements for particulate matter less than or equal to ten microns aerodynamic diameter (PM_{10}), and also for total suspended particulate matter (TSP). The SAS software package was used to assess the di-chot data to determine the relationship between total chromium and particulate matter. Total PM_{10} chromium, coarse fraction PM_{10} chromium, and fine fraction PM_{10} chromium, as related to PM_{10} particulate matter and TSP, were evaluated. Results showed a wide range of mean ratios and large standard deviations around the mean ratios. Correlation coefficients are all less than 0.61, indicating no statistically significant relationship between PM_{10} chromium, and PM_{10} particulate matter or TSP.

In addition, peak-to-mean ratios for PM_{10} chromium were calculated. Ratios were calculated for total (fine + coarse) chromium as well as for the coarse and fine fractions individually. Results are shown in Tables III-3, III-4, and III-5. Ratios calculated for total PM_{10} chromium (Table III-3) suggest that chromium source areas tend to be homogeneous; ratios are low at all but one of the nine sites. Results for the coarse and fine fractions individually (Tables III-4 and III-5) are more specific, and suggest impact from either intermittent or heterogeneous emission sources at one-third of the

TABLE III-2

SUMMARY OF AVERAGE CHROMIUM CONCENTRATIONS FROM ARB DICHOTOMOUS SAMPLES
(units are ng/m³)

Site Name	ARB Site Number	Coarse Fraction	Fine Fraction	Total Chromium	Total Samples
Bakersfield	1500203	2.91	1.09	4.00	56
Chico	0400628	2.75	0.85	3.60	34
China Lake	1500211	0.89	0.67	1.56	53
Fresno	1000234	2.21	1.57	3.78	41
Glendora	7000591	1.84	1.84	3.69	68
Lancaster	7000593	2.13	0.88	3.01	72
Long Beach	7000072	8.21	3.18	11.39	36
Riverside	3300146	2.06	1.61	3.67	72
Yuba City	5100895	2.49	1.35	3.84	51

TABLE III-3

PEAK TO MEAN RATIOS FOR TOTAL (FINE + COARSE) DICHOTOMOUS CHROMIUM
(units are ng/m³)

Site Name	ARB Site Number	Peak Chromium ^A	Mean Chromium ^A	P:M Ratios	Total Samples
Bakersfield	1500203	10.0	4.00	2.50	56
Chico	0400628	10.0	3.60	2.78	34
China Lake	1500211	3.0	1.56	1.92	53
Fresno	1000234	8.0	3.78	2.12	41
Glendora	7000591	10.0	3.69	2.71	68
Lancaster	7000593	16.0	3.01	5.32	72
Long Beach	7000072	39.0	11.39	3.42	36
Riverside	3300146	10.0	3.67	2.72	72
Yuba City	5100895	14.0	3.84	3.65	51

^A Total (hexavalent and trivalent) chromium

TABLE III-4

PEAK-TO-MEAN RATIOS FOR COARSE FRACTION DICHOTOMOUS CHROMIUM
(units are ng/m³)

<u>Site Name</u>	<u>ARB Site Number</u>	<u>Peak Chromium^A</u>	<u>Mean Chromium^A</u>	<u>P:M Ratio</u>	<u>Total Samples</u>
Bakersfield	1500203	6.89	2.91	2.37	56
Chico	0400628	7.78	2.75	2.83	34
China Lake	1500211	2.00	0.89	2.25	53
Fresno	1000234	5.78	2.21	2.62	41
Glendora	7000591	5.56	1.84	3.02	68
Lancaster	7000593	16.00	2.13	7.51	72
Long Beach	7000072	34.56	8.21	4.21	36
Riverside	3300146	6.78	2.06	3.29	72
Yuba City	5100895	11.78	2.49	4.73	51

TABLE III-5

PEAK-TO-MEAN RATIOS FOR FINE FRACTION DICHOTOMOUS CHROMIUM
(units are ng/m³)

<u>Site Name</u>	<u>ARB Site Number</u>	<u>Peak Chromium^A</u>	<u>Mean Chromium^A</u>	<u>P:M Ratio</u>	<u>Total Samples</u>
Bakersfield	1500203	5.55	1.09	5.09	56
Chico	0400628	2.22	0.85	2.61	34
China Lake	1500211	2.22	0.67	3.31	53
Fresno	1000234	3.33	1.57	2.12	41
Glendora	7000591	5.55	1.84	3.02	68
Lancaster	7000593	3.33	0.88	3.78	72
Long Beach	7000072	8.88	3.18	2.79	36
Riverside	3300146	7.24	1.61	4.50	72
Yuba City	5100895	13.32	1.35	9.87	51

^A Total (hexavalent and trivalent) chromium

sites evaluated for each individual size fraction. Although results indicate that source areas are in more cases homogeneous, it is apparent from the data that intermittent or heterogeneous sources do impact resulting chromium concentrations at some sites and that the size distribution of particles involved is just as likely to be in the fine fraction as in the coarse fraction.

The purpose of the analyses discussed above was both to determine whether particulate matter measurements could be used to estimate total chromium concentrations, and to determine the characteristics of chromium emissions. Results show that neither TSP or PM_{10} mass measurements provide adequate information for estimating corresponding chromium concentrations. No significant correlations were found using either dataset. Peak-to-mean ratios suggest that homogeneous source areas for chromium are present at many of the locations evaluated, while other sites show impact by local intermittent or heterogeneous sources or both, and that chromium from these sources is contained both within the fine fraction and coarse fraction particulate.

Work is being carried out to characterize the concentrations of total chromium and chromium(VI) in ambient air. Recent evaluation of ARB Method 106 indicates that chromium(VI) is unstable once collected, and that substances may be present in the samples which reduce the specificity of the method to chromium(VI). Because of these problems with Method 106, the validity of data produced by the method is uncertain. Until these questions of recovery and specificity for Method 106 can be resolved, data collected using Method 106 cannot be considered reliable, and will not be used in our analyses.

An alternative method to ARB Method 106 for the determination of chromium(VI) in ambient air is being developed. A copy of draft Method

ADDL006, Method for the Speciation and Analysis of Hexavalent Chromium at Ambient Atmospheric Levels, is attached.

During August 1985, four samples were collected in El Monte and analyzed for chromium(VI) using draft Method ADDL006. The four 24-hour samples showed chromium(VI) concentrations between 0.4 and 0.7 ng/m³, with an average of 0.5 ng/m³. These values are close to the estimated limit of detection (0.21 ng/m³) derived from laboratory evaluation of the method. Comparison of the limited information on chromium(VI) concentrations with total chromium concentrations in El Monte indicates that hexavalent chromium comprises between 3 and 8 percent of total atmospheric chromium. These estimates are based on preliminary chromium(VI) concentration measurements developed, using draft Method ADDL006. A validated method for sampling and analysis of chromium(VI) and additional information on chromium(VI) exposure will be prerequisite to the development of any control measures for chromium(VI).

B. ESTIMATES OF ANNUAL AMBIENT CHROMIUM EXPOSURE TO TOTAL CHROMIUM

Limitations to Analysis

Estimates of annual total chromium exposure were made for several areas in California. Because of the nature of the data used in making these estimates several important assumptions had to be made which impose certain limitations on the interpretation and use of the resulting data. The most important aspects of these limitations are summarized below:

- 1) The EPA data used to estimate annual population exposures for chromium were originally obtained from a number of different sources. It is probable that different collection and analysis methods and standards were employed by the various sources. Because

the accuracy of the chromium measurements is undocumented, the accuracy of the analyses presented here is unknown.

- 2) Data used to estimate annual population exposures for chromium are from a limited number of sites and based on a limited number of observations at those sites. Because of this, the true variability and magnitude of chromium concentrations may be more or less than those presented here. Also, because the spatial representativeness of each station is unknown, it is uncertain how differences in spatial representation between stations would affect the results presented.
- 3) Data used in these analyses are all representative of ambient outdoor concentrations; no consideration is given to indoor or workplace exposure. The exposure estimates presented here are based on the assumption that an individual's exposure was from the outdoor ambient air concentrations measured or calculated for the area in which the individual resides.
- 4) Chromium samples collected during 1977 and population data collected during 1980 have been used to make an estimate of annual population exposure to total chromium. These data were used because they allow estimation of annual average concentrations of total chromium. Changes may have occurred since these data were compiled; current total chromium concentrations and population exposures may be different. More recent data have become available which suggest that concentrations are lower, although these data are not adequate to estimate annual exposure.
- 5) Stationary sources of chromium are not explicitly considered in estimation of annual population exposure; they are considered

indirectly as a function of their contribution to chromium measured at the sampling sites. Exposures in receptor areas near large stationary sources of chromium are discussed separately.

- 6) Data presented here represent concentrations of total chromium. Limited preliminary data suggest that from 3 to 8 percent of total chromium may be chromium(VI) in areas not directly affected by chromium(VI) emissions.
- 7) Data from 1977 used for assessment of population exposure represent chromium particulate matter less than 50 micrometer (aerodynamic equivalent) diameter. Data on atmospheric concentrations of chromium particulate matter of respirable size (less than 10 micrometer diameter), gathered during 1982-1983, are presented in summary form in Table III-2 (page III-6).

Annual ambient population exposures were estimated using data from the EPA NADB database. As stated previously, the EPA comprise 24-hour total chromium concentrations collected with high-volume particulate samplers. All data were analyzed using the neutron activation analysis method. Although data are available for the years 1977 through 1981, much of the data for individual years are incomplete. Data for the year 1977 are the most suitable for use in evaluating annual total chromium exposures. The 1977 data were collected at sixteen stations. Although the sampling sites reflect a variety of land use parameters, all sites were established to provide data reflecting population oriented total chromium concentrations (EPA, 1984). Site-specific location and influence criteria are summarized in Table III-6.

Total chromium data collected at the sixteen sites during 1977 are summarized in Table III-7. Approximately two to three samples were collected at each site during each month of the year. Zero values comprised from three to seventy-seven percent of values reported at a given site; for all sites

TABLE III-6

Summary of Location Characteristics and Dominating Influences
Surrounding Sampling Sites Used in Exposure Analysis

Site Name	EPA Site Number	Location Characteristics	Dominating Influence
<u>SoCAB Sites:</u>			
Anaheim-Harbor Blvd.	0230001	Suburban	Commercial
Burbank-West Palm Ave.	0900002	Center City	Commercial
Long Beach-Pine Ave.	4100001	Center City	Commercial
Los Angeles- So. San Pedro	4180001	Center City	Commercial
Ontario Airport	5380001	Rural	Commercial
Pasadena-Cal Tech	5760002	Center City	Residential
San Bernardino-West 3rd Street	6680001	Center City	Commercial
Santa Ana-Ross Street	7180001	Center City	commercial
Torrance-Carson Street	8260001	Center City	Residential
<u>SFBAAB Sites:</u>			
Berkeley-Berkeley Way	0740001	Center City	Residential
Oakland-Fifth Street	5300001	Center City	Industrial
San Francisco- Grove Street	6860001	Center City	Commercial
<u>Other Sites:</u>			
Fresno-South Cedar Ave.	2800002	Center City	Commercial
Sacramento-Stockton Blvd.	6580001	Center City	Commercial
San Diego-Island Ave.	6800004	Center City	Commercial
San Jose- North 4th St.	6980004	Center City	Commercial

Table III-7

Summary of 1977 Chromium Data from the EPA
National Aerometric Data Bank
(units are ng/m³)

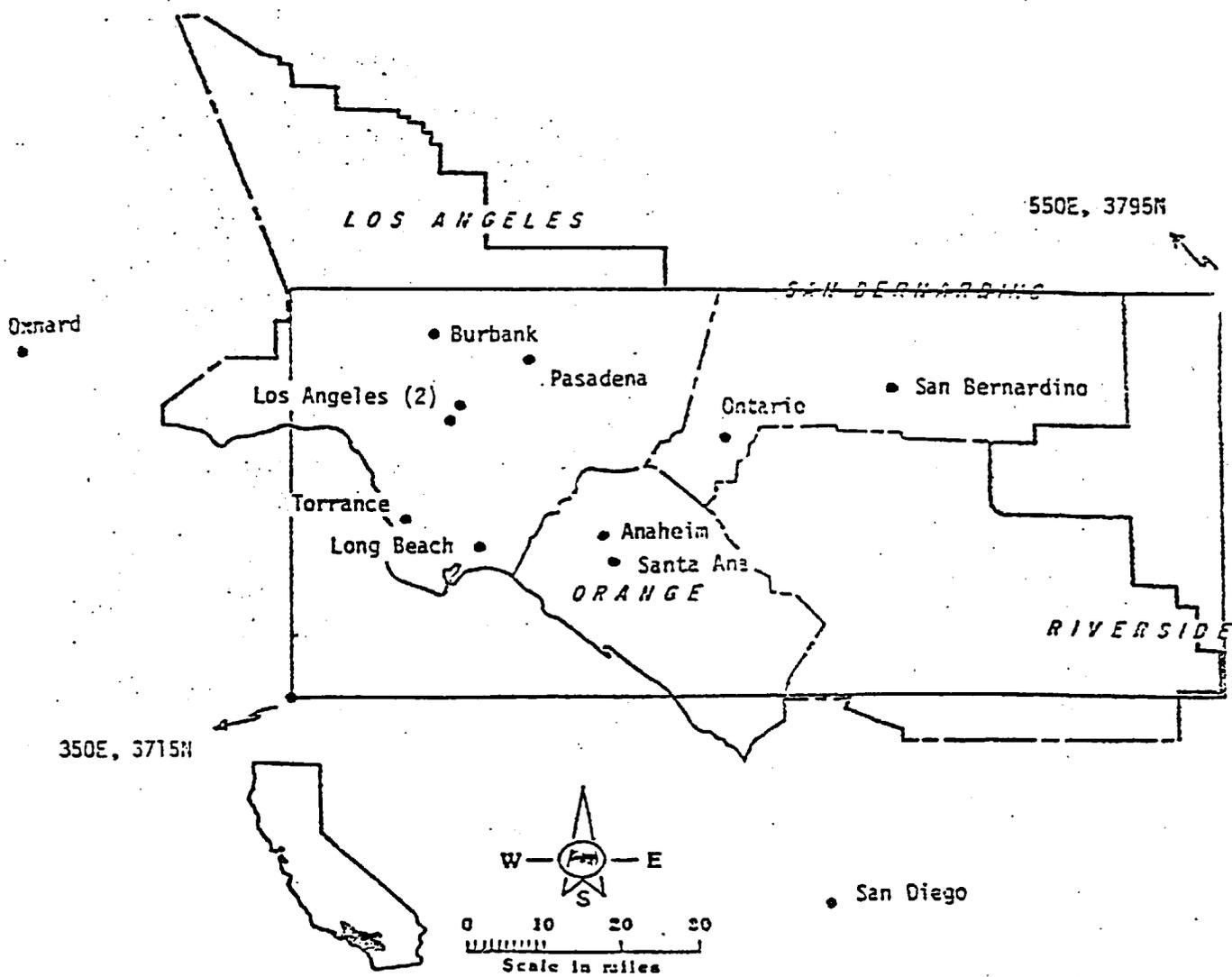
Site Name	EPA Site Number	Maximum Chromium	Average Chromium	Standard Deviation	Number of Samples: Total	Samples: Zero
SoCAB Sites:						
Anaheim- Harbor Blvd	0230001	28.3	6.4	5.2	30	23
Burbank- West Palm Ave	0900002	23.6	10.7	6.2	30	10
Long Beach- Pine Avenue	4100001	41.0	17.9	9.9	27	2
Los Angeles So. San Pedro	4180001	66.6	19.1	12.2	30	1
Ontario-Airport	5380001	34.2	18.5	6.7	30	1
Pasadena-Cal Tech	5760002	32.8	13.7	8.0	29	7
San Bernardino- West 3rd St.	6680001	103.3	33.3	24.1	29	2
Santa Ana- Ross Street	7180001	20.9	10.8	5.3	29	7
Torrance- Carson Street	8260001	315.2	30.6	56.2	29	5
SFBAAB Sites:						
Berkeley- Berkeley Way	0740001	72.9	9.0	13.7	30	19
Oakland-Fifth St.	5300001	60.3	19.0	10.1	29	1
San Francisco- Grove Street	6860001	14.8	6.2	3.6	30	21
Other Sites:						
Fresno-So. Cedar Avenue	2800002	32.4	12.3	8.3	30	10
Sacramento- Stockton Blvd.	6580001	23.6	10.8	5.7	30	7
San Diego- Island Avenue	6800004	23.6	11.7	6.3	30	7
San Jose- North 4th Street	6980004	29.1	14.3	7.6	30	5

N.B.- The minimum concentration reported at each site during 1977 was zero. The minimum non-zero value reported at any site was 8 ng/m³.

* These numbers represent the total number of samples included in the analysis and the number of samples for which a zero value was reported.

FIGURE III-1

LOCATION OF MODELING AREAS AND STATIONS, THE DATA FROM WHICH WERE USED TO INTERPOLATE CHROMIUM IN THE SOUTH COAST AIR BASIN



combined, twenty-seven percent of values were reported as zero. The number of zero values reported at each site is summarized in Table III-7. As stated previously, a reported zero concentration does not necessarily indicate an absence of chromium but rather that the chromium concentration was below the limit of the analytical techniques. There are several ways to treat zero values when calculating annual averages. Reported zero values can be assumed equal to zero, assumed equal to the lower limit of analysis, or assumed equal to one-half the lower limit of analysis. Including zero concentrations as zero results in estimates the lowest averages; assuming zero values equal the lower limit of analysis results in the highest averages. These two extremes likely bracket the possible range of concentration averages. Assuming zero concentrations equal one-half the lower limit of analysis provides a third estimate of concentrations.

In the following discussion, zero values were replaced with a concentration of one-half the lowest non-zero concentration sampled at any site during 1977, 4.0 nanograms per cubic meter. Alternatives to this approach are presented later in this section. We assume the lowest non-zero value reported during 1977 equals the lower limit of the analytical techniques used. Of the sixteen sites used in this analysis, three had more than fifty percent of all values reported as zero; nine sites had more than twenty percent of all values reported as zero. The occurrence of many zero values at a number of sites and the assumptions made in replacing them with a single concentration (4.0 ng/m^3) necessarily limits the confidence that can be placed in the results presented here.

Maximum twenty-four hour total chromium concentrations at each site range from 14.8 ng/m^3 to 315.5 ng/m^3 , while annual average chromium concentrations range from 6.2 ng/m^3 to 33.3 ng/m^3 . The highest twenty-four-hour average concentration and annual average concentration both occurred at stations located in the South Coast Air Basin.

As seen in Table III-7, the majority of sites for which chromium data are available are located in the South Coast (SoCAB) and San Francisco Bay Area (SFBAAB) air basins. Other stations are located in Fresno and San Diego. Using the appropriate annual average concentrations given in Table III-7, annual chromium concentrations were interpolated to 1980 census tract centroids for the SoCAB and SFBAAB using the McRae inverse distance-squared interpolation routine (McRae, 1982).

Total chromium concentrations in the SoCAB were interpolated for an area of 200 by 80 kilometers. The limits of the modeling area and the relative locations of stations used for interpolation are shown in Figure III-1. Barriers to interpolation, such as mountain ranges, were included as appropriate. Based on 1980 census data, total population in the SoCAB is approximately 11 million. Census tracts within the modeling area have a total population of just over 10 million. Figure III-2 is a graphic illustration of annual chromium concentrations interpolated to the modeling area. The plot indicates that annual concentrations during 1977 were highest in the eastern portion of the grid (San Bernardino station) with a secondary peak to the southwest (Torrance station). Areas with zero concentrations do not necessarily reflect an absence of chromium but rather, the influence of barriers to interpolation. Overall, annual average concentrations calculated for the modeling area are between 6.4 ng/m^3 and 33.3 ng/m^3 . A corresponding plot of population within the study area is shown in Figure III-3. Comparison of the two figures show the highest population density near the secondary peak at the Torrance-Carson site.

FIGURE III-2

SOCAB 1977 Total Chromium in 5 KM Cells

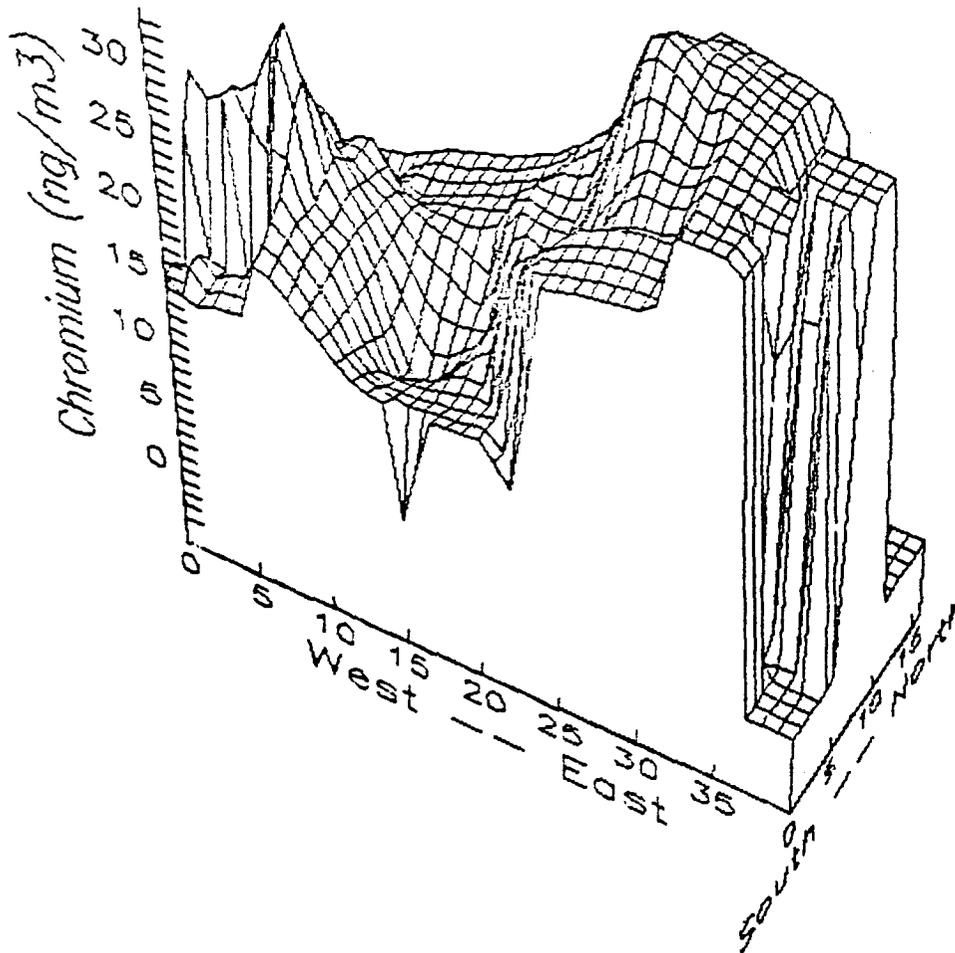


FIGURE III-3

SOCAB 1980 Population Density for 5 KM Cells

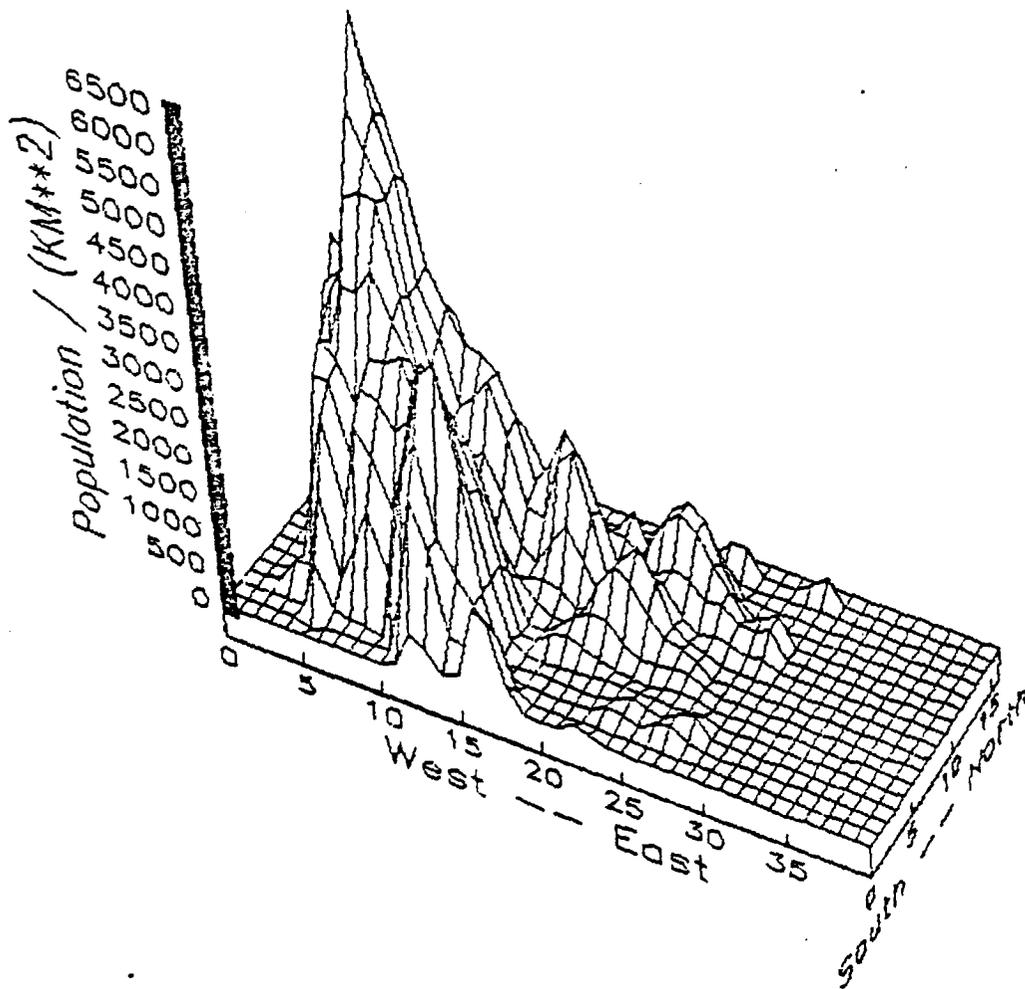


Figure III-4 shows the population exposed to various annual average chromium concentrations in the SoCAB. The majority of people were exposed to between 11.0 and 21.0 ng/m³ total chromium. The population-weighted average exposure in the SoCAB is 16.9 ng/m³ while the geographic average is 16.6 ng/m³. Figure III-5 shows the same data plotted in Figure III-4, but plotted as cumulative population versus annual average chromium. According to this figure, more than 2 million people were exposed to at least 20.0 ng/m³ total chromium in 1977.

Because the data available for the San Francisco Bay Area Air Basin lacked good spatial coverage, estimates of exposure could be estimated for only a forty by twenty-five kilometer area. The limits of the modeling area and the relative locations of stations used for interpolation are shown in Figure III-6. Barriers to interpolation were included as appropriate. Although there are approximately five million people in the SFBAAB, the total population in the modeling area is only about 1.5 million. A graphic illustration of annual chromium concentrations interpolated to the SFBAAB modeling area is shown in Figure III-7. Annual concentrations are greatest in the eastern portion of the grid (Oakland station). Areas with zero concentration reflect the influence of barriers to interpolation. A plot of population density in the study area is shown in Figure III-8. Comparison of Figures III-7 and III-8 show that the peak population density occurs to the west of the peak chromium concentrations; a secondary peak of population density occurs very near the point of peak concentration. Figure III-9 shows population exposures to total chromium in the SFBAAB modeling region. Almost 800,000 of the 1.5 million people in the study area were exposed to 9.0

FIGURE III-4

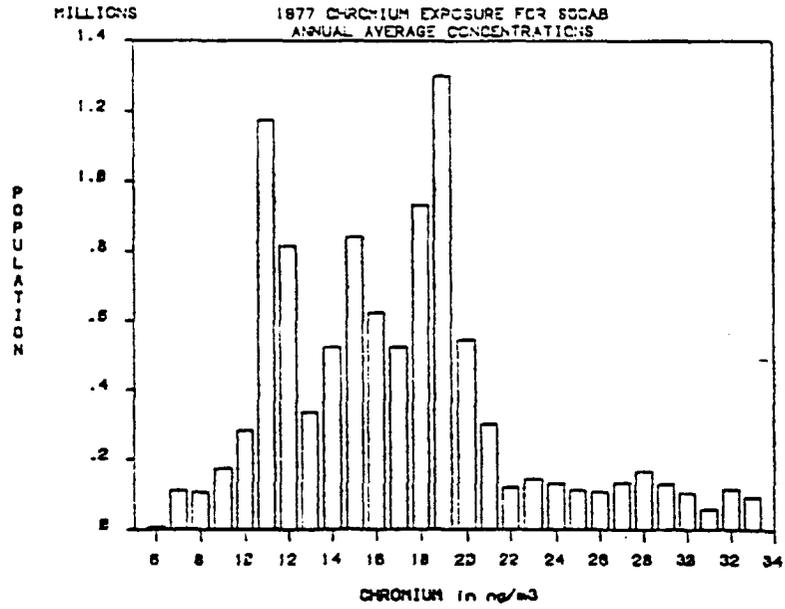


FIGURE III-5

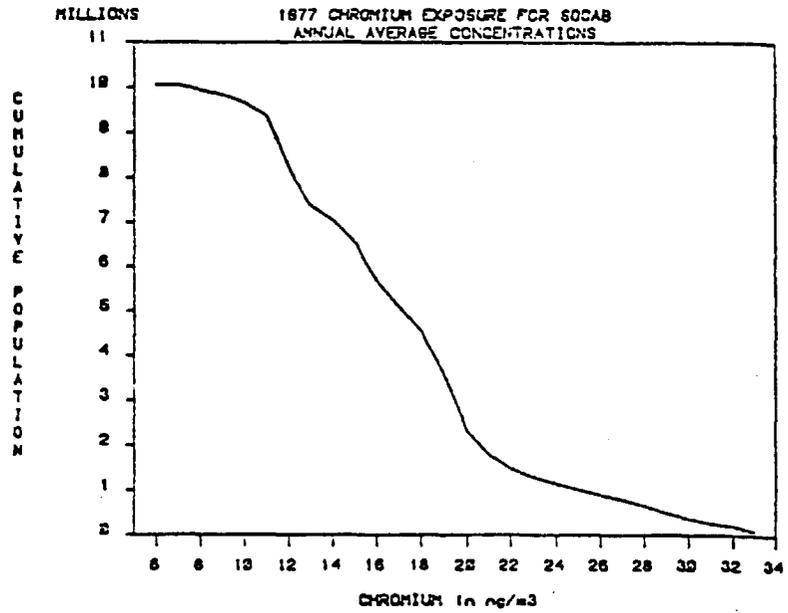


FIGURE III-6

LOCATION OF MODELING AREAS AND STATIONS USED, THE DATA FROM WHICH WERE USED TO INTERPOLATE CHROMIUM IN THE SAN FRANCISCO BAY AREA

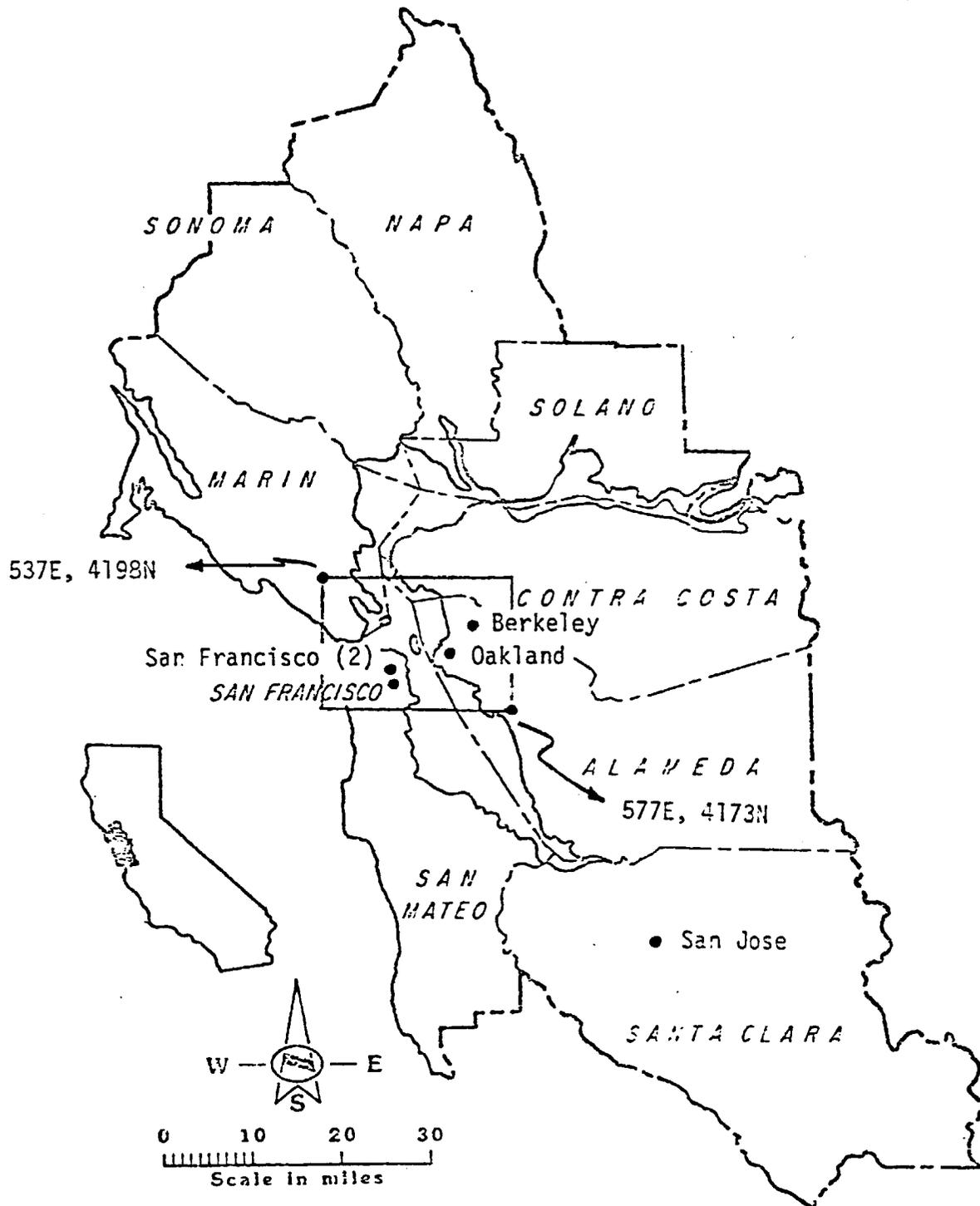


FIGURE III-7

SF Bay Area 1977 Total Chromium in 5 KM Cells

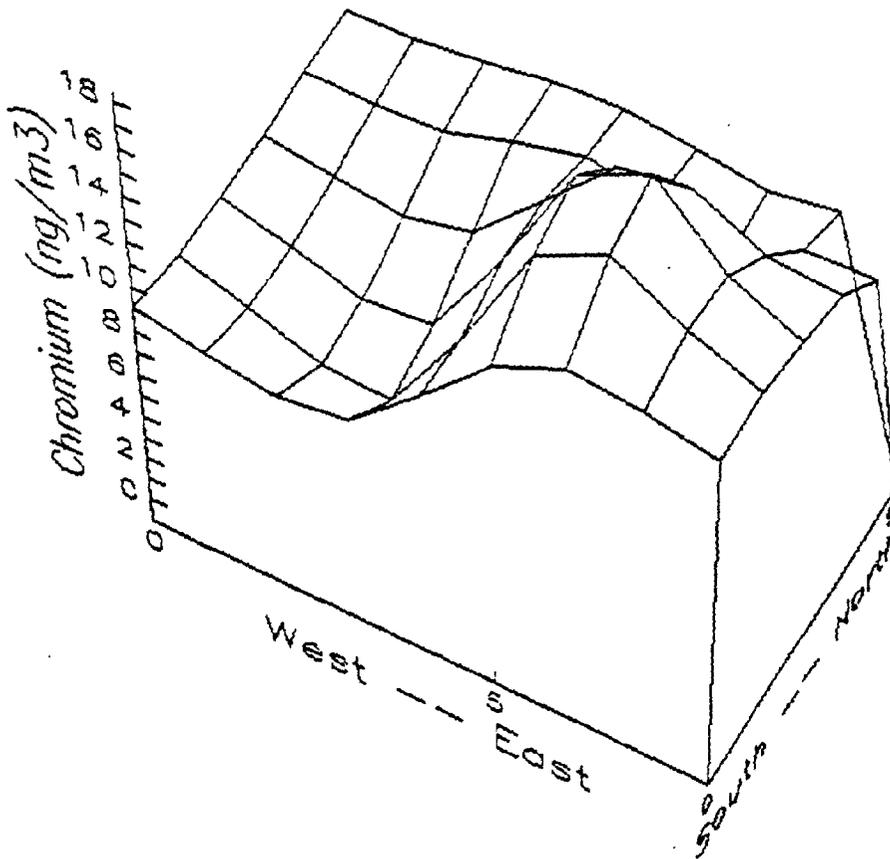


FIGURE III-8

S.F. Bay Area 1980 Population Density for 5 KM Cells

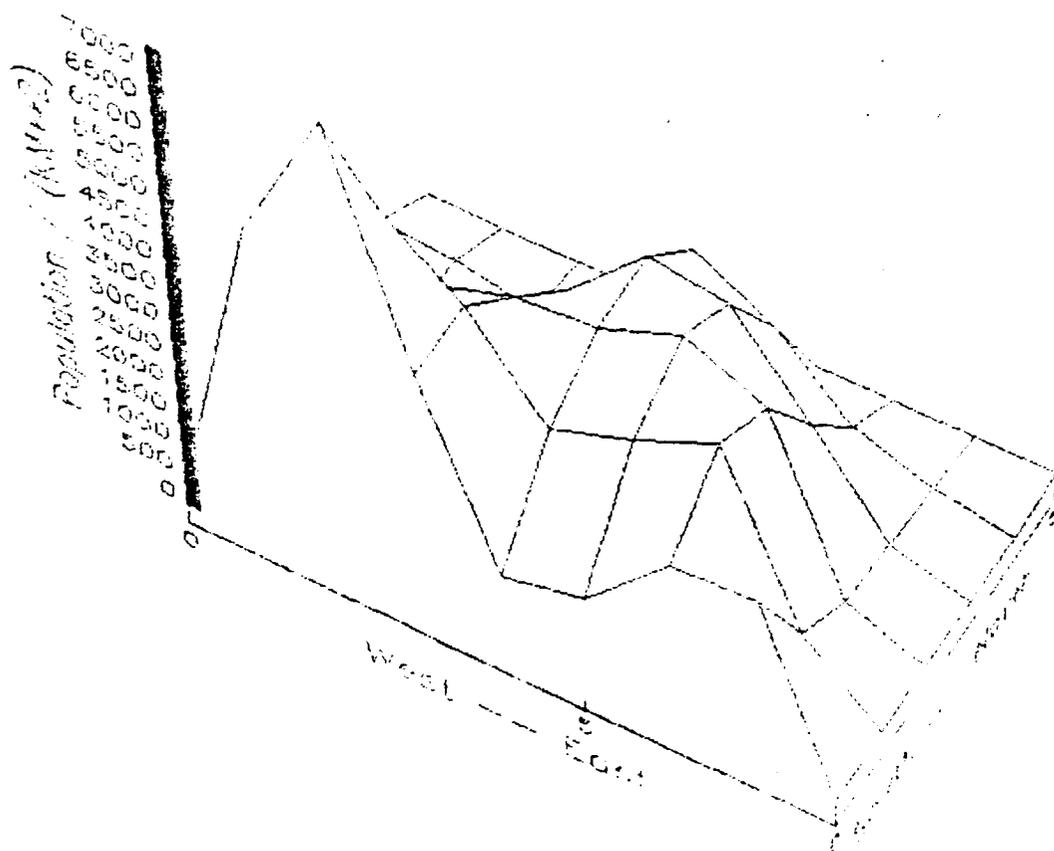
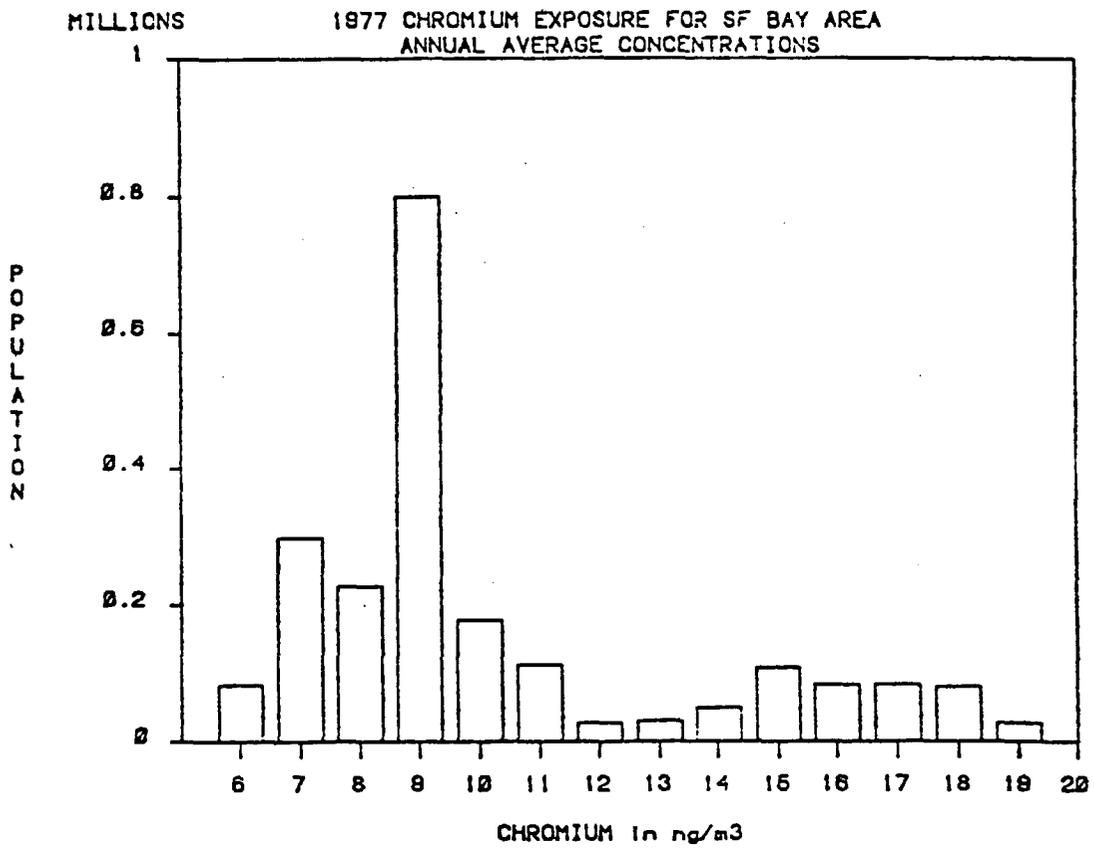


FIGURE III-9



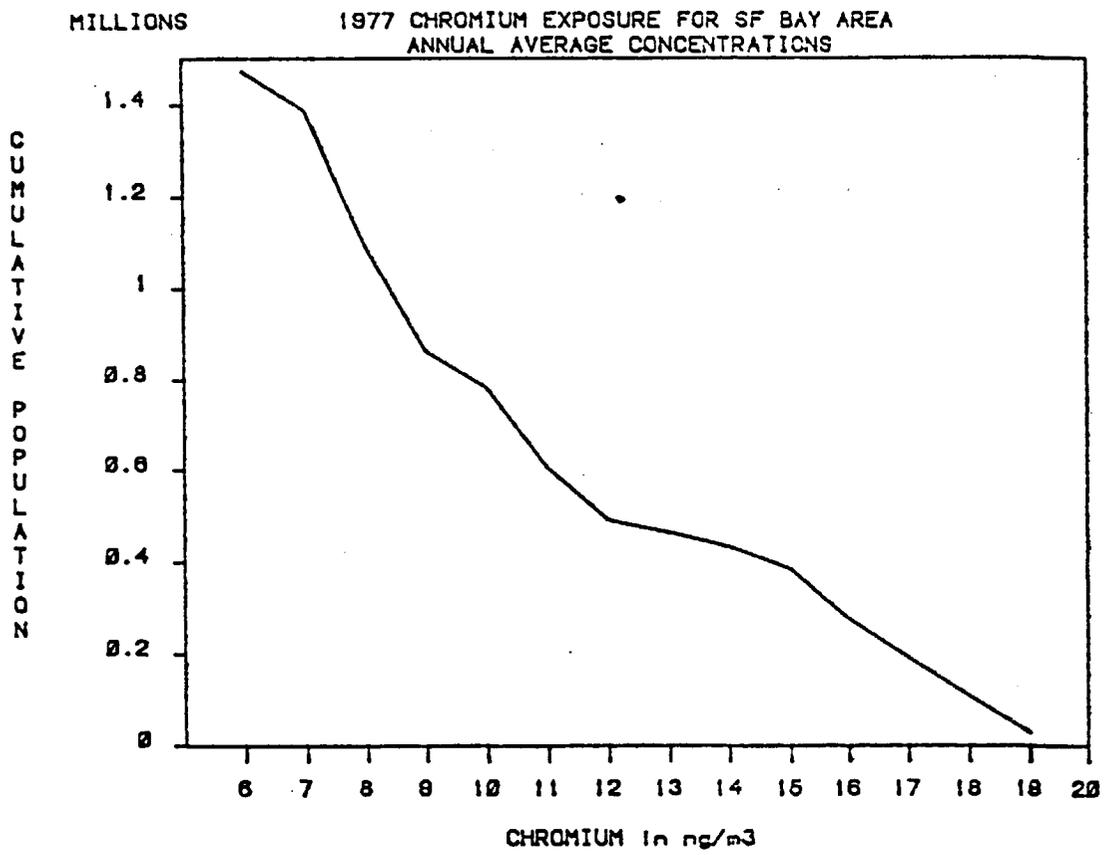
ng/m³ or more of total chromium during 1977. Cumulative exposures are shown in Figure III-10. In the SFBAAB, the population-weighted chromium concentration for 1977 was 10.8 ng/m³. The geographic mean was 11.3 ng/m³.

Annual total chromium exposure estimates for the other areas in the state were calculated somewhat differently from those for the South Coast and San Francisco Bay Area Air Basins. Data were available for only one site in each of four cities: Fresno, Sacramento, San Diego, and San Jose. For these cities, we assumed that the annual total chromium concentration at each site was representative of the exposure experienced by the population living in those census tracts with centroids not more than ten kilometers from the sampling site. The annual concentration at the sampling sites and the population exposed to that concentration are summarized in Table III-8. As shown in this table, annual population exposures to total chromium in these areas ranged from 10.6 ng/m³ to 14.3 ng/m³.

TABLE III-8
ANNUAL CHROMIUM EXPOSURE FOR SPECIFIC CENSUS TRACTS

<u>Site Name</u>	<u>EPA Site Number</u>	<u>Population Within 10 Kilometers</u>	<u>Annual Average Chromium (ng/m³)</u>
Fresno-South Cedar Avenue	2800002	250,612	12.3
Sacramento-Stockton Blvd.	6580001	376,283	10.6
San Diego-Island Avenue	6800004	477,482	11.7
San Jose-North 4th St.	6980004	608,945	14.3

FIGURE III-10



In addition to the approach discussed above, population exposures were determined using two alternative approaches to provide a range of possible values. The alternative approaches differ only in their treatment of zero concentrations. The first alternative approach assumes zero values in the database are actually zero concentrations. This approach provides a lower-bound estimate of population exposure. The second alternative approach assumes zero values in the database equal the lowest non-zero concentration reported during 1977 (7.9 ng/m³). This approach provides an upper bound estimate of population exposure. The effect of these alternative approaches on resulting concentrations is directly related to the number of zero concentrations reported at each individual site (refer to Table III-8). The greater the percentage of reported zero concentrations, the greater the variation in concentrations of one approach versus the other.

Exposure estimates based on these alternative approaches are summarized in Table III-9. Results based on the first approach show geographic averages ranging from 9.4 ng/m³ to 15.7 ng/m³ and population-weighted concentrations ranging from 8.9 ng/m³ to 16.1 ng/m³. Geographic average concentrations based on the second approach range from 11.7 ng/m³ to 17.5 ng/m³ while population-weighted averages range from 11.7 ng/m³ to 17.8 ng/m³.

Limited data on current ambient total chromium concentrations have recently become available as a result of the Air Resources Board's ongoing effort to document ambient levels of potentially toxic compounds. Data are available for nineteen locations for varying periods of time during January through June of 1985. These data represent twenty-four hour samples collected using either high volume or low volume particulate samplers and subsequently

analyzed for total chromium using atomic absorption or X-ray fluorescence, respectively.

The data are summarized in Table III-10. Minimum concentrations reported during the six months range from below the quantitation limit (1.0 ng/m^3) to 3.0 ng/m^3 . The maximum concentrations reported was 24.0 ng/m^3 . Averages of values at each site range from 1.9 ng/m^3 to 9.1 ng/m^3 . The average concentration for all sites combined is 4.7 ng/m^3 .

The 1985 ARB total chromium data are compared with the 1977 EPA total chromium data in Table III-11. Although all EPA sites are included in this comparison, only fourteen of the nineteen ARB sites are included. These fourteen sites are the only ARB sites located in the same areas as the EPA sampling locations. As is apparent from Table III-11, total chromium data from 1985 are different from chromium data of 1977. The 1977 data show higher concentrations. The maximum twenty-four hour concentration sampled during 1977 was 74.5 ng/m^3 whereas the maximum twenty-four hour concentration sampled during 1985 was 24.0 ng/m^3 . Average concentrations during 1977 ranged from 4.0 ng/m^3 to 34.5 ng/m^3 . This range compares with a range of 1.9 ng/m^3 to 9.1 ng/m^3 for the 1985 data. Overall concentrations reported by EPA for 1977 are approximately 1.5 to 3.5 times greater than those reported for 1985. Data summarized in Table III-11 suggest present total chromium concentrations are lower than those measured during 1977; however, several factors should be considered in comparing the data. These factors include:

1. Site locations during 1985 are not the same as those used in 1977;

TABLE III-9

Comparison of Population Exposures to Chromium During 1977

Using Three Approaches*

(units are ng/m^3)

Area Location	Approach #1 Geog Avg/Pop-Wt Avg	Approach #2 Geog Avg/Pop-Wt Avg	Approach #3 Geog Avg/Pop-Wt Avg
SoCAB Area- (150 x 80 km)	15.7 / 16.1	16.6 / 16.9	17.5 / 17.8
BAAB Area- (40 x 20 km)	9.4 / 8.9	11.3 / 10.8	13.1 / 12.7
Fresno Area- (10 km radius)	11.0 / 11.0	12.3 / 12.3	13.6 / 13.6
Scramento Area- (10 km radius)	9.8 / 9.8	10.6 / 10.6	11.7 / 11.7
San Diego Area (10 km radius)	10.7 / 10.7	11.7 / 11.7	12.6 / 12.6
San Jose Area- (10 km radius)	13.7 / 13.7	14.3 / 14.3	15.0 / 15.0

* The three approaches used differ in the way in which zero values in the database were treated:

Approach #1: Zero values were assumed equal to zero ($0.0 \text{ ng}/\text{m}^3$).

Approach #2: Zero values were assumed equal to one-half the quantitation limit ($0.6 \text{ ng}/\text{m}^3$).

Approach #3: Zero values were assumed equal to the quantitation limit ($1.2 \text{ ng}/\text{m}^3$).

TABLE III-10

Summary of ARB Chromium Data Sampled
January through June 1985
(units are ng/m³)

Site Name	EPA Site Number	Minimum Chromium*	Maximum Chromium	Average Chromium	Number of Samples: Total	Zero
SACRAMENTO VALLEY AIR BASIN						
Citrus Heights- Sunrise Blvd	3400293	2.0	11.0	5.4	13	0
SAN DIEGO AIR BASIN						
Chula Vista- El Cajon- Redwood Avenue	8000114	0.5	6.0	2.8	14	1
8000131		1.0	4.0	3.0	8	0
SAN FRANCISCO BAY AREA AIR BASIN						
Richmond-13th St.	0700433	2.0	5.0	3.4	14	0
Concord- 2975 Treat Blvd.	0700440	1.0	2.0	1.9	15	0
San Jose-4th St.	4300382	2.0	21.0	8.2	14	0
Fremont-Chapel Way	6000336	1.0	5.0	2.4	15	0
San Francisco- 23rd Street	9000304	2.0	6.0	3.9	15	0
SAN JOAQUIN VALLEY AIR BASIN:						
Fresno-Olive	1000234	2.0	10.0	4.3	12	0
Bakersfield- Chester Street	1500203	2.0	7.0	4.3	15	0
Stockton- Hazelton Street	3900252	3.0	6.0	4.1	12	0
Modesto- 418 14th Street	5000568	3.0	7.0	3.9	15	0
SOUTH CENTRAL COAST AIR BASIN:						
Santa Barbara- Canon Perdido	4200378	1.0	10.0	3.5	8	0
Simi Valley-	5600413	1.0	4.0	2.4	15	0
SOUTH COAST AIR BASIN:						
Riverside- Rubidoux	3300144	2.0	14.0	7.3	11	0
Upland	3600175	0.5	9.0	4.8	13	1
North Long Beach	7000072	2.0	11.0	6.3	12	0
Los Angeles- North Main	7000087	3.0	23.0	9.1	10	0
El Monte-ARB HSLD	7000579	3.0	24.0	8.6	50	0

* A concentration of 0.5 ng/m³ is equal to one-half the quantitation limit of 1.0 ng/m³ and was substituted for the value below the quantitation limit.

TABLE III-11

Comparison of 1977 EPA Chromium Data with 1985 ARB Chromium Data*
(units are ng/m³)

Characteristic Being Compared:	1977 EPA Chromium Data	1985 ARB Chromium Data
SAN FRANCISCO BAY AREA AIR BASIN SITES:		
Range of Minimum Concentrations	4.0 - 4.0	1.0 - 2.0
Range of Maximum Concentrations	13.9 - 28.2	2.0 - 21.0
Range of Average Concentrations (Each Site Individually)	7.2 - 16.8	1.9 - 8.2
Observations per Site	7	14 - 15
Average Concentration (All Sites Combined)	11.8	4.0
SOUTH COAST AIR BASIN SITES:		
Range of Minimum Concentrations	4.0 - 10.0	0.5 - 3.0
Range of Maximum Concentrations	4.0 - 74.5	9.0 - 24.0
Range of Average Concentrations (Each Site Individually)	4.0 - 34.5	4.8 - 9.1
Number of Observations	11 - 12	10 - 50
Average Concentration (All Sites Combined)	15.9	7.2
FRESNO AREA SITE:		
Minimum Concentration	4.0	2.0
Maximum Concentration	12.3	10.0
Average Concentration	6.8	4.3
Number of Observations	7	12
SACRAMENTO AREA SITE:		
Minimum Concentration	4.0	2.0
Maximum Concentration	17.8	11.0
Average Concentration	9.0	5.4
Number of Observations	7	13
SAN DIEGO AREA SITE:		
Minimum Concentration	4.0	0.5
Maximum Concentration	16.9	6.0
Average Concentration	10.0	2.8
Number of Observations	15	22
SAN JOSE AREA SITE:		
Minimum Concentration	4.0	0.5
Maximum Concentration	28.2	21.0
Average Concentration	16.8	8.2
Number of Observations	7	14

* Data included in this comparison are limited to samples collected from January through June of the two different years.

2. Meteorological conditions under which the 1985 data were collected may differ from those present during 1977;

3. The 1985 chromium data reflect a quantitation limit of 1.0 ng/m³. This concentration is approximately one eighth the quantitation limit for the 1977 data;

4. Chromium sampling during 1985 employed different collection and analysis methods than were used in 1977. The comparability of these various methods is not known.

Because data are available for the entire year of 1977, they were used to calculate annual exposure.

C. CONCENTRATIONS CLOSE TO SOURCES

To estimate concentrations of chromium close to sources of chromium(VI), emissions were calculated and air quality modeling done for a typical large chrome plater and for a bank of industrial cooling towers using chromate water treatment. Both sources are located in the South Coast Air Basin and are in populated areas.

After emissions from each source were calculated, an industrial source complex model (ISCST) was used to calculate annual average chromium concentrations at the points of a grid representing receptors surrounding each source. Residential population in the surrounding area was also gridded, and population exposure was estimated. The analysis encompassed an area 20 by 20 kilometers centered on the plating facility and an area 40 by 40 kilometer centered on the bank of towers. Deposition was not considered in this modeling.

The results of modeling are estimates of annual ambient concentrations based on worst case meteorology observed in the study areas. The modeled concentrations represent maximum annual average concentrations occurring outdoors. It is not known whether indoor concentrations are greater or less than those outdoors.

The concentrations and population exposures calculated from emissions from each source represent exposure above background from each source; possible additive or cumulative exposure from multiple sources is not addressed in this analysis.

Emissions of chromium from the chrome plating facility were calculated by the South Coast Air Quality Management District based on information provided by the company (Zwaicher, 1983). Chromium emissions from this source were estimated to be greater than 1,000 lbs/year. There are five chrome platers in the South Coast Air Basin which emit this or a greater amount of chromium per year. One facility was estimated to emit over 8,000 lbs/year of chromium per year. These figures reflect the assumption that 90 percent of chromium is removed by control equipment. Emissions were reported as chromium; no oxidation state was specified. Emission tests conducted by various agencies have indicated that worst-case chromium (VI) emissions from chromium platers comprise from 25 percent to 100 percent of total chromium emissions. (SCAQMD, 1985; Suzuki, 1984).

Results of modeling and population exposure assessment for the plating facility are presented in Table III-12, and shown in Figures III-11 and III-12. These numbers are estimated annual average chromium concentration above background. Because there is no information available to assess to what extent chromium(VI) reacts in the atmosphere after being emitted, the exposure is reported in terms of total chromium.

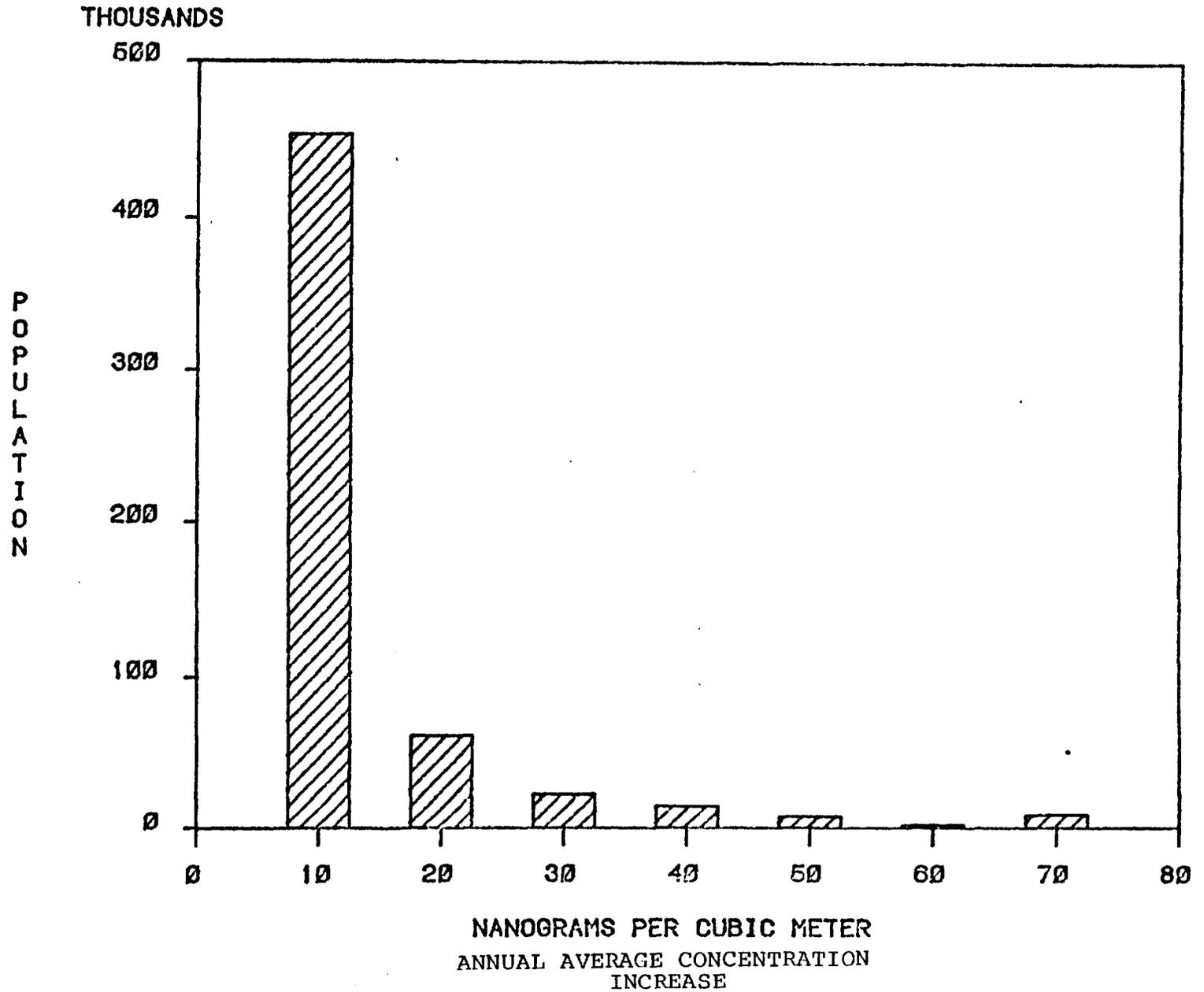
Table III-12

Increase in Population Exposure to Chromium
from a Plating Facility

<u>Annual Average Increase in Chromium Concentration, ng/m3</u>	<u>Population Exposed</u>	<u>Cumulative Population</u>
550	1,960	1,960
450	-0-	1,960
350	-0-	1,960
250	1,925	3,885
150	5,825	9,737
100	-0-	9,737
90	-0-	9,737
80	-0-	9,737
70	8,803	18,540
60	1,945	20,485
50	7,742	28,227
40	14,870	43,097
30	22,982	66,079
20	61,829	127,908
10	452,709	508,617
0.5 to 5.0	2,400,000	2,993,262

FIGURE III-11

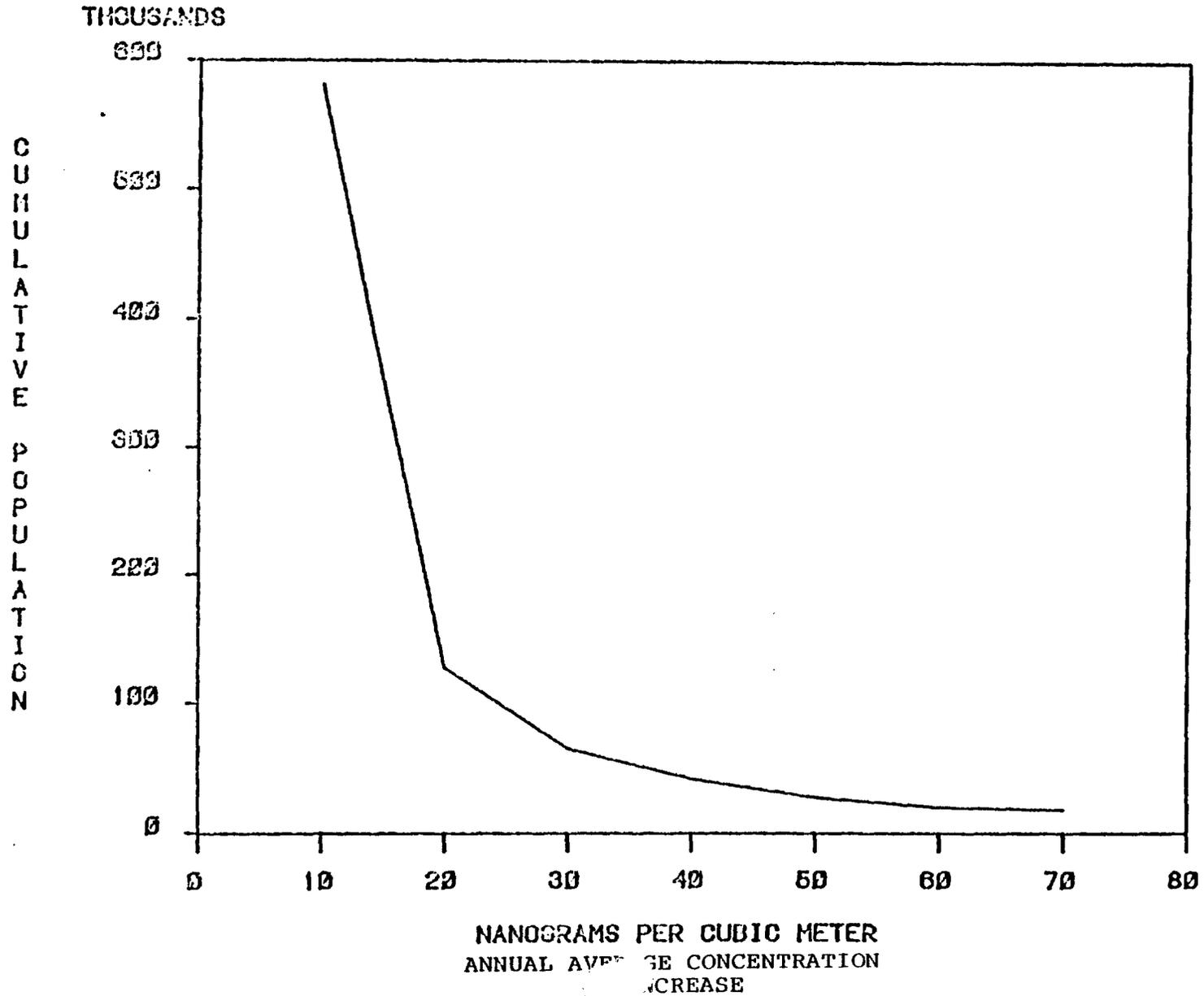
INCREASE IN
POPULATION EXPOSURE TO CHROMIUM FROM A PLATING FACILITY



III-35

FIGURE III-12

INCREASE IN
CUMULATIVE POPULATION EXPOSURE TO CHROMIUM FROM
A PLATING FACILITY



III-36

Relatively short distances are observed between the source and exposed population involved in this analysis; for instance, an elementary school is located within one kilometer of the source. Annual average concentrations of chromium at the school are estimated to fall between 100 and 500 ng/m³.

Emissions from a bank of industrial cooling towers were estimated based on recirculating water rate, average chromate treatment concentration in industrial towers, and information on the typical fraction of tower water emitted as drift. The annual emissions of chromium from these towers were estimated to be about 800 pounds. Results of modeling and exposure assessment are summarized in Table III-13 and shown in Figures III-13 and III-14. Values are reported as chromium because insufficient information exists to quantify the extent of reaction of emitted chromium(VI) occurring between the source and receptors.

TABLE III-13

Increase in Population Exposure to Chromium from a Bank of Industrial Cooling Towers

Annual Average Increase in Chromium Concentration, ng/m ³	Population Exposed	Cumulative Population
5.0	8,886	8,886
4.0	2,993	11,879
3.0	23,942	35,821
2.0	96,565	132,386
1.0	730,336	862,722

In summary, estimates of concentrations of chromium close to sources of chromium(VI), and resulting population exposures have been made for two typical sources of chromium(VI) emissions. These health conservative estimates indicate that significant increases in population exposure to chromium may occur close to large sources.

FIGURE III-13

INCREASE IN
POPULATION EXPOSURE TO CHROMIUM FROM A BANK OF
INDUSTRIAL COOLING TOWERS

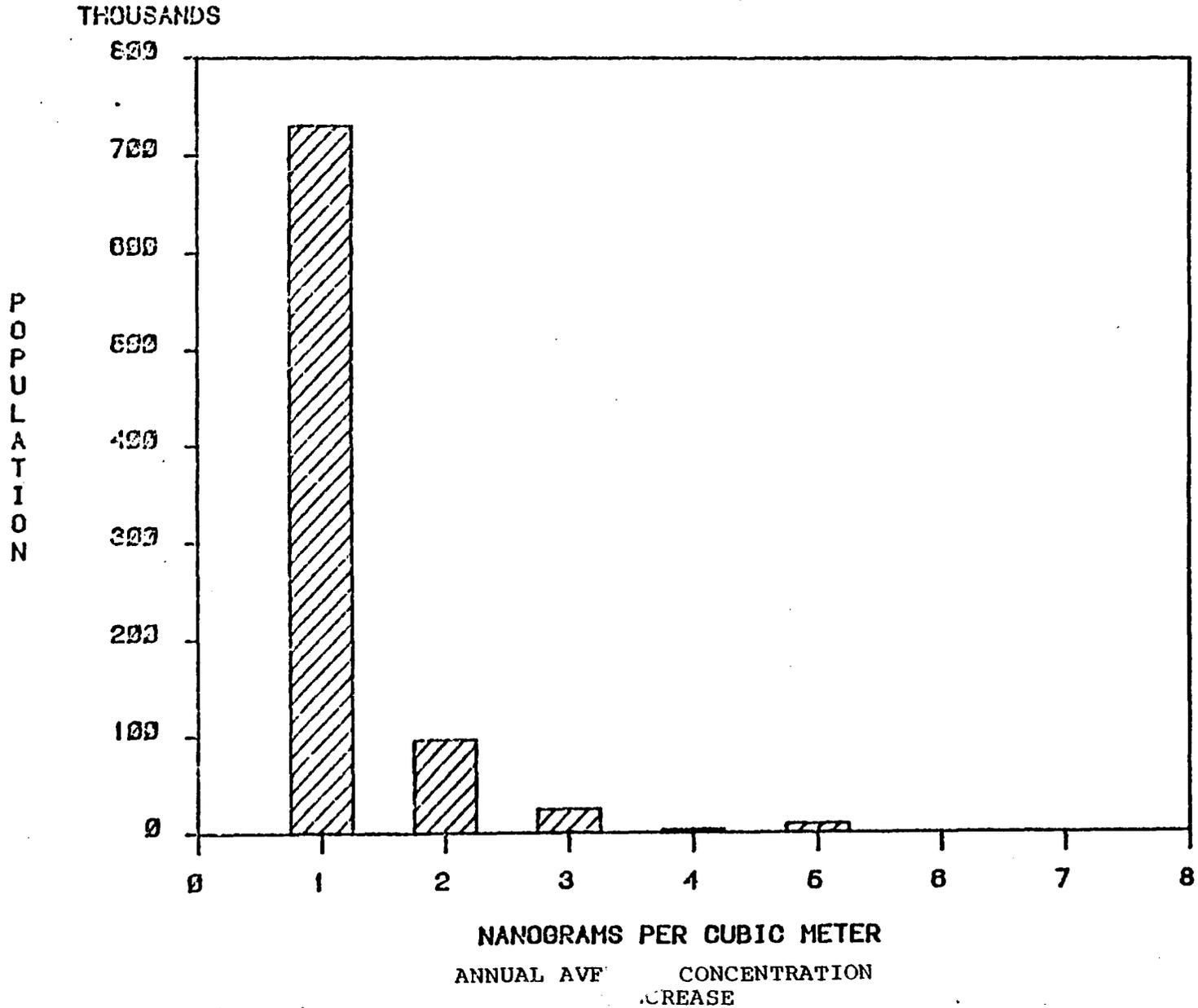
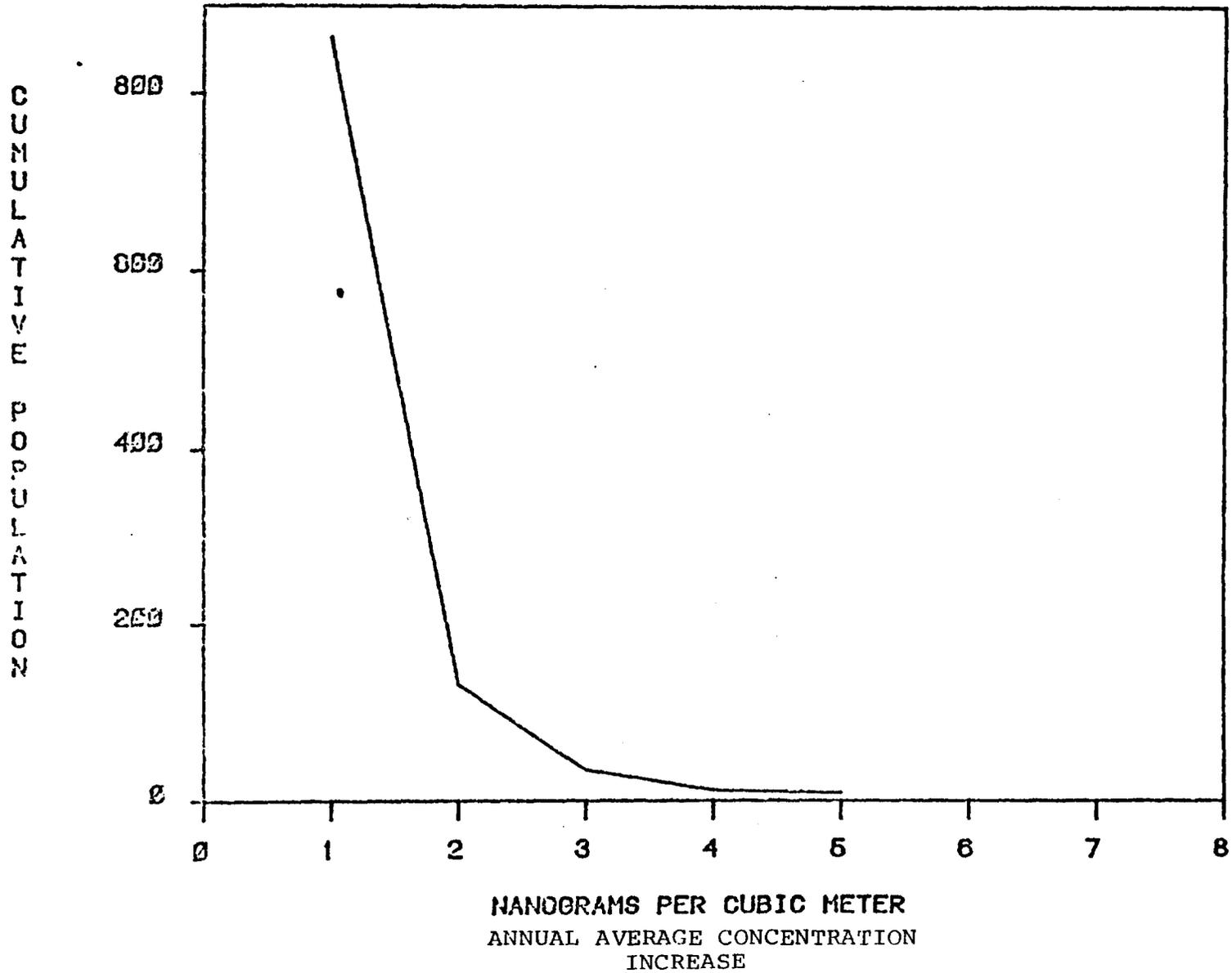


FIGURE III-14

INCREASE IN
CUMULATIVE POPULATION EXPOSURE TO CHROMIUM FROM A BANK
OF INDUSTRIAL COOLING TOWERS

THOUSANDS



III-39

D. EXPOSURE BY ROUTES OTHER THAN AMBIENT AIR

Human intake of chromium(III) occurs through consumption of chromium-containing foods. Chromium is found as a trace element in various foods. Data on the oxidation state of chromium in food are unavailable; only chromium or total chromium concentrations have been reported. Because chromium(VI) is a strong oxidizing agent, it is reasonable to expect that in the presence of bulk organic matter and water in food, chromium(VI) would be reduced to chromium(III). The chromium concentration in different types of foods has been measured at between 0.02 ug/g and 0.51 ug/g (Thomas, 1974). Chromium intake from a typical American diet of 43 percent fat was determined to be 62 ± 28 ug/day; from a typical American diet of 25 percent fat, intake of chromium was determined to be 89 ± 56 ug/day (EPA, 1984a). The DHS has found that trivalent chromium is an essential nutrient and is necessary for maintenance of normal glucose metabolism. Also, it is known that chromium(III) compounds are poorly absorbed from the gastrointestinal tract of animals, and that they are practically non-toxic when administered orally.

There is some evidence that human exposure to chromium may occur from drinking water. Chromium has been measured at low concentrations in some surface and groundwaters in California. Concentrations of up to 21 ppb were found in four of 72 spring water and three of 63 well water samples taken in the state (Silvey, 1967). In other California studies, no chromium was detected in 65 stream and 24 seawater samples (Soukup, 1972). The average chromium concentration in United States water supplies was determined to be 2.3 ppb (Schroder, 1962). A national mean daily intake of 17 ug/day of chromium in drinking water has been reported, with a range of 1 to 224 ug/day based on 2 l/d drinking water consumption (NAS, 1980). Chromium in water is

virtually all in the chromium (III) state, although chromium (VI) has been known to exist in natural waters with extremely low organic content. The extent to which anthropogenic sources are responsible for the presence of chromium detected in the hydrosphere is not known.

The extent of exposure to airborne chromium in the indoor environment, other than in the workplace, is not known. There are no direct consumer uses of chromium which could lead to emission of chromium compounds. Although cigarettes are known to contain chromium, the intake of chromium from smoking is not known.

The intake of chromium via these routes is summarized in Table III-14.

TABLE III-14
Intake of Chromium by Exposure Routes
Other Than Ambient Air

<u>Exposure Route</u>	<u>Chromium Oxidation State</u>	<u>Mean Daily Intake, ug (range, ug)</u>
Ingesting of Food	+3	62 (37-130)
Ingestion of drinking water	+3	17 (1-122)

Because chromium intake from food and water is in the trivalent state, chromium (as chromium (VI)) from ambient air represents the exposure route having the most significant public health effect.

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APPENDIX A

INFORMATION REQUEST LETTER WITH
ATTACHMENTS AND RESPONSES

AIR RESOURCES BOARD

1102 Q STREET
BOX 2815
SACRAMENTO, CA 95812



July 31, 1984

Dear Sir or Madam:

Subject: Request for Information Regarding Chromium

I am writing to request information on the health effects of chromium as part of our toxic air contaminant program. This program is based on Health and Safety Code Sections 39650, et seq. which require the ARB to identify compounds as toxic air contaminants and once identified to develop and adopt control measures for such compounds. After consultation with the staff of the Department of Health Services (DHS), we have selected chromium as a candidate toxic air contaminant to be evaluated in accordance with the provisions of Health and Safety Code Sections 39650, et seq. During our evaluation of chromium, we will consider available health information on all forms and compounds of chromium. Additionally, we are soliciting information regarding environmental and biological transformations of chromium and its compounds.

Before the ARB can formally identify a compound as a toxic air contaminant, several steps must be taken. First, the ARB must request the Department of Health Services to evaluate the health effects of candidate compounds. Second, the ARB staff must prepare a report which includes the health effects evaluation and then submit the report to a Scientific Review Panel for its review. The report submitted to the Panel will be made available to the public. Information submitted in response to this request will be considered in the ARB report to the Panel. Although any person may also submit information directly to the Panel for its consideration, I urge you to submit all information at this time for our consideration in the development of the report for the Panel. The Panel reviews the sufficiency of the information, methods, and data used by the DHS in its evaluation. Lastly, after review by the Scientific Review Panel, the report with the written findings of the Panel will be considered by the Air Resources Board and will be the basis for any regulatory action by the Board to officially identify a compound as a toxic air contaminant.

Prior to formally requesting the DHS to prepare a health effects evaluation of chromium, we are providing, pursuant to the provisions of Section 39660(e) of the Health and Safety Code, an opportunity to interested parties to submit information on the health effects of chromium which he or she believes would be important in DHS's evaluation of chromium as a candidate toxic air contaminant.

July 31, 1984

In July 1984, ARB staff received a reference search on chromium health effects using the MEDLARS II and DIALOG Information Services. These information services include material available to the public on or before December 1983. The attached bibliography lists the references from this information search. We are requesting pertinent information on chromium health effects, including any material that may not be available to the public, that is not included in the attached bibliography.

Pursuant to the provisions of the Public Records Act (Government Code Sections 6280 et seq.), the information you provide will be a public record and subject to public disclosure, except for trade secrets which are not emission data or other information which is exempt from disclosure or the disclosure of which is prohibited by law. The information may also be released to the Environmental Protection Agency, which protects trade secrets and confidential information in accordance with federal law, and to other public agencies, which are also required to protect such information.

To expedite the review process, we ask that any information which you believe should be regarded as "trade secret" be clearly marked and separated from other information. You may identify portions of the information you submit as "trade secret" in accordance with Health and Safety Code Section 39660(e). The claim of trade secrecy must be supported upon the request of the Air Resources Board. Other information claimed to be trade secret and information otherwise claimed to be exempt from disclosure may be identified as confidential in accordance with Section 91011, Title 17, California Administrative Code. Section 91011 requires that the claim of confidentiality be accompanied by specified supporting information.

I would appreciate receiving any relevant information you wish to submit by August 31, 1984. Your help in expediting our review will be greatly appreciated. Please send the information to the attention of:

William V. Loscutoff, Chief
Toxic Pollutants Branch
Re: Chromium
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

If you have any further questions regarding health effects information, please contact Mr. John Batchelder at (916) 323-1505. For any other questions, please contact Mr. Robert Barham at (916) 322-7072.

If you are not the person to whom this request should be addressed, please forward it to the appropriate person in your organization. Also, please let us know whether you would like to continue to receive information inquiries

July 31, 1984

for other candidate compounds, and if not, if there is anyone in your organization to whom such requests should be sent.

Sincerely,

A handwritten signature in cursive script, appearing to read "Peter D. Venturini".

Peter D. Venturini, Chief
Stationary Source Division

cc: Alex Kelter, DHS
Lori Johnston, DFA
Wayne Morgan, President, CAPCOA
Jan Bush, Executive Secretary, CAPCOA
David Howekamp, EPA Region IX
Assemblywoman Sally Tanner
APCOs

Attachment

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DOUGLAS AIRCRAFT COMPANY

3855 Lakewood Boulevard Long Beach, California 90846
TWX: 9103416842
Telex: 674357

August 13, 1984
C1-711-WB-84-177

William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Subject: Request for Information Regarding Chromium

Dear Mr. Loscutoff:

Douglas Aircraft Company, a division of the McDonnell Douglas Corporation, acknowledges receipt of the subject request.

Concerning information on the health effects of chromium as a candidate toxic air contaminant, Douglas Aircraft Company can be of no help.

Although Douglas Aircraft uses chromic acid in anodizing operations, the only physical fallout that Douglas experiences is the discharge of gaseous components expressed as hydrocarbons, particulate matter, sulfur dioxide and nitrogen dioxide. The discharge of these compounds arise from the painting, degreasing, abrasive blasting, oven use, and other manufacturing operations in which the Douglas Aircraft Company is involved.

Very truly yours,



W. Barnack, Jr.
Environmental Control Engineer
Plant Engineering

CONCURRENCE:



G. M. French
Manager - Plant Engineering
Design & Facilities Acquisition

WB/scc



IT CORPORATION

August 14, 1984

Mr. William V. Loscutt, Chief
Toxic Pollutants Branch
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Dear Bill:

CHROMIUM

A quick review of your bibliography on chromium indicates a couple of things:

a. The data bases you are searching may not include books and monographs. Two examples are:

Paul B. Hammond and Robert P. Bellies "Metals" - Chapter 17 In "Casarett and Doull's Toxicology: The Science of Poisons" 2nd Edition. MacMillan Publishing Co. (New York) 1980. Pages 409-467.

Marshall Sittig "Toxic Metals" Chapter on Chromium, pages 97-131. Noyes Data Corporation (Park Ridge, N.J.) 1976.

b. The data bases and/or search strategy are not picking up papers that discuss substances such as Cr in connection with another, perhaps broader topic. As you know, these are people who assert that a threshold for carcinogenesis must exist for metals, particularly trace metals that are found in all humans in measureable concentrations. Without prejudging that issue, it seems important that your bibliography at least include such papers from the literature. Two important examples that deal with Cr are:

William V. Loscutoff
August 14, 1984
Page 2

IT CORPORATION

George Claus and Karen Bolander "Environmental Carcinogenesis: The Threshold Principle: A Law of Nature", In "Pollution and Water Resources" (G. J. Halajl-Kun, Editor) Pergamon Press (New York) 1982. Pages 153-182.

Thomas H. Jukes "Chasing a Receding Zero: Impact of the Zero Threshold Concept on Actions of Regulatory Officials". J. Amer. Coll. Toxicol. 2 (3): 147-160, (1983).

Another paper on this subject, although not explicitly discussing Cr, is:

R. Koch "A Threshold Concept of Environmental Pollutants" Chemosphere. 12(1): 17-21 (1983).

I hope these references are helpful. Please continue to send me your data requests and exposure and health effects reports.

Very truly yours,



R. N. Hazelwood, Ph.D.
Project Manager
Environmental Affairs

RNH/sp

^{10/3} This could be very useful for calculating actual doses at the tracheal level as f (concentration) in air Last

Chromate Inhibition of Metabolism by Rat Tracheal Explants II. *In Vivo* Exposures

UNIVERSITY OF CALIFORNIA

Last

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Air Resources Board

William V. Loscutoff, Chief
Toxic Pollutants Branch
Re: Chromium
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

asis
xplan

animals.

In an earlier study (Last *et al.*, 1977), we demonstrated that the secretion of mucus glycoproteins by tracheal slices incubated for 24 hr in tissue culture is inhibited by inclusion of Na₂CrO₄ in the culture medium. The extent of such inhibition was dependent upon the concentration of chromate in the medium; a biphasic dose-response curve was observed. In the second phase, at higher concentrations of chromate (above 0.27 mM), we also observed inhibition of precursor [³H]glucosamine uptake and gross cytotoxicity. In the present study, analogous studies have been performed with tracheal

explants from rats exposed to Na₂CrO₄ *in vivo*, administered as an aerosol. We find that for equivalent concentrations of Na₂CrO₄ administered *in vivo* and *in vitro* (calculated as described below), there is equivalent inhibition of glycoprotein secretion rate in the tracheal explant assay (Last *et al.*, 1977). In addition, we have extended the previous findings of chromate-induced cytotoxicity by histochemical staining techniques.

Such a quantitative comparison of pollutant effects *in vivo* and *in vitro* is, to the best of our knowledge, a completely novel approach with no published precedents.

August 16, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

Reference: Chromium

Regarding July 31, 1984 ARB request for information on the health effects of Chromium. We have no data to submit at this time.

We would like to continue to receive information inquiries, etc. for other potential toxic air contaminants.

Sincerely,

Dale B. Hanson
Dale B. Hanson
Director, Engineering

DBH/dpc

cc: P. Charley
G. Sweeney

adcoat, inc.

172 East La Jolla Road, Placentia, California 92670 — (714) 630-7311

August 17, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
Re: Chromium
California Air Resources Board
P.O. Box 2815
Sacramento
CA. 95812

Dear Mr. Loscutoff:

Adcoat, Inc. does not, at this time, use any chromium or chromium compounds in its products.

We have, from time to time, considered the use of chromium containing pigments, so we would like to remain on your mailing list for information on chromium.

Very truly yours,
ADCOAT, INC.



HUGH H. MULLER
PRESIDENT

HHM/mw



DEPARTMENT OF BIOPHYSICS
AND MEDICAL PHYSICS
BERKELEY, CA 94720

UNIVERSITY OF CALIFORNIA, BERKELEY
6701 SAN PABLO AVENUE
OAKLAND, CA 94608
TELEPHONE (415) 642-7160

17 August 1984

Mr. Peter D. Venturini
Stationary Source Division
Air Resources Division
1102 Q Street
PO Box 2815
Sacramento, CA 95812

Dear Mr. Venturini:

Thank you for your letter of July 31 regarding chromium.

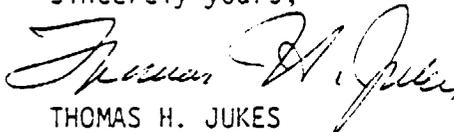
Any discussion or regulation concerning chromium should include consideration of the fact that, in small amounts, it is a nutritionally essential element. The recommended dietary allowance is 0.05 to 0.20 milligrams per day (National Academy of Sciences). See Recommended Dietary Allowances, 9th ed., 1980, National Research Council, Washington, D.C.

Chromium deficiency in human beings causes disturbances of carbohydrate metabolism, and marginal deficiency states may exist in the USA.

Kindly refrain from throwing the baby out with the bathwater. Thank you.

Enclosed is a publication by me.

Sincerely yours,


THOMAS H. JUKES

cc: William V. Loscutoff
R.N. Hazelwood
Assemblywoman Sally Tanner

Oil, Chemical and Atomic Workers
International Union

J. E. (JACK) FOLEY
DIRECTOR, DISTRICT NO. 1



304 FREEWAY CENTER BUILDING
3605 LONG BEACH BOULEVARD
LONG BEACH, CALIFORNIA 90807
PHONE: (213) 426-6961

August 10, 1984

State of California
Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Attention: Peter D. Venturini, Chief
Stationary Source Division

Dear Mr. Venturini:

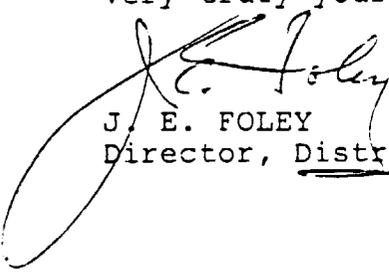
In response to your communication of July 31, 1984,
please continue to send this, and like correspondence to this
office and I would appreciate your forwarding the same
material to:

Mr. Dan Edwards, Director
Health and Safety Dept.
Oil, Chemical & Atomic Workers
International Union
P. O. Box 2812
Denver, CO 80201

I have taken the liberty of forwarding a copy of your
July 31st letter to him at our Denver office.

May I take this opportunity to thank you in advance for
your cooperation on the above request.

Very truly yours,


J. E. FOLEY
Director, District 1

JEF:ajs
cc: Dan Edwards
File

RECEIVED
AUG 14 1984
Stationary Source
Division
Air Resources Board

Allied Chemical

P. O. Box 1139R
Morristown, New Jersey 07960

August 24, 1984

Mr. William V. Loscutoff
Chief
Toxic Pollutants Branch
Re: Chromium
California Air Resources Board
P. O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

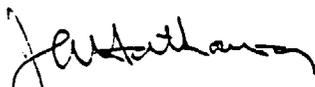
Re: Request for Information Regarding Chromium

We are enclosing copies of comments provided last year to the EPA's Science Advisory Board during their deliberations on the EPA's Health Assessment Document for Chromium. A number of the specific references mentioned in our comments were not listed in your bibliography and should be reviewed. The concerns we expressed to the EPA should also apply to both your review and that of the Department of Health Services.

Also enclosed is a copy of a lifetime intratracheal injection study in rats. A manuscript for publication related to this study is currently in preparation and will be forwarded when available. Additional studies on detoxification mechanisms for chromates have also been completed and manuscripts are in preparation. These studies provide substantial additional support for a threshold phenomenon for chromate carcinogenesis and will also be forwarded when available.

Please be sure we are included in future mailings related to chromium.

Sincerely,



F. A. Hathaway, M. D.
Director - Medical Services
Chemical Sector

JAH/hmw
Enclosures



Chevron Environmental Health Center, Inc.

A Chevron Research Company Subsidiary
15299 San Pablo Avenue, Richmond, California
Mail Address: P.O. Box 4054, Richmond, CA 94804

R. D. Cavalli
Manager
Product Evaluation

August 22, 1984

William V. Loscutoff
Chief, Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

This letter is in response to your request for information on the health effects and environmental fate of chromium and its compounds. Upon review of our files we did not identify any in-house toxicology or environmental fate data on these materials. Several published reports were identified, however, which we believe will significantly contribute to the information already collected by the Air Resources Board. These references are listed below:

Ecological Analysts, Inc. (November 1981). The Sources, Chemistry, Fate and Effects of Chromium in Aquatic Environments. Available from API Publications, order No. 847-89600.

Environmental Protection Agency (July 1983). Health Assessment Document for Chromium, EPA 600/8-83-014A.

National Institute for Occupational Safety and Health (1975), Criteria for a Recommended Standard. Occupational Exposure to Chromium VI, HEW Publication No. 76-129.

National Institute for Occupational Safety and Health (1973), Criteria for a Recommended Standard. Occupational Exposure to Chromic Acid, HEW Publication No. 73-11021.

Please contact R. M. Wilkenfeld of my staff at (415) 231-6018 should you have questions concerning the information we are submitting.

Sincerely,

RDCAVALLI/AUE

**KAISER ALUMINUM
& CHEMICAL CORPORATION**

August 24, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Subject: CHROMIUM

Dear Mr. Loscutoff:

Kaiser Aluminum & Chemical Corporation thanks you for the opportunity to respond to your request for information regarding chromium. We are interested in chromium compounds because some are the basis for the manufacture of heat and chemical resistant materials known as refractories, which is the business of our Refractories Division.

Our concern centers exclusively around trivalent chromium present in the ore of chromium. We call this ore "chromite." Chromite is among the materials most resistant to chemical change. It is insoluble in water and in all common bases and acids including aqua regia. It is also relatively insoluble in most of the aggressive leaching substances designed to categorize hazardous wastes. Examples of such leaching substances include citric and acetic acids.

Many of the references cited in the attachment to the "Request for Information Regarding Chromium" attest to the absence of exposed worker health effect from chromite.

Battelle Memorial Institute, Columbus, Ohio, published a study in February 1983 regarding their investigations to determine the extent of health hazard from trivalent chromium compounds used in the refractories industry. We suggest you refer to a copy of that study (Exhibit A, attached) and add their bibliography to the chromium references provided with the State's request for information on chromium.

Exhibit B, attached, is a report by Joseph J. Durek, Ph.D., which was part of a submission to the Department of Health Services in the latter part of 1983. Dr. Durek's report indicates the permanence of chromite, since the mineral is found unaltered in the environment.

The third attachment, Exhibit C, by Dr. Harry Mikami, an acknowledged expert on chromite, is further substantiation for the permanence of chromite in the environment. Dr. Mikami's paper and the references he cites should be part of the references used in rule making.

Because of potential concern about trivalent chromium in solution (water) we hired a Bay Area engineering company to perform preliminary toxicity tests on rainbow trout using 750 grams of chromite per liter of water. Rainbow trout are exceedingly sensitive to toxic substances and are a good choice for delicate testing. There were no fatalities in the 96 hours of exposure.

Kaiser Aluminum & Chemical Corporation believes that any regulation on chromium compounds emitted to the atmosphere should recognize the distinct difference in health effects between trivalent and hexavalent compounds.

Sincerely,



Rod E. Ewart, CIH
Industrial Hygiene Manager

- Attachments:
- Exhibit A, "Report on Evaluation of the Potential Health Effects of Trivalent Chromium Compounds in the Refractories Industry," by Joiner, Rensch, Zanetos, and Brauning, Battelle Columbus Laboratories, Columbus, OH, February 18, 1983
 - Exhibit B, "Chromite Distribution in California," by J. J. Durek, Kaiser Aluminum & Chemical Corporation, Oakland, CA, August 24, 1984.
 - Exhibit C, "Chromite," by H. M. Mikami, from Industrial Minerals and Rocks, 4th Ed., A.I.M.E., 1975



Diamond Shamrock
Chemicals Company

Technical Center

August 23, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

In response to Mr. Peter Venturini's solicitation for information on the toxicity of chromium, I have included several pieces of information to aid in your review. These include:

1. "Chromates Symposium 80"
2. U.S. EPA list of references taken from a 7/83 draft of their health assessment document on chromium.
3. "Testing Sodium Dichromate and Soluble Calcium Chromate for Carcinogenicity in Rats" - final draft.

Another study, sponsored by the American Wood-Preservers' Institute, titled "Effects of Chemical Preservatives on the Health of Wood Treating Workers in Hawaii, 1981 - Clinical and Chemical Profiles and Historical Prospective Study - July, 1983" was not included but contains findings related to worker exposure to chromium containing wood preservatives. A copy of this study can be obtained by contacting:

J. E. Wilkinson
Reichold Chemicals, Inc.
2340 Taylor Way
Tacoma, Washington 98401

The proceedings from the Industrial Health Foundation's "Chromates Symposium 80" is an excellent collection of pertinent information describing the acute & chronic toxic effects that have been attributed to exposure to chromium containing compounds.

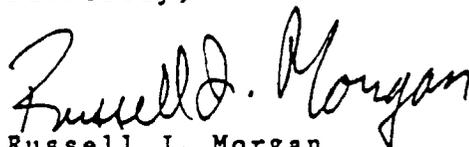
Mr. William V. Loscutoff, Chief
California Air Resources Board
August 23, 1984
Page 2

The list of references is from an external draft of the Office of Health and Environmental Assessment's (OHEA) "Health Assessment Document for Chromium" which was released for review and comment in July, 1983. The document itself was returned to EPA for further revision and is expected to be released shortly. This health assessment document was developed for use by the Office of Air Quality Planning and Standards to support decision-making regarding possible regulation of chromium as a hazardous air pollutant. If you contact Dr. Si Duk Lee of OHEA of the U.S. EPA, I'm sure he'd be happy to provide you with a copy of the revised document when it is available.

The study "Testing Sodium Dichromate and Calcium Chromate for Carcinogenicity in Rats" conducted by Bayer AG, Institute of Toxicology is a final draft and should be regarded as confidential until its publication in the journal, Cancer. I have included it because the findings are significant and the study itself is one of the best done on this subject to date. This work was planned, designed and sponsored within the framework of the Industrial Health Foundation by a number of the world's chromium chemicals producers.

In closing, we here at Diamond Shamrock appreciate the opportunity to participate and contribute toward your evaluation of air borne chromium. Please don't hesitate to contact me if we can be of any further help.

Sincerely,



Russell J. Morgan
Chromium Chemicals Group
Research & Development

kjv

PACIFIC GAS AND ELECTRIC COMPANY

PG&E + 77 BEALE STREET • SAN FRANCISCO, CALIFORNIA 94106 • (415) 781-4211 • TWX 910-372-6587

H. M. HOWE
CHIEF SITING ENGINEER

August 29, 1984

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Re: Chromium
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

Information Inquiries Mailing List
Requests for Public Health Information

Pacific Gas and Electric Company received your July 31, 1984 request for additional public health information regarding chromium. We reviewed the bibliography and concluded that we are unaware of any additional public health effects information which would be of use to you.

It is generally recognized that hexavalent chromium is far more potent than trivalent chromium. In fact, your bibliography includes references addressing such differences. However, by requesting information on "chromium" you appear to be overlooking such differences.

As a matter of general principle, PGandE thinks that any risk assessment document forwarded to the Science Review Panel for their review should include separate risk assessments for each compound or valence state of concern -- particularly when the available data suggest that such differences may be significant.

Please continue to send future information inquiries to me at the above address.

Thank you.

Sincerely,

*B. B. Wroblewski for /
J. F. McKenzie*

J. F. MCKENZIE
Supervising Civil Engineer



3801 West Temple Avenue
Pomona, California 91768
Telephone (714) 598-4592

August 29, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
Re: Chromium
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

Pursuant to your request for information regarding chromium health effects, I have determined that the University does not have any information which I believe would be important in the Department of Health Services' evaluation of chromium as a candidate toxic air contaminant.

Sincerely,

A handwritten signature in cursive script that reads "Michael R. Ceser".

Michael R. Ceser
Environmental Health & Safety Officer

MRC:cb

cc: President La Bounty
Dorothy Roberts

Agriculture
Arts
Business Administration
Engineering
Environmental Design
Science
Teacher Preparation

Member of The California State University

301 Pigeon Point Road
New Castle, Delaware 19720
(302) 652-3301
Telex 905033
Answerback: AMMIN NCST
Cable AMINPAR Newcastle, DE

American Minerals

September 4, 1984

Mr. William Loscutoff, Chief
Toxic Pollutants Branch
Re: Chromium
California Air Resources Board
Box 2815
Sacramento, Ca. 95812

Dear Mr. Loscutoff:

This is in reply to your request for information concerning the toxicity of Iron Chromite. We have just received a copy of the letter from Mr. Venturini and, therefore, were not able to respond by the indicated deadline. It is hoped that you will consider our evidence in spite of it being late.

American Minerals is a supplier of Iron Chromite to the glass industry in California, so these hearings are very important to us. Iron Chromite is really a natural ore of Chromium which we import from South Africa and grind in our plants in El Paso, Tx. and Wilmington, Del. Although we have been involved with Iron Chromite for more than 25 years, we have never noted an unusual incidence of cancer in any of our plants.

Iron Chromite has the essential formula of $FeO.Cr_2O_3$ which means that the Chromium is in the trivalent state. We should like to submit in evidence, pages 18 to 29 of a report by Battelle Institute entitled, "Evaluation of the Potential Health Effects of Tri-Valent Chromium Compounds in the Refractories Industry".

The pages enclosed contain a good summary of the experimental work that has been carried out in this field. Please note on page 27, "The information available on human exposure to chromium compounds suggests that exposure to the trivalent chromium

Received
SEP 07 1984
N.W.

301 Pigeon Point Road
New Castle, Delaware 19720
(302) 652-3301
Telex 905033
Answerback: AMMIN NCST
Cable AMINPAR Newcastle, DE

American Minerals

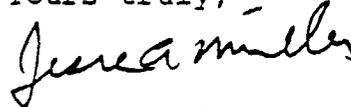
compounds does not produce a significant increase in cancer incidence."

We can send you a copy of the entire report if this would be of interest to you, but we did not want to burden your files.

We are also enclosing a copy of a letter from Dr. L.E. Thompson who serves as a consultant for us. His opinion is that "The probability of hexavalent chromium being produced in any substantial quantity in the reactions assumed in the fusing of glass, is relatively small."

Please place my name on your mailing list to receive notifications of hearings concerning Chromium. If we can supply you with any further information, please write or call us.

Yours truly,



Jesse A. Miller
Vice President

OCAW

Oil, Chemical & Atomic Workers
International Union, AFL-CIO



Joseph Misbrenner, President
Michael Ricigliano, Secretary-Treasurer
L. Calvin Moore, Vice President
Robert E. Wages, Vice President

International Offices:
255 Union Blvd., Lakewood, CO 80228
303/987-2229

Mail: P.O. Box 2812, Denver, CO 80201

→ Bill
Adjunct
Manufacturing
[Signature]

August 27, 1984

RECEIVED

SEP 4 1984

Stationary Source
Division
Air Resources Board

Peter D. Venturini, Chief
Stationary Source Division
State of California,
Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Re: Request for Information
Regarding Chromium

Dear Mr. Venturini:

Reference is made to your letter of July 31, 1984, regarding the above, addressed to Director Foley, and Director Foley's August 10, 1984, response to you (copy attached).

First, I concur with Director Foley's request to direct future requests of this nature directly to this office, while continuing to direct a copy of such requests to his office.

Regarding Chromium, this office has no unpublished or other information other than that contained in the standard reference literature, which I'm sure you already have. We also have no information regarding environmental and/or biological transformations of chromium and its compounds.

Thank you for the opportunity to provide information.

Yours truly,

[Signature: Dan C. Edwards]

Dan C. Edwards, Director
Health and Safety Department

c-R. E. Wages, Vice President
J. E. Foley, Director



CALIFORNIA CAST METALS ASSOCIATION

1722 J Street • Suite 14 • Sacramento, CA 95814 • (916) 442-6233

Frederick J. Simonelli
Executive Director

William P. Conway, Jr.
Administrative Director

Hazel Kagan
Legislative Analyst

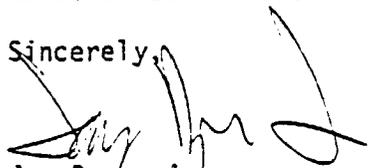
September 5, 1984

Mr. Peter D. Venturini
Stationary Source Division
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Venturini:

I have no information regarding the toxicity of chromium, but wish to continue to receive inquiries for other candidate compounds.

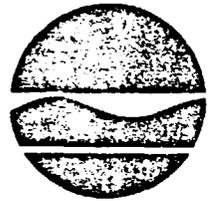
Sincerely,



Jay Dyer, Jr.
Administrative Assistant

JD:em

New York State Department of Environmental Conservation
50 Wolf Road, Albany, New York 12233-0001



Henry G. Williams
Commissioner

September 6, 1984

Mr. William V. Loscutoff, Chief
Toxics Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

At your request for information regarding Chromium as a toxic air contaminant (TAC), we are enclosing copies of "New York State Air Guide-1 - Guidelines for the Control of Hazardous Ambient Air Contaminants" and "Part 212 - Processes and Exhaust and/or Ventilation Systems" for environmental ratings in the State of New York.

After extensive research done by New York State Department of Environmental Conservation and the Department of Health, hexavalent chromium and derivatives have been classified as high toxicity air contaminants. After reviewing your enclosed references, I do not think that we could add any more useful information at the present time. We are enclosing the above documents that our Regional Air Pollution Control Engineers (RAPCEs) use as a reference guide in trying to minimize the hazards of toxic contaminants in our environment.

We would be very interested in receiving a copy of your report on Chromium when available.

Sincerely,

A handwritten signature in black ink, appearing to read 'Carlos L. Montes', is written over a horizontal line. The signature is stylized and somewhat cursive.

Carlos L. Montes
Asst. Research Scientist
Bureau of Air Toxics
Division of Air

Enc.

SEP 10 1984



REPLY TO
ATTENTION OF

DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010-6422

05 SEP 1984

Occupational and Environmental
Medicine Division

Mr. William V. Loscutoff
Chief, Toxic Pollutants Branch
California Air Resources Board
P. O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

This Agency has no information which would be pertinent to your evaluation of the health effects of chromium. However, we are aware of a recent EPA draft document which you may want to review if you have not already done so. The draft document, Health Assessment Document for Chromium, SRC TR-84-628, May 7, 1984, and any public comments thereto should provide important information on the current assessment of chromium's health effects. This document was published by the U.S. Environmental Protection Agency, Office of Research and Development, Research Triangle Park, North Carolina 27711. Project coordinator is Si Duk Lee, Ph.D.

Questions or comments to this Agency should be addressed to Major Robert W. Petzold, M.D., M.P.H., telephone (301) 671-2464.

Sincerely,

Joel C. Gaydos
Joel C. Gaydos, M.D.
Colonel, Medical Corps
Director, Occupational and
Environmental Health

SEP 10 1984

19/8

Memorandum

To : William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Date : September 6, 1984

Place : Sacramento

From : **Department of Food and Agriculture**

Subject: Response to Request for Information Relevant to DOHS Evaluation of Chromium as a Candidate Toxic Air Contaminant

In response to your request, I am enclosing a copy of the print-out of references in the Department of Food and Agriculture's Registration Library. Please be advised that some of these references may be confidential access and as such may fall under the Department's policy on such matters.



Lori Johnston, Assistant Director
Pest Management, Environmental
Protection and Worker Safety
(916) 322-6315

Attachment



HEUBACH INC.
256 VANDERPOOL STREET
NEWARK, NEW JERSEY 07114
201-242-1800

[Handwritten signature]

September 24, 1984

Air Resources Board
1102 Q Street
P.O. Box 2815
Sacramento, CA 95812
ATTN: Mr. Peter Venturini

Dear Mr. Venturini:

We received through our California sales office a request for information on Chromium. I suggest that this request be directed to the Dry Color Manufacturers' Association who should be in a position to provide you with comprehensive information on health effects of chromium based pigments. You may wish to address this request to:

Dry Color Manufacturers' Association
P.O. Box 931
Alexandria, VA 22313
ATTN: Mr. J. Lawrence Robinson
Executive Vice President

I am sure this will enable you to get pertinent information for your study.

Sincerely,

[Handwritten signature]

P. A. Wriede
Vice President, R&D

PAW:mr

cc: J. L. Robinson - DCMA

RECEIVED
OCT 1 1984
Stationery Source
Division
Air Resources Board

Representing the Color Pigments Industry

SUITE 202, 206 NORTH WASHINGTON STREET
ALEXANDRIA, VA 22314 (703) 684-4044

Mailing Address:
P.O. BOX 931, ALEXANDRIA, VA. 22313

December 20, 1984

William V. Loscutoff, Chief
Toxic Pollutants Branch
Re: Chromium
California Air Resources Board
P.O. Box 2815
Sacramento, California 95182

Dear Mr. Loscutoff:

The Dry Color Manufacturers' Association is pleased to provide you with additional references as a result of your request of October 4 concerning information regarding chromium.

The Dry Color Manufacturers' Association is an industry trade association representing small, medium and large pigment color manufacturers throughout the United States and Canada, accounting for approximately 95% of the production of color pigments in this country. Foreign pigment manufacturers with sales in the United States and Canada and suppliers of intermediates to the pigments industry are also members of the Association. The Lead Chromate Committee of the DCMA represents manufacturers of lead chromate pigments and the enclosed comments are prepared by that committee.

You will find enclosed a copy of a report entitled, "The Effect of a Range of Chromium-Containing Materials on Rat Lung", a study conducted by the University of Aston in Birmingham, England, sponsored by the DCMA and others. You will note that this study indicates significant differences in different chromium compounds. In particular, the solubility of chromium pigments is much lower than other chromium compounds, and their impact on the environment is significantly less.

Also enclosed is a paper entitled, "Mutagenicity of Chromium Compounds" by F. L. Petrilli and S. De Flora which appeared in the Proceedings of the Chromate Symposium 1980. In that paper you will note the importance that the authors place on threshold levels.

We trust that this information is of assistance to you. Should you have any questions concerning lead chromate pigments, please feel free to call upon us.

Sincerely,



J. Lawrence Robinson
Executive Vice President

Enclosures

DEC 27 1984

APPENDIX B

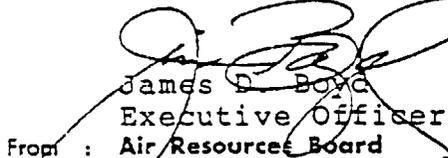
HEALTH EFFECTS REQUEST TO
THE DHS AND LETTER OF RESPONSE

Memorandum

o : Peter Rank, Director
Department of Health Services
714 P Street
Sacramento, CA 95814

Date : October 3, 1984

Subject: Evaluation of
Chromium


James D. Boyd
Executive Officer
From : Air Resources Board

I am writing to formally request that the Department evaluate the health effects of chromium as a candidate toxic air contaminant in accordance with Assembly Bill 1807 (Tanner). According to Health and Safety Code Sections 39660-62, your Department has ninety days to submit a written evaluation and recommendations on the health effects of chromium to the Air Resources Board and may request a thirty day extension.

Attached for your staff's consideration in evaluating chromium are: Attachment I - a suggested list of topics that we believe should be included in your chromium evaluation and recommendations; Attachment II - a list of references on chromium health effects which were identified in an ARB letter of public inquiry; Attachment III - additional references received from the public in response to the inquiry letter; Attachment IV - comments provided by Allied Chemical to EPA's Science Advisory Board during SAB's deliberations on EPA's Health Assessment Document for Chromium; and Attachment V - ambient chromium concentration data and emission trends which should be used to estimate the range of risk to California residents as required in Health and Safety Code Section 39660(c).

My staff is available for consultation in conducting this health effects evaluation. We look forward to continuing to work closely with you and your staff in carrying out this legislative mandate. If you have any further questions regarding this matter, please contact me at 445-4383 or have your staff contact Peter D. Venturini, Chief of the Stationary Source Division, at 445-0650.

Attachments

cc: Gordon Duffy
Alex Kelter w/attachments
Raymond Neutra w/attachments
Peter D. Venturini
Assemblywoman Sally Tanner
Claire Berryhill
Emil Mrak, Chairman and Members
of the Scientific Review Panel

CHROMIUM: TOPICS TO BE INCLUDED IN FINAL STAFF REPORT ON CHROMIUM

- I. CHEMICAL AND PHYSICAL PROPERTIES
 - A. Valence States
 - B. Chromium Containing Compounds
 - C. Environmental Transport
 - D. Industrial Uses
- II. INHALATION TOXICOLOGY OF CHROMIUM
 - A. Occurrence of Chromium in Particulate Matter
 - B. Deposition in the Lung
 - C. Defense Responses of the Lung
 - D. Inhibition of Normal Pulmonary Functions
 - E. Fibrogenic Potential of Chromium
- III. CARCINOGENICITY (REVIEW ARTICLES: U.S. EPA, DRAFT DOCUMENT, 1983; IARC, 1980)
 - A. Human Evidence (Hayes, 1982; Norseth, 1981; Langard, 1983; and Leonard and Lauwerys, 1980)
 1. Epidemiologic studies of workers in the production of chromium compounds
 - a. Strong association between industrial exposure and respiratory cancer
 - b. Undefined exposure levels
 - c. Exposure may include chromite ore, Cr(III) and Cr(VI) compounds with various solubilities.
 2. Epidemiologic studies of workers in the production and use of chromium pigments
 - a. Some indication that workers in chromium pigment production had increased respiratory cancer.
 - b. The risk associated with the use of such pigments and products containing such pigments is less certain.
 - c. Major exposure is to Cr(VI) in compounds such as lead and zinc chromates.
 3. Epidemiologic studies of workers in chrome plating industry
 - a. Data are inconclusive to determine the risk of respiratory cancer
 - b. Chromium oxides are the major exposure
 4. Epidemiologic studies of workers in ferro-chromium industry
 - a. Some indication of increased lung cancers
 - b. Exposure to Cr(III), Cr(VI) compounds and possibly other carcinogens such as asbestos and benzo(a)pyrene

- B. Animal Evidence (Hayes, 1982; Norseth, 1981; Langard, 1983; and Leonard and Lauwerys, 1980)
1. The carcinogenicity of different compounds containing chromium has been studied in laboratory animal species through various routes of exposure.
 2. Sufficient evidence exists for Cr(VI) compounds in causing cancer in animals--e.g., calcium chromate, strontium chromate and zinc chromate.
 3. Chromium (VI) compounds have been shown to be carcinogenic by different routes of exposure--e.g., intrabronchial, intrapleural, intramuscular implantation and subcutaneous injection.
 4. Both Cr(III) and Cr(VI) compounds have been ineffective in producing lung tumors in animals.
 5. Cr(III) compounds have not been shown to be carcinogenic in animals by oral administration.

IV. SHORT-TERM TESTS FOR GENOTOXICITY

IARC (1982) considered the evidence for the genotoxic activity of hexavalent chromium to be sufficient and the evidence for trivalent chromium to be inadequate.

The most recent review articles on the genotoxicity of chromium compounds include those by: Levis and Bianchi (1982); Sirover (1981); Hatherill (1981); and EPA (1983). The following outline on the genotoxicity of chromium compounds emphasizes articles published subsequent to the IARC monograph review (1980) and complements the above-listed reviews. The outline is not meant to be comprehensive. Representative articles in each category are listed.

- A. Gene Mutation or DNA Damage in Bacteria or Fungi
1. Gene Mutations - Hexavalent Chromium (Cr VI) was mutagenic in several Salmonella strains. Trivalent chromium (CrIII) was negative. (Bennicelli, et al., 1983; Petrilli and DeFlora, 1981.)
 2. DNA Damage - Cr(VI) induced DNA damage as determined by B. Subtilis rec repair assay. (Kada, et al., 1980.)
- B. Gene Mutation or DNA Damage in Mammalian Cells (excluding human cells)
1. Gene Mutation - Cr(VI) was mutagenic in V79 Chinese hamster cells in culture (Paschin, et al., 1983; Newbold, et al., 1979). Cr(III) was inactive in V79 cells (Newbold, et al., 1979).
 2. DNA Damage - Cr(VI) induced DNA cross-links, strand breaks, and DNA-protein cross links in chick embryo hepatocytes (Tsapakos, et al., 1983). Rainaldi, et al. (1982) reported that Cr(VI) induced sister chromatid exchanges in V79 cells in vitro in a dose-dependent manner.
- C. DNA Damage in Human Cells
1. In vitro - Stella, et al. (1982) reported that Cr(VI) induced sister chromatid exchanges (SCE) in human lymphocytes in culture in a dose-dependent manner. Cr(III) was inactive.

2. In vivo - Workers exposed to chromic acid (Cr[VI]) had increased SCE's compared to unexposed controls (Sarto, et al., 1982).

D. Chromosomal Effects

1. Stella, et al. (1982) reported significant increase in chromatid-type aberrations (gaps and breaks) in human lymphocytes in vitro at Cr(VI) concentrations above 2.5×10^{-7} M. One hundred times more Cr(III) was required compared to Cr(VI) to increase the frequency of chromosomal aberrations.
2. Sarto, et al. (1982) reported increased chromosomal aberrations in workers exposed to chromic acid (Cr[VI]).

E. Other Short-Term Tests for Genetoxicity

1. Dominant lethal assay - Cr(VI) was positive in mice. There was a dose-dependent relationship (Knudsen, 1980).
2. Mouse spot test - Welding fumes and Cr(VI) were positive (Knudsen, 1980).

V. REPRODUCTIVE EFFECTS

A. Animal Studies

1. Teratogenesis:

<u>Species</u>	<u>Method of Administration</u>	<u>Oxidation State</u>	<u>Author(s)</u>	<u>Effects</u>
a. Mice	I.P. Injection	Cr(III)	(Matsumoto, <u>et al.</u> 1976)	Fetal deaths exencephaly, open eyelids, cleft palate, skeletal mal- formations
b. Hamsters	I.V. Injection	Cr(VI)	Gale, 1978)	Fetal deaths, cleft palate, skeletal de- fects
c. Hamsters (pregnant)	I.V. Injection days 7,8,9	Cr(VI)	Gale and Bunch, 1979)	Fetal deaths, cleft palate
d. Mice/Blasto- cysts & egg cylinders	In Vitro	Cr(VI)	Ijima, <u>et al.</u> 1983)	Degeneration of Inner Cell Mass, ↑ in No. of S.C.E.'s, ↓ in develop- ment and crownrump length
e. Mice (pregnant)	I.P. Injection day 8	⁵¹ Cr (III)	(Ijima, <u>et al.</u> 1983)	Neural tube defects

1. Teratogenesis (continued):

<u>Species</u>	<u>Method of Administration</u>	<u>Oxidation State</u>	<u>Author(s)</u>	<u>Effects</u>
f. Chicken Eggs	Air Sac Injection	Cr(VI)	(Gilano & Marano, 1979)	Skeletal Malformations, exencephaly, microphthalmia, evisceration/ decreased body size
g. Chick Fibroblast	In Vitro	Cr(III), Cr(VI)	(Denker, et al., 1983)	Inhibition of cartilage formation (skeletal defects)

2. Impaired Fertility

<u>Species</u>	<u>Method of Administration</u>	<u>Oxidation State</u>	<u>Author(s)</u>	<u>Effects</u>
a. Sea Urchin	Pre-treatment of sperm Gametes	Cr(VI) Cr(III)	Pagano, <u>et al.</u> 1983)	↓ Fertilization No Malformation
b. Marine Polychaete	2-Generation Toxicity Test	Cr(VI) Cr(III)	Oshida & Word, 1982	↓ # of Offspring Change in Spawning Time No Change
c. Rabbit	IP, 2 mg/kg	Cr(III), or Cr(VI)	Behari, 1978 (From Lee, 1983)	↓ Testicular Succinic dehydrogenase ↓ ATP-Ase Multi-nucleated Germ Cells Degeneration of Spermatocytes

- B. Human Effects
 - 1. Chromium levels in placentas and in maternal and fetal blood in 25 maternal-fetal sets from each of eight geographic areas in the United States. Stable maternal-fetal chromium ratio demonstrated in spite of geographic variation. (Creason, et al. 1976)
 - 2. Lack of relationship between levels of chromium in drinking water in 48 local areas in South Wales and increased CNS malformation rates. (Elwood, et al. 1974)

- C. Discussion of Animal Data
 - 1. Mechanism of Action - Maternal Toxicity
 - 2. Effects on Fertility

D. Human Data (insufficient)

VI. ACUTE TOXICITY (REVIEW ARTICLE: IARC, 23 (1980))

- A. Cr(VI)
 - 1. Fatal ingestion (1.5 - 6 g) causes hemorrhage in various organs, shock and death
 - 2. Toxic to renal tubules and liver
 - 3. Corrosive to nasal septum
 - 4. Contact sensitivity in the skin
 - 5. Bronchial asthma and pulmonary edema
 - 6. Irritation of mucus membranes (including conjunctivitis and corneal injury and respiratory irritation)
- B. Cr
 - 1. Chromium metal is relatively nontoxic
- C. Cr(III), Cr(II)
 - 1. Inhalation of insoluble chromite dust produces pneumoconiotic changes consisting of thickening of interstitial tissue, fibrosis and hyalinization of the lungs.
 - 2. Inhalation of soluble chromic and chromous salts have produced no established acute toxicity with the exception of dermatitis.

VII. PHARMACOKINETICS

A. Absorption, Distribution and Excretion

Chromium is absorbed from the gastro-intestinal tract and the airways of the lungs. Following inhalation exposure, it may deposit in the pulmonary tissues. Chromium is excreted in the urine and also from the GI tract where biliary excretion plays an important role (Langard, 1982).

B. Metabolism

Chromate, Cr(VI), is reduced in the cells of the body to produce Cr(III). Molecules containing sulfhydryl groups easily reduce chromate. Several proteins contain chromate-reductase activity. This activity is found in the microsomes and mitochondria. (Connett and Wetterhahn, 1983.)

- VIII. RISK ASSESSMENT (REVIEW ARTICLES: U.S. EPA, DRAFT [1983]; IARC, VOL. 23 [1980]; AND SUPPLEMENT [1982])
- A. Threshold Determination
 - 1. Solubility of Compounds
 - 2. Valence States
 - 3. Route of Administration
 - B. Dose-response Assessment Based on:
 - 1. Available Animal Data
 - 2. Human Epidemiology and Monitoring
 - 3. Workplace Evidence
 - C. Range of Potential Risks
 - 1. Study of Manusco (1975) - See EPA Draft
 - 2. CAG Estimate
 - 3. Population at Risk

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Environmental Affairs IV Co.

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Submitted by J. A. Hathaway, M.D. Director - Medical Services Chemical
Sector Allied Chemical

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Medical Physics and the Dept. of Nutritional Sciences, U.C. Berkeley:

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Submitted by Russell J. Morgan Chromium Chemicals Group Research
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EPA Health Effects References. See original bibliography

Testing Sodium Dichromate and soluble Calcium Chromate for carcinogenicity in rats.
See reference submitted by J.A. Hathaway.

Allied
Chemical

P.O. Box 1132A
Morristown, New Jersey 07960

August 24, 1984

Mr. William V. Loscutoff
Chief
Toxic Pollutants Branch
Re: Chromium
California Air Resources Board
P. O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

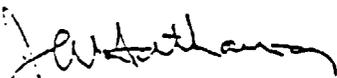
Re: Request for Information Regarding Chromium

We are enclosing copies of comments provided last year to the EPA's Science Advisory Board during their deliberations on the EPA's Health Assessment Document for Chromium. A number of the specific references mentioned in our comments were not listed in your bibliography and should be reviewed. The concerns we expressed to the EPA should also apply to both your review and that of the Department of Health Services.

Also enclosed is a copy of a lifetime intratracheal injection study in rats. A manuscript for publication related to this study is currently in preparation and will be forwarded when available. Additional studies on detoxification mechanisms for chromates have also been completed and manuscripts are in preparation. These studies provide substantial additional support for a threshold phenomenon for chromate carcinogenesis and will also be forwarded when available.

Please be sure we are included in future mailings related to chromium.

Sincerely,



F. A. Hathaway, M. D.
Director - Medical Services
Chemical Sector

JAH/nmw
Enclosures



Allied Corporation
Corporate Health,
Safety and Environmental Sciences
P.O. Box 2332A
Morristown, New Jersey 07960

October 28, 1983

Members, Science Advisory Board
Environmental Health Committee
U. S. Environmental Protection Agency

Reference: Health Assessment Document for Chromium,
Review Draft, EPA-600/8-83-014A

Allied Corporation is a major United States producer of basic chromium chemicals. In the very limited time available to us, we have tried to review the above referenced document. We have identified numerous areas where we disagree with the interpretations, methods of analysis, and/or conclusions expressed. In a few instances we have noted errors in the factual information presented in the document, or omissions of recent pertinent scientific papers related to chromium compounds. We would like to stress that our review is limited in scope due to the short time-frame allowed by the Environmental Protection Agency. We were unable to review most of the references in their original form and suspect that had more time been available, additional errors in fact or interpretation would have been discovered.

In addition to our specific concerns noted below we would make the general observation that the document has internal inconsistencies related to interpretation of scientific data. While we can appreciate the difficulty of preparing a cohesive document of this size when numerous authors are drafting different sections, we believe that it was premature of the Environmental Protection Agency to present the document to the Science Advisory Board in its present condition. It would have seemed advisable for the Agency to reexamine the document for editorial consistency as well as consider the comments of external reviewers before submitting it to the Scientific Advisory Board. The summary, which can be expected to be relied upon by the public and regulatory agencies to a large degree, is particularly troublesome inasmuch as the conclusions expressed therein are usually incomplete or unrepresentative of important scientific studies and interpretations discussed in the body of the report.

We do agree with one of the major conclusions of the report that there is sufficient evidence for the carcinogenicity of calcium chromate, strontium chromate and zinc chromate from animal studies and for similar moderately insoluble chromates from epidemiology studies. But we disagree with many other interpretations and conclusions. Of particular concern is that both the qualitative and quantitative risk assessments for all chromium compounds are unsupported by the available scientific data and clearly exaggerate the risk to human populations exposed to low doses. We also believe that the scientific data supports the conclusions that chromates do not pose a human teratogenic risk and that trivalent chromium compounds are not mutagenic or carcinogenic in

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Members, Science Advisory Board
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U. S. Environmental Protection Agency

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man. In contrast the document, particularly the summary, implies that the evidence is inconclusive on these issues. Our specific comments will address these concerns as well as other issues in more detail.

1. Epidemiology Studies of Chromate Production Workers

Sixteen epidemiology studies of chromate manufacturing plants are reviewed in the document (pages 7-36 to 7-55). While the studies clearly demonstrate an increased risk of lung cancer associated with work in these plants, the qualitative risks as discussed in the summary on pages 7-64 and 7-65 implies a far greater risk than actually exists for current workers. Relative risks quoted in the summary are 29, 32, 23, and 38. These relative risks are from studies with small sample sizes, inappropriate controls and/or reflect studies performed in the 1940's or 1950's which included workers whose exposures were primarily in the 1910-1930 time frame. Unfortunately no mention is made in the summary of the three studies of more contemporary cohorts. The three more current studies discussed in the body of the EPA document demonstrate much lower risks for workers initially hired from the 1940's to about 1960. For workers hired since 1960 two of the three studies show no excess risk of lung cancer. All three studies compared cohorts initially exposed during different time periods corresponding to improvements in industrial hygiene or modification of processes. The cohorts correspond to the following time frames:

	<u>I</u>	<u>II</u>	<u>III</u>
Leverkusen	approx. '40-'48	'48-'57	'57-'79
Uerdingen	approx. '40-'48	'48-'63	'63-'79
Eaglescliff	* '49-'60 (only)	+ '49-'60 (or later)	'61-'77
Baltimore	'45-'49	'50-'59	'60-'74

* 1949-1960 cohort includes workers hired after 1949 with no exposure after 1960. + 1949-1960 includes workers hired during this period but who also worked after 1961. All other cohorts in this Table include workers hired exclusively during the indicated time periods.

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The results of the studies are summarized below:

<u>Author</u>	<u>Country</u>	<u>Location</u>	<u>S M R</u>		
			<u>Time Frame</u>		
			<u>I</u>	<u>II</u>	<u>III</u>
Korallus, et al.	W. Germany				
		Leverkusen	2.76	2.60	0.96
		Uerdingen	2.85	1.97	0.54
Alderson, et al.	Great Britain				
		Eaglescliff	3.03	2.03	1.87
Hayes, et al	United States				
		Baltimore			
		Short-term	1.8	1.8	No Cases
		Long-term	3.0	3.4	No Cases

When the three studies are considered together there is a clear trend showing a decreasing risk for more recently hired cohorts. The rates even for workers initially hired in the 1940's and 1950's are much improved over those quoted in older studies whether one looks at the relative risks of 20-30 or the SMR of 8.5 observed by Taylor (page 7-44) using more modern epidemiology methods. Rates for workers hired since about 1960 are even more favorable and excess risks may have been eliminated in the German and United States plants studied.

The authors of the document noted that the favorable trends within each study are not statistically significant but the identical trend in all three studies should be considered strongly suggestive of a substantial decrease if not elimination of excess lung cancer risk in these plants. Another argument raised by the authors is that the amount of time that has passed since 1960 may be an insufficient latent period for lung cancer in chromate production workers. We concur that this is a possibility; however, in

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reviewing several older epidemiology studies the authors noted a higher relative risk for lung cancer in workers less than 45 years of age compared to older workers. This situation clearly does not exist in the cohorts first hired since 1960 since many of these individuals would now be approaching age 45 even if hired at age 20. It is our opinion that even though the risk of lung cancer has not been proven to have been eliminated in these workers, it is certainly markedly reduced from early time periods. This conclusion should be adequately addressed in both the body of the document and its summary.

2. Quantitative Risk Assessment

Allied Corporation strongly disagrees with both the methodology used in making the quantitative risk assessment as well as the final result. Based on animal studies and mutagenicity tests we believe the lifetime estimate of cancer of 1.2×10^{-2} for continuous exposure to 1 ug/m^3 of chromium is overestimated by several orders of magnitude or even more probably that there is no risk whatsoever at that level of exposure. Our opinion is based on the following points, several of which we understand will be discussed in even more detail by the Industrial Health Foundation's Chromium Chemicals Environmental Health and Safety Committee.

- The one-hit model used by the EPA to estimate risk is inappropriate.
- Any of the commonly discussed mathematical models, including the one-hit model, used to estimate low dose exposures to carcinogens are designed for systemic acting carcinogens. Since carcinogenic effects for chromates are a local phenomenon, none of these models are appropriate for quantitative risk assessment.
- The EPA did not seriously consider the substantial amount of pharmacokinetic information on chromates that support the concept of a threshold for carcinogenesis.

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- All chromium compounds, regardless of valence or solubility, were inappropriately considered of equivalent toxicity in calculating the quantitative risk assessment.
- The exposure levels used from the Mancuso epidemiology study to develop risk estimates were too low.
- Comparisons to real-life exposures to chromium compounds demonstrate that the quantitative risk estimate does not reflect reality.

(a) One-Hit Model

The use of this model appears to follow outmoded policy and outdated methodology rather than current scientific judgment. One would have expected a more balanced presentation on this issue in pages 7-66 and 7-67. There is insufficient discussion of arguments against the one-hit model. Further discussion on the substantial controversies that exist in selection of mathematical models to predict low exposure cancer risks, should be made in the document.

In fact, there are numerous articles that make significant points against the blind political use of the one-hit model in scientific risk assessment. A few of these include:

- (1) Final Report of the Scientific Committee of the Food Safety Council, June 1980, Food Safety Council, 1725 K Street, N.W., Washington, DC 20000.
- (2) Ryzin, J.V., Quantitative Risk Assessment, Journal of Occupational Medicine, 22:321-326, 1980.

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- (3) Park, C.N. and R.D. Snee, Quantitative Risk Assessment: State-Of-The-Art for Carcinogenesis. Fundamental and Applied Toxicology, 3:310-333, 1983.

In addition, there are several articles in the January-February 1981 issue of Fundamental and Applied Toxicology that discuss the ED₀₁ study performed at the National Center for Toxicology Research which was referenced on page 7-67 in support of using a one-hit model. These articles clearly point out the inappropriateness of the one-hit model as it relates to exposure to 2-acetylaminofluorene and bladder cancer. When time to tumor considerations are applied the one-hit model is also not supported by the data on liver cancer, contrary to the claim made in the EPA's draft document.

(b) Inappropriateness of Mathematical Models in Predicting Low Dose Risks from Chromate Exposures

Chromates have been shown in animal or epidemiology studies to only produce tumors at the site of initial contact; that is, at implant sites or respiratory tract surfaces. Despite numerous animal experiments, no tumors have been seen at distant sites. Mathematical models implicitly assume random and even distribution of dose to the animal or man. This is simply not the case with chromates. The animal chromate inhalation versus implant studies reinforce this point when lung cancer is manifested in the latter and not the former. Any risk assessment that works with average exposures or time-weighted average exposures based on samples with extreme variations in time and space, cannot be expected to give reliable risk extrapolation estimates. This point will become clearer when the exposures in the Mancuso study and similar industrial hygiene experience at Allied's Baltimore Plant is discussed later.

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(c) Pharmacokinetic Data on Chromates

Contrary to the statement on page 5-22, there is a substantial amount of information on the pharmacokinetics of chromate metabolism. In addition to the numerous studies referenced in the document, the following should be added:

Petrilli, F. L. and S. DeFlora,
Interpretations on Chromium Mutagenicity and
Carcinogenicity in Mutagens In Our
Environment, pages 453-464, Alan R. Liss,
Inc., 150 Fifth Ave., New York, NY 10011,
1982.

This information, along with the results of a recently completed life-time intratracheal injection study (to be provided with the submission from the Industrial Health Foundation's Chromium Chemicals Environmental Health and Safety Committee), provide substantial evidence for a threshold for mutagenic and carcinogenic responses to chromate exposure.

Hexavalent chromates can be effectively reduced to the much less toxic and nonmutagenic (in vivo and using whole cells in vitro) trivalent chromium. This reduction takes place rapidly in the skin, saliva, gastric juice, red blood cells, and liver. Chromate can also be reduced by compounds normally present in cytoplasm such as ascorbic acid and reduced glutathione. Lung cells can also reduce chromates to a small degree and with repeat exposures this reduction is enhanced in a manner suggestive of enzyme induction.

The knowledge of these pharmacokinetic mechanisms provides understanding to the observations that chromates do not produce cancers at distant sites and do not enter fetal tissues from reasonable routes of maternal exposure. This knowledge and the further observation that it is difficult to produce tumors in the respiratory tracts of animals unless material is held directly in contact with tissue (intratracheal implantation) or by large dose bolus

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administration (Industrial Health Foundation Study) provides good evidence of a threshold effect for chromate carcinogenesis.

(d) Solubility and Valence State

The EPA document does not differentiate between different forms of chromium compounds in its quantitative risk assessment. This is acknowledged to be inappropriate but is justified by lack of separate exposure information on hexavalent chromates. It is our opinion that this justification is unsupportable scientifically. If there is insufficient information to make a quantitative risk assessment because of lack of exposure information, this fact should have simply been acknowledged and no attempt at risk assessment should have been made. In fact, as previously discussed, there are ample additional reasons for not performing the risk assessment using mathematical models and certainly for not using the one-hit model.

The numerous references on trivalent chromium throughout the document provide sufficient information to conclude that trivalent chromium is not a carcinogen or mutagen. This is in contrast to the statement in the document that the data on these effects relative to trivalent chromium are inconclusive. In fact, studies on trivalent chromium have consistently shown a lack of carcinogenic activity and lack of mutagenic activity. While some interaction of trivalent chromium with DNA has been demonstrated, these have been in artificial cell extracts. Whenever whole organism including yeast and bacteria have been used the results have been negative. The inability of trivalent chromium to penetrate cell membranes has been clearly established by the studies cited in the draft document. This fact, coupled with the lack of mutagenic activity in vitro and the negative results in carcinogenicity studies, should logically lead to the conclusion that trivalent chromium compounds do not pose a carcinogenic or mutagenic risk to humans.

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Solubility considerations are discussed in the document, it is even stated that the authors believe some chromates do pose greater carcinogenic risk than others. In general they express agreement that intermediately soluble compounds such as calcium, strontium, and zinc chromates pose a greater carcinogenic risk than aqueously soluble materials. It seems totally inappropriate to us to then lump all chromium compounds, regardless of solubility or valence statement, into one category for risk assessment. Any result of such an assessment can only yield scientifically invalid results. We are not persuaded by the authors' arguments attempting to justify their approach (see pages 7-69 and 7-70). We see no reason to perform a risk assessment at all if one knows the results will be invalid.

(e) Exposure Levels used in Quantitative Risk Assessment

The exposure levels used in the draft document are based on those presented in Mancuso's 1975 paper, which are in turn based on levels reported by Bourne and Yee in their 1950 paper. Although it is difficult to be absolutely certain, a careful review of Mancuso's reported exposure levels strongly suggests they were based on Figures 1-4 from the Bourne and Yee study. The exposure levels reported in these figures represent time-weighted average exposures for nine different departments under "normal operating conditions." It appears that no consideration was given to reported exposures under maintenance and repair conditions even though such work occurred very frequently. Thirty percent of the workforce was reported as maintenance workers and their time-weighted average maximum exposures as reported in Table 5 varied from 0.13 to 5.67 mg/m³ with most over 1.0 mg/m³. The minimum exposures also listed in this table are related to "normal operating conditions" and are similar to Figures 1-4. Bourne and Yee state that "it was observed huge volumes of dust were generated during the repair and cleaning of dust collectors, [and] process equipment or building structure [was] overlaid with an accumulation of dust." Any risk assessment that does not consider these frequent excursions of much higher exposures will grossly exaggerate the estimated risk from chromate exposure.

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Experience at Allied's Baltimore Plant in 1947, when over 2,500 industrial hygiene samples were taken, also supports our belief that exposures were much higher than estimated by Mancuso. The plant he studied in 1949 was similar in operation to ours and we believe exposures were similar. We suspect that even the "normal operating levels" reported by Bourne and Yee represent ideal conditions at the plant during visits by inspectors from the State of Ohio Health Department.

If the data collected in the first half of 1949 and reported by Bourne and Yee and Mancuso were similar in nature to that collected by Allied in 1947, no reasonably representative low dose risk estimates can be derived using simple models derived for average exposure. Based on samples taken at the Allied plant over a 12 month period in 1947, monthly average samples from 39 areas ranged from 0.01 to 50.0 mg/m³ hexavalent chromium expressed as CrO₃. The yearly average of all locations was 0.9 mg/m³. Individual samples show an even greater spread. Also, yearly area averages ranged from 0.03 to 6.8 mg/m³ hexavalent chrome as CrO₃, revealing large location differences of a factor of more than 200 fold. Representative exposures are difficult, if not impossible, to derive from such data because of the order of magnitude differences in average levels. We believe similar variations occurred at the plant studied by Mancuso and that the real exposures also varied in a similar manner. The extremely high levels of variation in workplace chromium levels and the enormously high exposure (often over 10.0 mg/m³) that existed at many plant locations in the late 1940's dramatize the serious problems in developing meaningful low dose risk extrapolations from average chromium levels that do not realistically represent actual exposures.

Besides the problem of extreme variation, there is a problem of data representativeness over time. The data that was collected in the first half of 1949 by Bourne and Yee and that has subsequently been used in the EPA's chromium risk assessment estimates, cannot be considered

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representative of exposures for employees followed between 1931 and 1974 in the Mancuso study. Bourne and Yee point out such deficiencies and limitations of the data in paragraphs 4 and 5 of their paper. Any risk assessment model developed from such data is ignoring the fact that the data represents only a half year in a forty-three year follow-up period (1931-1974) and hence assumes conditions were "static". The static assumption is also presumed when using these types of models since there is a long lag time between dose (chromium exposure) and response (respiratory cancer). If the dose is not constant throughout the period then a lag relationship needs to be considered. Otherwise a biased or distorted relationship between dose and response can result. In the case of chromium exposures in the workplace, the assumption of constancy of dosage is probably the least supportable assumption that can be made.

(f) Comparison of Predicted Risks to Real-Life Situations

While the authors of the draft document caution on page 7-70 that the quantitative risk assessment should be only used for certain chromium compounds, the fact that it is derived without regard to solubility or valence considerations will undoubtedly leave others to apply it to all forms of chromium. The inappropriateness of the predicted risk of 1.2×10^{-2} at continuous exposure to 1 ug/m^3 for developing cancer can be illustrated by the following two examples.

The first example is normal ingestion of chromium in the diet which is estimated by the National Academy of Sciences (NAS, 1960) to be 62 ug/day in food and 17 ug/day in drinking water for a total of 79 ug/day.³ This compares to an intake of about 20 ug/day at 1.0 ug/m^3 if one assumes the chromium is 100 percent respirable and totally retained and that air exchange equals $20 \text{ m}^3/\text{day}$. From this normal dietary intake about five percent of the population ought to develop lung cancer as a result of this exposure according to the quantitative risk assessment. If this were valid, most of the lung cancer in the United States could be attributed to chromium ingestion. Obviously, this is not the case as numerous

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epidemiology studies linking cigarette smoking and lung cancer have clearly demonstrated. The only conclusion one can reach is that the estimated risk predicted by the EPA model does not represent reality and should, therefore, be disregarded.

The second example involves a study in a Swedish County with two communities heavily polluted with chromium compounds from ferro-alloy industries. (Before discussing the article in detail, we would like to comment that it seems incredible that the EPA authors would omit such an epidemiology study from its consideration, particularly in a document developed for use by the Office of Air Quality Planning and Standards). The citation for this study is:

Axelsson, G. and R. Rylander,
Environmental Chromium Dust and Lung
Cancer Mortality, Environmental
Research, 23:469-476, 1980.

Two ferro-alloy industries are situated in the County studied. Chromium air levels are reported as 0.1 to 0.4 ug/m³, which is 50-100 times higher than most other rural areas in Sweden. The plants started operations in 1912 and 1913. The quoted exposures refer to 1976-1979, and one could speculate that past exposures were likely to have been even higher since air pollution control has received considerable recent attention in Sweden.

If one assumes that the average exposure was 0.25 ug/m³ for the communities studied then about 0.3% of the population would be expected to suffer lung cancer as a result of the air pollution using the results of the EPA risk assessment estimate. While this amount of lung cancer risk in males may not be enough to be statistically discernible, it should have caused at least a 50% increase over control groups for females. Such an increase was not seen, casting serious doubt on the credibility of the risk estimate. The study concluded that there was no excess risk of lung cancer in the two communities with higher levels of airborne pollution from chromium compounds.

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It is our opinion that risk estimates which do not conform to reality should be disregarded. Such is the case with the risk estimated for chromium in the draft document.

3. Errors in Airborne Chromium Levels Reported for Baltimore

The airborne chromium levels reported for Baltimore in the summary on page 2-2 and on pages 3-21 to 3-23 are in error. Copies of the 1977 and 1979 Maryland State Yearly Air Quality Data Reports, prepared by the State Department of Health and Mental Hygiene, are attached so that the actual levels can be verified.

In fact, the maximum observed value is not 2.48 ug/m^3 , as reported in the draft document for 1977, but is rather 0.247 ug/m^3 . The arithmetic average is actually 0.036 ug/m^3 not 0.1568 ug/m^3 , as reported in the draft document. For 1979 the data are also incorrect with a maximum value of 0.31 ug/m^3 (one value of 0.690 ug/m^3 was disregarded according to procedures specified by the Maryland Health Department when there was only one sample in a quarterly reporting period) and an arithmetic average of 0.0468 ug/m^3 . These levels are more in line with reports from other communities; however, in view of the errors noted for Baltimore, the EPA authors should review the reported results for all locations to verify their accuracy.

4. Allied's Epidemiology Experience

This discussion supplements comments made previously in paragraphs #1. and #2.e concerning results of epidemiology studies and exposure measurements at Allied's Baltimore facility. Allied's epidemiology experience since a major process change in 1961 (a new chromic acid plant) shows no significant excess of respiratory cancer among production workers who were first hired after this date. One case of respiratory cancer has been reported in this cohort and 1 to 2 cases would have been expected based on Baltimore City cancer incidence rates. Although five to ten more years of follow-up are desired to improve the power of the statistical test, there is no evidence of excess risk in the Allied production workers whose initial employment at the chromium facility occurred in the past 21-3/4 years based upon the Hayes et al. study on these workers through mid-1977 and our review of Company records on active employees and retirees through September 1983.

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Major process changes in 1951 (a new bichromate plant) and in 1961 (a new continuous chromic acid plant) have led to significant reductions in the average and peak chromium exposures at the Allied plant. These reductions correlate with no apparent respiratory cancer excess risk in production workers hired after 1961.

From samples collected in 1961 and 1962, the plant average level was estimated to be .07 mg CrO₃/M³ or a factor of at least 10 below the levels in 1947. The area averages ranged from .01 to .5 mg CrO₃/M³. These were followed by further reductions to an average of .02 mg CrO₃/M³ as evidenced in 1968 and also in the period 1976-1978. Area average readings typically ranged from nondetectable to .14 mg CrO₃/M³ in the years 1976-1978. During this period, the value of .1 mg CrO₃/M³ was only exceeded on the average in 4 of the 154 sampling areas (3%) where the worker density per workday was approximately 1 person for the four areas combined or .3% of the workforce. This contrasts with 30 of 39 sampling areas (77%) exceeding .1 mg CrO₃/M³ during 1947.

As seen above, over the past three and one half decades major changes have occurred in the average chromium exposure levels as well as in the size and number of extreme exposures.

In addition to the changes in dust levels of chromates, we believe the changes in the Chromic Acid Plant in 1961 may have had a major effect on the excess risk of lung cancer that previously was associated with work in that area. Both internal Company observations as well as the Hayes study identified the End Products area as having the highest lung cancer risk. Chromic acid is manufactured in this area and is sometimes referred to in our comments as the Chromic Acid Plant.

Prior to 1961, chromic acid was produced in batches. This method of production was accompanied by the production and evolution of large but unquantified levels of chromyl chloride in the workplace. Contamination of Soda Ash by salt used in the roasting of chromite ore resulted in chloride contamination of product streams. The chromate streams with the greatest contamination of chloride were directed to the Chromic Acid Plant where the chloride was removed essentially by boiling it off as chromyl chloride.

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We speculate that chromyl chloride may have been the major factor for the observed greater risk of lung cancer among workers in the old (pre-1961) Chromic Acid Plant. Since chromyl chloride was present as a vapor it might well be able to more easily penetrate the non-dividing layer of epithelial cells lining the lower respiratory tract than other chromates and once in contact with dividing cells exert a carcinogenic action. Another possibility is that chromyl chloride might have a carcinogenic action independent of the fact that it is a hexavalent chromium compound. In the attached article on the Chemistry of Chromyl Compounds by W. H. Hartford and M. Davrin, reaction of chromyl chloride with organic compounds resulting in chlorinated adducts is described. If such reactions occurred within DNA molecules a carcinogenic mechanism different from that of other chromates is possible.

Changes in the chromic acid manufacturing plant in 1961 eliminated chromyl chloride exposures. As previously discussed in paragraph #1 and earlier in this paragraph, no excess lung cancer has been observed at our Baltimore Plant since this time.

5. Systemic Toxicity of Chromates

Discussion of this subject on pages 7-1 and 7-140 to 7-143 do not cover the known acute toxicity of chromates very well. Acute renal failure is the predominant finding following either accidental ingestion or cutaneous exposure to chromates (typically in conjunction with a thermal or acid burn). A few recent literature citations are provided so the authors of the document may improve this section.

- (a) Schiff, H., P. Weidmann, M. Weiss, and S. G. Massry, Dialysis Treatment of Acute Chromium Intoxication and Comparative Efficacy of Peritoneal versus Hemodialysis in Chromium Removal, Mineral Electrolyte Metabolism, 7: 28-35, 1982.

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- (b) Ellis, E.N., B. H. Brouhard, R. E. Lynch, E. B. Dawson, R. Tisdell, M. M. Nichols, F. Ramirez, Effects of Hemodialysis and Dimercaprol in Acute Dichromate Poisoning. J. Toxicol: Clin Toxicol 19: 249-258, 1982.
- (c) Leonard, L.G., J. J. Scheulen, A.M. Munster, Chemical Burns: Effects of Prompt First Aid. The Journal of Trauma, 22: 420-423, 1982.
- (d) Korallus, U. C., Harzdorf, and J. Lewalter, The Experimental Bases for Ascorbic Acid Therapy of Poisoning by Hexavalent Chromium Compounds. International Archives of Occupational and Environmental Health (in press) - prepublication copy attached.

In addition to the above references, Allied's Department of Toxicology has recently completed an animal study demonstrating the efficacy of ascorbic acid in the treatment of acute dichromate exposures.

Acute accidental exposures to chromates can produce serious and sometimes fatal kidney failure. Conversely there does not appear to be a similar chronic effect. Mortality studies have not identified chronic renal disease, nor has renal damage been seen in lifetime carcinogenesis animal bioassays. Clinical testing of employee groups has also not demonstrated chronic renal problems. This has been Allied's experience in its medical examinations and is the result reported in the paper by Satoh et al.

6. Epidemiology Study of Ferrochromium Industry

The remarks on page 7-64 of the document referring to a study of ferrochromium industry employees in Sweden by Axelsson et al (1980) are an incorrect interpretation of the data reviewed on page 7-63. Although the negative results of this study are correctly reported by the EPA authors, their comment that "because of the confounding due to smoking and exposure to asbestos, no definite conclusions can be drawn from this study." is incorrect. In fact, any confounding from these two variables was in the direction of an increased risk of lung cancer among exposed workers. This type of

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confounding in a negative study only strengthens the conclusion that there was no association between work in the Swedish ferrochromium industry and lung cancer. The subsequent comment in the summary on pages 7-64 and 7-65, that two studies of the ferrochromium industry reported an increased risk of lung cancer mortality is obviously inaccurate.

7. Summary

Allied Corporation would hope that this document would receive extensive and careful revision before approval by the EPA's Scientific Advisory Board. Errors in fact, and editorial inconsistencies need to be corrected. The review of the literature needs to be expanded in many areas -- a number of citations are provided in our comments to assist with this effort. The views expressed by Allied as well as those of the Industrial Health Foundation's Chromium Chemicals Environmental Health and Safety Committee need to be seriously addressed, particularly as they relate to interpretation of epidemiology studies and the inappropriateness of mathematical models to assess low exposure cancer risks. Finally, the results of the Industrial Health Foundation's lifetime intratracheal study needs to be considered along with more recent mutagenicity studies that provide substantial evidence for a threshold of chromate carcinogenicity.



J. A. Hathaway, M. D.
Director-Medical Services
Chemical Sector
Allied Corporation

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Diamond Shamrock

T. R. Evans Research Center

October 5, 1983

Project Officer for Chromium
Environmental Criteria and Assessment Office (MD-52)
U.S. Environmental Protection Agency
Research Triangle Park, N.C. 27711

Dear Sir:

The Chromium Chemicals Environmental Health and Safety Committee of International Health Foundation appreciates the opportunity to comment on the draft Health Assessment Document for Chromium (EPA 600/ 8-83-014A July 1983). The time period allowed for review of the document has limited our initial comments to the Summary and Conclusions Section, and the Cancer Assessment Group estimated lifetime cancer risk. We feel the Summary and Conclusions Section will be widely read and will be the basis for decisions made concerning possible chrome regulations at the Federal and local levels. The estimated lifetime cancer risk will also be an important factor in possible regulatory action; therefore these sections have been the major focal point of our present review. Although a line-by-line critique was not possible at this time, the committee will submit further comments and additional information in the future. We have requested an extension of the comment period so as to permit input from studies just completed and to allow time for comments from European members of the committee.

Our conclusion is that studies of the chrome industry and recent animal studies show that exposure to high levels of chromium are of concern to human health, but ambient levels of chromium do not pose a concern for human health or the environment. Further, the data does not support the theory of linear extrapolation from high to low levels of exposure, thus the assessment of carcinogenic risk is inappropriate as applied to chrome.

2. Summary and Conclusions

General: The Summary and Conclusions section ineffectively summarizes the main text of the document and the section does not present any conclusions. The organization of the total document is poor in that certain sections and even subsections of the main body contain summaries and conclusions, the contents of which are not represented in this overall Summary and Conclusions section. The organization of the headings in this section does not follow the main document and makes little sense.

For example: 2.3 Biological Significance and Adverse
Health Effects of Chromium
2.5 Human Health Risk Assessment of Chromium

It would seem that the risk assessment should be a sub-part of the biological significance.

References to material discussed are given in some paragraphs and not in others.

2.1 Background Information

The text should indicate that Cr (0) as well as Cr (III) and Cr (VI) states are the most stable. The word anthropogenic is good and correctly used in the document but it would be clearer to refer to man made sources.

2.2 Analysis of Chromium

X-ray fluorescence is only able to analyze large amounts of chrome in compounds and would not be useful for environmental analysis.

The section should include the colormetric method using diphenylcarbazide. This method is widely used by industry. The method is accurate and precise at levels of 10 ppb and greater.

2.3 Biological Significance and Adverse Health Effects of Chromium

2.3.1 Chromium Pharmacokinetics: This subsection offers little in understanding chrome absorption, metabolism and excretion. The discussion does not even indicate, as does the main body of the report, that inhalation is an important route of exposure to chromium compounds. The background information on particulate inhalation is inappropriate for a summary section. Speculation should not be included in a summary section such as:

"Reduction of Cr (VI) to CR (III) appears to occur rapidly in biological systems, while the mechanism and kinetics are not completely understood."

2.3.2 Subcellular and Cellular Aspects of Chromium Toxicity: The document should avoid the use of jargon, such as "critical levels" without an explanation. The paragraph on mutagenicity neither summarizes the studies completed nor offers any understanding of valence state or solubility as factors in the conduct and interpretation of the results. It is doubtful that one looking for a summary of mutagenicity or genotoxicity would find the material under this organization.

2.3.3 Systemic Toxicity of Chromium: Adds nothing to the understanding of this topic.

2.3.3.1 Animal Data: To use the words ingestion/orally and soluble CR (VI) solutions/chromium salts in one sentence does not aid the reader, even a technically astute one, to gain an understanding of what the document is trying to say.

"Ingestion of soluble Cr (VI) solutions can cause local irritation but, generally chromium salts are relatively non-toxic when administered orally."

The main body of the document (7-2) states:

"Kidney effects are the primary result of acute exposure to chromium by various routes."

The summary section states:

"Acute exposure (intraperitoneal) result in kidney failure, liver, heart and brain micropathology."

It would appear that the understanding of the experiments in demonstrating the kidney as a target organ for acute chrome toxicity was lost on the individuals summarizing the document.

2.3.4 Chromium Carcinogenesis: This section can be easily summarized by stating as in the second sentence:

"Animal studies have provided sufficient evidence for the carcinogenicity of the following Cr (VI) compounds calcium chromate, strontium chromate and zinc chromate."

Speculation about other forms of Cr (VI) and unfounded statements on solubility modification of carcinogenicity does not have a place in a summary.

Many statements in this section could be omitted, but one sentence in particular should be deleted.

"Cr (VI) is mutagenic in multiple tests while the data for Cr (III) is inconclusive."

To attempt to bring a one sentence discussion of chromium mutagenicity into the section on carcinogenicity shows a naive understanding of proposed genotoxic mechanisms as they may apply to metals.

It is interesting to note the many references to IARC criteria (3 times in this section). If EPA is accepting this criteria for evaluation of a chemicals carcinogenicity, then I think it should be stated and applied to all chemicals.

2.3.5 Dermatological Aspects of Chromium: The section should point out that adherence to personal hygiene practices have been shown to reduce the industrial incidences of ulceration and have in general eliminated chrome dermatitis.

2.4 Human Biological Monitoring: The section should clearly differentiate environmental measurements from those taken in industrial settings.

2.4.1 Chromium in Blood: Reintroduces points included in the pharmacokinetics section but in a much more positive manner.

Section 2.3.1 "Chromium may be absorbed via the skin, lungs or gastrointestinal tract."

Section 2.4.1 "Chromium is absorbed through both the respiratory tract and gastrointestinal tract."

2.4.2 Chromium in Urine; 2.4.3 Chromium in Human Hair: These sections present data but do not summarize or offer a conclusion. The presentation of values without any discussion or indication of meaning is not placing the information in perspective.

2.5 Human Health Risk Assessment of Chromium

2.5.1 Health Effects Summary: If the CAG estimated lifetime cancer risk is to be included in this document the uncertainties, as discussed in the main body 7-77 and 7-82, must be included in the summary section.

2.5.2 Populations at Risk: This section offers nothing to be included in a Summary Section.

The Summary and Conclusions section is a very important part of the Health Assessment Document. The section must represent the main body of the document and the conclusions must be well founded in the data and must be clearly stated. The present section does not represent the main body of the report (for example no mention of teratology or other reproductive effects), fails to include conclusions and should be redone.

RISK ASSESSMENT

The Industrial Health Foundation's Chromium Chemicals Committee has sponsored the conduct of an extensive program of toxicology studies on chromates during the past five years, including studies to develop therapies and first aid treatment for the nephrotoxicity of accidental poisonings and studies to characterize the acute toxicity, mutagenicity, and carcinogenicity of chromium compounds. These last two sets of studies have, of course, direct bearing on the question of a risk assessment for chromium.

The entire issue of a risk assessment for chromium as presented in the Health Assessment Document is one which requires extensive review and revision. The model used for the risk assessment and the data to which this model was applied are open to numerous questions. The agency document itself, on pages 7-44 and 7-44a, states that both the data and conclusions of Mancuso (the basis for the risk estimate which is presented) are of limited value, particularly in that the exposures are not well characterized. New information now available from the IHF studies may provide a better data base on which to base a risk assessment.

The final report and a manuscript for publication on the carcinogenicity study are in the final stages of review. These describe the results of a carcinogenesis bioassay of sodium bichromate and calcium chromate, administered intratracheally in solution form. Benzopyrene and dimethylcarbamoyl chloride were included as positive controls. Intratracheal administration provided direct exposure to the lungs. Separate groups of rats were dosed with calcium chromate or sodium dichromate at lifetime total dose levels approximating one half the present TLV, three and fourteen times the present TLV. To test the effect of concentration, each total dose was administered to one group of animals either once per week or as a divided dose to a different group of animals five times per week. The method of administration, in a single bolus, resulted in peak concentrations delivered to the target tissue approximately 10^3 times what would be expected from continuous exposure by inhalation. Even at the highest tolerated doses, the frequency of tumor formation was low compared to the positive controls; no tumors were observed within the first 27 months of chrome administration; there was excellent survival, and none of the tumors, which were small, caused the death of the test animals.

Significant tumor incidences were observed only in the lungs of the highest dosage once-per-week groups and in the positive controls, there being no lung tumors in negative control animals. The same amount administered five days per week did not produce any tumors. Hence, at the maximum tolerated dose (1.25 mg/kg administered once per week), tumorigenic effect is related to peak concentration of repeated doses rather than the total administered dose.

This study strongly supports the conclusion that there is a no-effect level for chromate carcinogenesis, based on multiple physiological and biochemical defense mechanisms. It also helps explain the progress which

has been made over the past 35 years within the chromate-producing industry in control of lung cancer by advanced engineering and process improvements, and the lack of credible evidence of abnormal lung cancer risk in consuming industries other than pigment manufacture.

Mutagenicity testing (Ames Test) has indicated that Cr (VI) compounds had a similar mutagenic potency. Cr (VI) elicited both frameshift errors and basepairs substitutions in *S. typhimurium*. Cr (III) compounds were negative in Ames Tests. Cr (VI) mutagenicity was decreased by S9 fractions from various tissues through NADPH - requiring pathways reducing Cr (VI) to Cr (III). The findings may contribute to interpret carcinogenicity data; for example, reduction of Cr (VI) to Cr (III) by gastric juice is consistent with the lack of carcinogenicity following ingestion of chromates (Cr VI). Also the reversal of Cr (VI) mutagenicity by erythrocyte lysates is consistent with Cr (VI) detoxification in the blood and supports the finding of tumors only at implant sites. Since Cr (III) is trapped by cytoplasmic ligands, this may also indicate an intracellular detoxication mechanism; that is, a barrier affecting the ability of Cr (VI) to enter the nucleus and then to interact with DNA (probably as Cr III).

In view of this information, the following points about the risk assessment presented in the agency's document need to be addressed.

- 1) Chromium is an essential dietary component for man, with an estimated adequate and safe intake (EASI) and recommended daily allowance (RDA) of 200 micrograms per day. The level of intake for which the agency is here proposing a risk of 1.2×10^{-2} of cancer is only 10% of this EASI/RDA.
- 2) The linear extrapolation model utilized, and in fact, any pure linear model is inappropriate. The model is not one of the agency's "standard" models and even though used by the agency for arsenic, it is not a generally accepted total body burden model.
- 3) Further the model used projects a risk based on total chromium exposure, not on exposure to hexavalent chromium. Hexavalent chromium is now generally accepted to be the source of concern. The extensive mutagenicity data base developed under the sponsorship of the IHF also supports the view that it is hexavalent chromium, at high local concentrations, which must be viewed with concern.
- 4) The original data base the agency's estimates are based on is not accurate. The base does not differentiate in exposures between the different valence states of chromium, just as importantly, it does not in any manner account or allow for the episodic high exposures of workers to chromium which did occur in the older plants. The resulting predicted risk of 1.2×10^{-2} incidences of cancer per $\mu\text{g}/\text{m}^3$ of total chromium is contrary to observed lung cancer incidence levels.

- 5) One microgram of chromium per cubic meter of air equals 20 ug/day in the average man, or a total of approximately 300 ug per year and about 36.5 mg over the course of fifty years. In a seventy kilogram "standard" man this amounts to 0.521 mg/kg. The high dose in the final intratracheal study was equivalent to 541.7 mg/kg over the course of the study, or 10^3 times greater total exposure. Fifty years at the EASI is equivalent to 52.14 mg/kg, or 10^2 times greater exposure. The observed results from either of these situations, occurring as doses distributed over the course of a life time, do not correspond at all to what the model purposed in this document would predict.
- 6) Using the background levels of chromium in urban areas presented in the document, one would expect matching variations in the lung cancer rates. The variation in mean chromium levels (page 3-4) are 30 fold, yet no corresponding variations in lung cancer incidence has been reported.
- 7) Based on total body burdens of chromium and using the IHF rat carcinogenicity study, one would expect a cancer rate in the high dose, once a week exposure group (the worst case from the intratracheal study) some 10-20 times higher than was found. In addition, one would expect significantly greater tumor incidence levels in all of the groups in the study. Every group would have been expected to show a significant incidence of tumors.

In summary, based on the IHF rat study data, and other recent epidemiology data (Franchini, et al, Scand J Work Environ Health 9 (1983) 247-252) a linear model is inappropriate. However, using the EPA linear model with the IHF rat data (1x per week) an upper bound risk of approximately 6.75×10^{-5} was calculated. An appropriate model should not however be based on total chromium but rather on hexavalent chromium.

Members of the Chromium Chemicals Environmental Health and Safety Committee would like to expand on the points of concern with the HAD as indicated in this letter and further would like to share the data of the several studies recently completed. Copies of completed reports will be submitted to the project officer by the end of 1983. The Committee would be prepared to present and discuss the results of these reports and other new data with appropriate agency people as soon as a meeting can be arranged.

Sincerely,

David M. Serrone, Ph.D.
dlg

David M. Serrone, Ph.D.
for the Chromium Chemicals
Environmental Health and
Safety Committee

DMS/dlg/9.13

ATTACHMENT V

Ambient Chromium Concentrations and Emission Trends

Data from the U.S. EPA's National Aerometric Data Bank show mean concentrations of total chromium between 0 (below detectable limit) and 29.9 ng/m³, with 68 percent (59 of 87) of the means falling above 4 ng/m³. This data represents total particulate chromium 50 um and smaller collected from ambient air at sites throughout California from 1965 to 1983.

Data on total chromium in particulate matter 10 um and smaller, collected at ten sites throughout the state by the ARB in 1983 and 1984, show mean concentrations of chromium from 1.6 to 14.9 ng/m³. At most (7 of 8) of the urban sites, mean chromium concentrations fell between 3.0 and 4.2- ng/m³.

The contribution of the various uses of chromium compounds in California to the presence of chromium in the ambient air is currently being investigated by ARB staff. Chromium compounds are used in chrome plating, refractory brick production, glass manufacture, wood preservatives, paint pigments, and cooling towers as anticorrosion agents. Other potential sources of chromium in air are emissions from fuel combustion, sewage sludge incineration, refractory brick wear from the glass, cement and secondary steel production furnaces, and entrainment of chromite-bearing soil.

National consumption of chromium has decreased steadily due to continued weak demand for steel and reduced need for refractory materials. Whether this trend is reflected in California is uncertain; primary steel production facilities do not exist in this state.

Memorandum

To : James D. Boyd
Executive Office
Air Resources Board
1102 Q Street
B-4

Date : FEB 25 1985

Subject: Health Effects
Chromium (CR)

Handwritten signature/initials

From : Office of the Director
714 P Street, Room 1253
B-1248

Attached is the document prepared in response to your memo requesting the assistance of the Department of Health Services in evaluating the health effects of chromium (CR).


Stanley Cubanski
Director

Attachment

cc: C. Berryhill
G. Duffy
Assemblywoman Tanner
P. Venturini

Memorandum

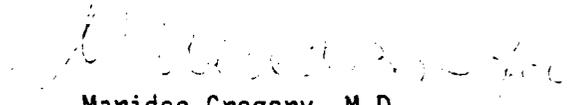
To : William V. Loscutoff, Chief
Toxics Pollutants Branch
Air Resources Board
1102 Q Street
B-4

Date : September 18, 1985

Subject: Chromium Health
Evaluation Document

From : Public Health
8/1253 5-2927

Attached please find the revised chromium health evaluation document to be sent to the Science Review Panel.


Maridee Gregory, M.D.
Acting Deputy Director

Attachment

SEP 19 1985

APPENDIX C

DISCUSSION OF EMISSION ESTIMATES

1. Chrome Plating Emissions

A. Emission Factors

Emission factors were derived based on data presented in the Naval Shipyard Study,^{1/} from information provided by industry representatives, and using certain assumptions.

Emission factors were calculated as follows:

$$\text{Emfac} = E_i / S_i \quad (1)$$

Where:

Emfac = Emission factor, lb/hr. ft.²

E_i = Emission rate of the i th tank, lb/hr.

S_i = Surface area of the i th tank, ft.²

Emission rate of the i th tank is calculated according to equation 2 below:

$$E_i = E_T * (S_i / \sum_{i=1}^n (S_i f_i)) * f_i \quad (2)$$

Where:

E_T = Total emission rate for each test, lb/hr.

f_i = Fractional current density applied in the i th tank, unitless (for hard chrome, $f_i = 1.0$, for decorative, $f_i = 0.4$).

For uncontrolled emission factors, emission rates, E_i 's were calculated from the emission rates at the inlet of the scrubber.. The emission rates at the outlet of the scrubber were used to calculate the controlled emission factors.

The emission rates and resulting emission factors are shown in the table below:

Test-Run	Emission Rate, E_T (lb./hr) ¹		Emission Factors (lb/hr.ft ²)			
	Inlet	Outlet	Decorative		Hard	
			Uncontrolled	Controlled	Uncontrolled	Controlled
4-1	0.0674	0.00316	2.05×10^{-4}	9.60×10^{-6}	5.12×10^{-4}	2.40×10^{-5}
4-2	0.0338	0.00534	1.03×10^{-4}	1.62×10^{-5}	2.56×10^{-4}	4.05×10^{-5}
4-3	0.171	0.00215	5.20×10^{-4}	6.53×10^{-6}	1.30×10^{-3}	1.64×10^{-5}
4-4	0.0639	0.00592	1.94×10^{-4}	1.80×10^{-5}	4.85×10^{-4}	4.50×10^{-5}
Ave.	0.0840	0.00414	2.56×10^{-4}	1.26×10^{-5}	6.37×10^{-4}	3.15×10^{-5}
sd	0.0599	0.00178	1.82×10^{-4}	5.41×10^{-6}	4.54×10^{-4}	1.35×10^{-5}

B. Estimates of Emissions

An average size chromic acid tank used in chrome plating has been estimated by an industry association representative to be about 1,000 gallons with the dimensions of 12 feet long, 4 feet wide and 3 feet deep.^{2/} The number of these tanks used by each company is estimated to range from at least one, to four. The Long Beach Naval Shipyard has four chrome plating tanks and was assumed to have the most number of chromic acid tanks per plater. For calculation purposes, it was assumed that the platers used an average of 1.5 tanks for chrome plating.

Using the estimated number of chrome platers (400 platers) in California and an industry association estimate^{3/} that three-fourths of chromium used for plating is used for for hard chrome, and one-fourth for decorative chrome, the surface area, S's are calculated as follows:

$$\text{Average surface area per plater} = 1.5 \text{ tanks } (12' \times 4') = 72 \text{ ft}^2$$

Hard chrome:

$$S_{\text{Hard}} = (400 \text{ platers}) (3/4) (72 \text{ ft}^2/\text{plater}) = 21,600 \text{ ft}^2$$

Decorative chrome:

$$S_{\text{Decorative}} = (400 \text{ platers}) (1/4) (72 \text{ ft}^2/\text{plater}) = 7,200 \text{ ft}^2$$

Emissions were calculated assuming that on the average chrome plating is done 8 hours per day, 250 days per year. Emissions from chrome platers are tabulated below:

	Hexavalent Chromium Emissions (tons/year)	
	Controlled	Uncontrolled
Hard Chrome	0.68	13.8
Decorative Chrome	0.09	1.8
Total	0.77	15.6

NOTE: The controlled emissions were calculated based on an average scrubber efficiency of 92 percent as reported in the Naval Shipyard Study^{1/} The figures presented here for controlled emissions represent estimates based on technically achievable control efficiencies, and not on control efficiencies observed in the industry. On the average, we would expect lower than 92 percent control efficiency for typical wet scrubbers.

2. Cooling Towers Emissions

Chromium emissions from cooling towers were estimated using two sources of information. Method 1 is based on a survey conducted by SAI^{5/} on emissions from cooling towers in California. Method 2 is based on information from a Radian report^{4/} on the national population exposure to ambient chromium emissions. Both methods divide cooling towers into two groups, industrial and those associated with electrical power plants (utilities). This division is maintained in the following summary of methods used to calculate chromium emissions.

Where upper and lower estimates are given, the lower estimate was determined by using the lowest reported values for each parameter in an equation and the highest reported value was used for the upper estimate.

Method 1:

Based on an SAI report^{5/}, equation (1) was used to estimate chromium emission from cooling towers. The fraction of cooling towers using chromates, the concentration of chromium in the cooling tower water and the circulating water flow rate were determine from a survey of utilities and industry.

$$\text{Cr. Ems} = C_1 * F * Q * D_f * C_{Cr} \quad (3)$$

Where:

Cr. Ems = tons per year

C_f = units conversion factor (0.563 ton/min/year. M^3)

F = fraction of cooling towers using chromates

Q = Circulating water flowrate in cubic meters per minute

D_f = Fraction of circulating water lost to the atmopshere (drift fraction)

C_{Cr} = Weight fraction of chromium in circulating water in parts per million

To calculate the conversion factor, it was assumed that cooling towers operated 24 hours per day, 355 days per year. Ten days were allowed for maintenance or holiday stoppage. The drift losses, D_f , reported ranged from 10^{-5} to 10^{-4} gallons lost per gallon of circulating water. The concentration of chromium in the circulating water varied from 15.5 ppm to 16.1 ppm by weight. The fraction of all cooling towers, F, reported to be using chromates was 0.191. Using the above values, equation (1) can be simplified to yield the following equations for lower and upper estimates:

$$\text{Lower estimate} \quad \text{Cr. Ems} = 1.67 \times 10^{-5} Q_l \quad (4)$$

$$\text{Upper estimate} \quad \text{Cr. Ems} = 1.73 \times 10^{-4} Q_u \quad (5)$$

The average circulating water flow rate was different for industrial and utilities cooling towers and was determined separately as follows:

a) Utility Cooling Towers

The total circulating water flow rate was estimated to be 7,670 M³/minute for cooling towers associated with electrical power plants in California.^{5/} This does not include the Geysers, Magnolia, Olive or the Grayson plants (chromium emissions of these plants are negligible as calculated by Rogozen). Using equations (2) and (3), the contribution of chromium emissions from utility cooling towers is estimated to range from 0.12 ton to 1.3 tons per year.

b) Industrial Cooling Towers

SAI estimated that there are between 874 and 1,887 cooling towers in use in California. Of this total, it was reported that 392 towers had a total circulation rate of 2,960 M³/min or an average circulation rate of 7.55 M³/min tower.^{5/} Using the average circulation rate and the estimates for the number of towers in California, upper and lower estimates for the total amount of water circulating in towers, Q, can be calculated.

Lower estimate $Q_l = 7.55 \text{ M}^3/\text{min tower} (874 \text{ tower}) = 6600 \text{ M}^3/\text{min}$

Upper Estimate $Q_u = 7.55 \text{ M}^3/\text{min tower} (1,887 \text{ tower}) = 14250 \text{ M}^3/\text{min}$

Substituting the appropriate values into equations (2) and (3) gives a range of estimates emissions from 0.11 ton to 2.5 tons per year of chromium for industrial cooling towers. Adding the upper and lower estimates for both utilities and industrial towers gives the following estimate for the total emission rate:

	<u>Lower Estimate</u>	<u>Upper Estimate</u>	<u>Average</u>
Utilities	0.12	1.3	0.7
Industrial	<u>0.11</u>	<u>2.5</u>	<u>1.3</u>
Total Chromium Emissions (tons/year)	0.23	3.8	2.0

Method 2:

This method uses estimates from a Radian report^{4/} on chromium emissions from cooling towers and some values from the SAI report. Equation (6) was used to calculate chromium emissions.

$$\text{Cr Ems} = C_2 * F * D_w * C_{Cr} \quad (6)$$

Where:

C_2 = Units conversion factor (4.2×10^{-9} ton/gallon)

F = The fraction of cooling towers using chromates

D_w = The amount of water lost to drift

C_{Cr} = The concentration by weight of chromium in the circulating water

Because the Radian report estimated emissions nationwide, equation (6) was changed to include a correction factor for the number of towers in California compared to the nation. It was assumed the fraction of towers in California was the same as the fraction of the population in California. Thus, equation (5) was used for the California estimates.

$$\text{Cr. Ems} = C_2 * F * F_p * D_w * C_{Cr} \quad (7)$$

Where:

F_p = The fraction of the population in California

The fraction of the population in California is approximately 0.10. The fraction of cooling towers using chromate, F , was taken from Method 1. Because the chromium concentration, C_{Cr} , used in the Radian report was not specific to the measured concentration in California cooling towers, an average of chromium concentration of 15.8 ppm from method 1 was used in the method 2 equation. The water lost to drift nationwide in 1983 was estimated to be 1.436×10^9 gallons per year for industry and 2.656×10^9 gallons per year for utilities. Using the above values in equation (7) gives:

Industry estimate:

$$\begin{aligned} \text{Cr. Ems} &= (4.2 \times 10^{-9} \text{ ton/gal})(0.10)(0.191)(1.436 \times 10^9 \text{ gal/yr}) \\ &\quad (15.8 \text{ ppm}) \\ &= 1.8 \text{ tons/year} \end{aligned}$$

Utilities estimate:

$$\begin{aligned} \text{Cr. Ems} &= (4.2 \times 10^{-9} \text{ ton/gal})(0.10)(0.191)(2.65 \times 10^9 \text{ gal/yr}) \\ &\quad (15.8 \text{ ppm}) \\ &= 3.4 \text{ tons/year} \end{aligned}$$

The Radian report^{4/} also included a second estimate for the water lost from utility cooling towers. This second method estimates the drift based on the amount of water needed for cooling per kilo-watt-hour of power produced. The estimate for D_w from this approach is 5.83×10^9 gallons per year nationwide.

Using equation 5 the estimates for utility emissions is

$$\begin{aligned} (\text{Cr. Ems}) &= (4.2 \times 10^{-9} \text{ ton/gal})(0.10)(0.191)(5.83 \times 10^9 \text{ gal/yr}) \\ &\quad (15.8 \text{ ppm}) \\ &= 7.4 \text{ tons/year} \end{aligned}$$

Using the two estimates for utility emissions, an upper and lower estimate can be determined.

	<u>Lower Estimate</u>	<u>Upper Estimate</u>	<u>Average</u>
Utilities	1.8	1.8	1.8
Industrial	<u>3.4</u>	<u>7.4</u>	<u>5.4</u>
Hexavalent Chromium Emissions (tons/year)	5.2	9.2	7.2

Because there was no reason to select either method 1 or 2 as the "best" estimate, results from both methods were used for the report.

The estimate for the average chromium emissions from cooling towers was the average of the methods 1 and 2 estimate or $(2.0 + 7.2)/2 = 4.6$ tons/year. The possible upper and lower estimates were taken to be the highest and the lowest estimate determined by either method or 0.23 tons per year from method one and 9.2 tons per year from method two.

3. Waste Incineration Emissions

Chromium emission factors are usually presented as a weight percent of the particulate matter (PM) emissions. The chromium content of PM is highly dependent on the amount of chromium in the waste being burned. Unfortunately, the chromium content of waste is usually not known and an average emission factor has to be applied to the PM emissions.

A review of six reports indicates that the percent chromium in PM emissions can range from 0.017 percent to 0.13 percent with an average for refuse and/or sludge incinerators of 0.058 percent.^{6,7,8,9,11/} The total PM emissions from refuse/sludge incineration in 1981 was estimated to be 126.2 tons.^{10/}

Using the above numbers, the estimates for chromium emissions are:

Lower estimate Cr. Ems = $\frac{(0.017)(126.2 \text{ tons})}{100} = 0.021 \text{ tons/year}$

Upper estimate Cr. Ems = $\frac{(0.13)(126.2 \text{ tons})}{100} = 0.16 \text{ tons/year}$

Average Cr. Ems = $\frac{(0.058)(126.2 \text{ tons})}{100} = 0.074 \text{ tons/year}$

4. Residual Oil Combustion:

In 1981, 85.5 million barrels of residual oil were burned within California which resulted in an estimate of 18,300 tons of particulate matter (PM) being released to the atmosphere. Of this oil use, the electric utility industry consumed for 45.0 million barrels and released 9,000 tons of PM emissions.^{12/}

In 1983, electric utilities in California consumed 10.4 million barrels of residual oil^{13/} which are estimated to emit 2,080 tons of PM.

All other sections, except electric utilities, are estimated to consume 38.8 million barrels of residual oil and emit 8,730 tons of PM^{14/}; the total California consumption of residual oil and its PM emissions in 1983 would be 49.2 million barrels (10.4 MMbbl + 38.8 MMbbl) and 10,800 tons (8,730 tons + 2,080 tons) of PM emissions, respectively.

Chromium emissions based on residual oil combustion are estimates as follow:

$$\text{Cr Ems} = (8.47 \times 10^6 \text{ tons/yr})(1.2 \times 10^{-3} \text{ lb.Cr/ton oil})^{15/} \\ (\text{ton}/2,000 \text{ lb}) = 5.1 \text{ tons}$$

In another method, chromium emissions are calculated as a fraction of PM emissions. The emission factor was calculated based on tests using #6 fuel oil. The calculation is presented below:

$$\begin{aligned} \text{Cr Ems} &= (10,800 \text{ tons PM/yr})(1.85 \times 10^{-3} \text{ ton Cr/ton PM}) \underline{15/} \\ &= 20 \text{ tons} \end{aligned}$$

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APPENDIX D

ARB ANALYTICAL METHODS FOR SAMPLING AND ANALYSIS
OF ATMOSPHERIC TOTAL CHROMIUM AND
ATMOSPHERIC HEXAVALENT CHROMIUM

AIR RESOURCES BOARD
PROCEDURE FOR THE SAMPLING AND ANALYSIS
OF
ATMOSPHERIC TOTAL CHROMIUM, LEAD, MANGANESE AND NICKEL
METHOD 105

Haagen-Smit Laboratory Division
State of California
Air Resources Board
9528 Telstar Avenue
El Monte, CA 91731

Procedure for the Sampling and Analysis
of
Atmospheric Total Chromium, Lead, Manganese and Nickel
Method 105

1. Introduction

- 1.1 This procedure describes a method of sampling and analyzing atmospheric concentrations of total chromium (Cr), lead (Pb), manganese (Mn) and nickel (Ni).
- 1.2 Normal concentrations of total chromium usually are about 0.007 $\mu\text{g}/\text{M}^3$; lead usually is about 0.2 $\mu\text{g}/\text{M}^3$; manganese is about 0.01 $\mu\text{g}/\text{M}^3$ and nickel is about 0.005 $\mu\text{g}/\text{M}^3$.
- 1.3 With a sample volume of 24 cubic meters, the lower detectable limit for Cr, Mn, and Ni is 0.002 $\mu\text{g}/\text{M}^3$, while the lower detectable limit for Pb is 0.005 $\mu\text{g}/\text{M}^3$.

2. Method

- 2.1 A low-volume sampler is used to collect ambient suspended particulates containing total chromium, lead, manganese and nickel in air parcels.
- 2.2 A measured volume of air passes through a Teflon filter where particulates are collected.
- 2.3 The procedure and apparatus for low-volume sampling is described in Appendix C, "Procedure for Lo-Volume Sampling."
- 2.4 The Teflon filter is removed from the sampler and returned to the laboratory for elemental measurement by X-ray fluorescence (XRF) analysis:
 - 2.4.1 The sample is irradiated with X-rays, which knock out inner-shell electrons.
 - 2.4.2 When the inner-shell vacancies are filled by valence electrons, the excess energy may be released in the form of (fluorescent) X-rays whose energies are characteristic of the atom from which they originate.
 - 2.4.3 Both the number and characteristic atomic energies of the fluorescent X-rays are measured by a solid-state detector.
 - 2.4.4 The XRF simultaneously measures concentrations of most elements, including Cr, Pb, Mn, and Ni, at the nanogram to microgram level.

3. Apparatus

3.1 The XRF analyzer consists of the following:

3.1.1 A sample holder which contains an X-ray tube, detector, preamplifier and liquid nitrogen trap.

3.1.2 Amplifier

3.1.3 Multichannel analyzer

3.1.4 Buffer unit

3.1.5 Calculator with printer

3.1.6 The buffer unit and calculator can be replaced by a computer.

3.1.7 A separate unit houses the X-ray tube power supply and control.

3.2 Figure 3.2 is a block diagram of the instrumentation employed. The detector is solid-state, lithium-drifted silicon. Its resolution is about 150 electron volt (eV) full width half maximum (FWHM) at an X-ray energy of 2.3 KeV; its resolution decreases with increasing X-ray energy. The multichannel analyzer sorts the pulses from the amplifier into channels according to the energy of the pulse, which is proportional to the energy of its parent X-ray. It may be used to process the spectrum in a number of ways. The buffer stores pulses from the analyzer and feeds them into the calculator at an acceptable rate. The calculator is programmable; its program subtracts the background of the raw spectrum, removes contributions from secondary X-rays, calculates net atmospheric concentrations and sends them to the printer.

4. Procedure

4.1 The sample is placed in the X-ray sample holder where a molybdenum X-ray tube irradiates the sample.

4.2 The resulting fluorescent X-rays are detected and converted into electrical pulses, amplified, and sent into a multi-channel analyzer.

4.3 After a scan is completed, the pulses are converted into elemental concentrations of Cr, Pb, Mn, and Ni and the results are typed out automatically on the printer.

5. Calculations

5.1 Elemental concentrations are obtained assuming a proportionality between net counts and concentration; the proportionality constant is obtained from calibration standards, stored in cassette tapes and entered into the Tektronix 31 calculator.

5.2 The standards are thin films obtained from μ matter Company or dried solutions on filters obtained from Columbia Scientific Industries.

5.3 Fluorescent count rates from these standards are proportional to elemental concentrations of Cr, Pb, Mn and Ni expressed in micrograms per cm².

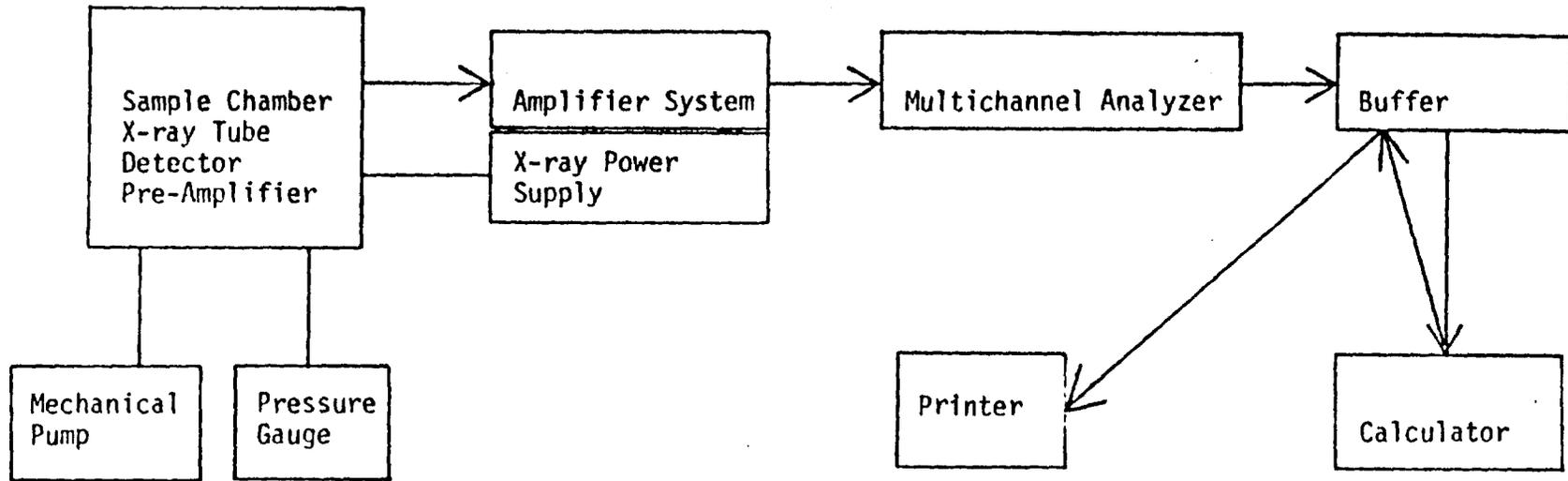
6. Critiques and Comments

6.1 Molybdenum L X-rays were chosen to maximize count rates from elements which fluoresced in the region between 5 and 12 KeV, particularly manganese and lead. The molybdenum L X-rays near the sulfur K region were absorbed using two thicknesses of Whatman 41 filter paper.

6.2 X-ray fluorescence analysis is a rapid, non-destructive analytical method.

Figure 3.2

Block Diagram of Instrumentation



DRAFT

D R A F T

ADDL006

METHOD FOR THE SPECIATION AND ANALYSIS OF
HEXAVALENT CHROMIUM AT AMBIENT ATMOSPHERIC LEVELS1. SCOPE

This document describes the determination of chromium +6 in aqueous media after sampling ambient air. The method has been tailored to concentrations which would be expected in ambient air. Although the procedure described is known to complex other metal ions, the procedure has not been validated for any metal species other than hexavalent chromium.

2. SUMMARY OF METHOD

If sampling is performed by aqueous impinger, the water may be treated directly. If sampling by low volume filter, the filter is added to 100 ml of water and the complexation procedure carried out in the presence of the filter.

The aqueous solution is buffered to pH 7 and an aqueous solution of APDC added. After mixing, the solution is filtered through a disposable cartridge containing C₁₈-bonded silica gel. The complex is absorbed onto the gel. The water, remaining ions, and uncomplexed APDC are passed through into a filtering flask and discarded. The absorbed Cr+6-complex is desorbed with acetone, the acetone evaporated, and the resultant residue diluted to 1.0 ml with 10% nitric acid in water.

This solution is then analyzed by flameless atomic absorption spectrophotometry (FAAS) for chromium.

3. LIMITATIONS AND INTERFERENCES

- 3.1 The concentration ranges expected for Cr+6 in ambient air (1-5 ng/m³) require that extreme care must be taken to insure that glassware and reagents do not contribute to the measured levels. Blanks must be analyzed with every batch of samples.
- 3.2 Trivalent chromium at levels ten times the Cr+6 concentration does not interfere in the method. Iron (Fe+3) does not interfere, except that excess ferric ion will compete with Cr+6 for available complexing agent. This effect has been minimized by performing the complexation step at pH 7. The other metals known to form APDC complexes at pH 7 (copper and cobalt) do not occur at sufficiently high levels to deplete the complexing agent.
- 3.3 Matrix effects have been reduced or eliminated by the extraction of the complex into an organic solvent and matching the final aqueous diluent to the 10% nitric acid solution used for diluting standards.

4. APPARATUS

- 4.1 Varian Model 375 Atomic Absorption Spectrophotometer equipped with a CRA-90 flameless accessory and strip chart recorder.

- 4.2 Vacuum filtering apparatus equipped with Sep-Pak C₁₈ cartridge adaptor and teflon tubing.
- 4.3 micro-Snyder concentrator, 5 ml capacity.
- 4.4 Sep-Pak cartridge: Waters Assoc. #51910. Prepare cartridge for use by first filtering 5 ml of methanol through it, then washing with 10 ml distilled water.

5. REAGENTS

- 5.1 Nitric acid, Ultrex grade.
- 5.2 Stock standard, 250 mg/l: Dissolve 141.4 mg K₂Cr₂O₇ in 10% nitric acid solution and dilute to 200 ml in a volumetric flask. 1 ml = 0.25 mg Cr+6.
- 5.3 Intermediate standard, 0.5 mg/l: Dilute 100 ul of the stock standard in 50 ml of 10% nitric acid in a volumetric flask. 1 ml = 0.5 ug Cr+6.
- 5.4 Working standard: Dilute 2.0, 4.0, 8.0, 12.0 ml in 100 ml of 10% nitric acid. These correspond to 10 ng/ml, 20 ng/ml, 40 ng/ml, and 60 ng/ml Cr+6. Prepare working standards daily.
- 5.5 Buffer, pH 7: 0.05 M KH₂PO₄/NaOH buffer, Fisher Scientific.

5.6 APDC solution: Dissolve 3 gms ammonium pyrrolidine dithiocarbamate in 100 ml distilled water. Filter the solution through a glass fiber to remove the insoluble sediment. The resultant solution will be a clear yellow. Filter entire 100 ml through a prepared Sep-Pak C₁₈ cartridge. The resultant solution will be colorless.

6. INSTRUMENT CALIBRATION

6.1 Prepare instrument for the flameless analysis of chromium. Insure that the carbon tube is properly aligned.

6.2 Inject 10 ul of 10% nitric acid solution. Start CRA-90 heating cycle. Auto zero the data system using this value. The absorbance value should be no more than 0.005.

6.3 Inject 10 ul of 60 ng/ml standard. After the analysis, calibrate the data system to 60 ng/ml. Repeat Step 6.2 to insure that the system reads 0.0.

6.4 Inject 10 ul of 60 ng/ml standard twice more. Recalibrate if values differ from 60 ng/ml by more than +15%.

6.5 Inject 10 ul of 40 ng/ml, 20 ng/ml, and 10 ng/ml standards in triplicate. Determine the least squares fit of the resultant data; the analysis must result in a slope of $1.00 \pm 15\%$. This calibration procedure must be performed weekly.

6.6 The blank and 60 ng/ml standard must be analyzed at least every ten samples.

7. SAMPLE ANALYSIS

7.1 If the sample has been taken using a 37 mm glass fiber or teflon filter, place the filter in a 125 ml glass stoppered flask, add 100 ml deionized water, 2 ml of pH 7 buffer, and 1 ml of APDC solution. Place on horizontal shaker for 30 minutes.

7.2 If sample has been collected in a liquid impinger, add 2 ml/100 ml solution pH 7 buffer; mix well, and then add 1 ml/100 ml solution APDC solution. Mix well.

7.3 Aspirate aqueous solution through a prepared Sep-Pak C₁₈ cartridge.

7.4 Using a 10 ml syringe, desorb the trapped Cr⁺⁶-APDC complex with 5 ml acetone directly into a micro-Snyder concentrator.

7.5 Using a hot water bath (more than 80°C), concentrate the acetone solution to dryness. Note: There will be a small liquid residual, mostly residual water. As much acetone must be removed as possible, since it causes problems during the analysis step.

7.6 While hot, add 0.1 ml concentrated Ultrex nitric acid (2 drops); let cool.

- 7.7 Add deionized water to the micro-Snyder receiver and quantitatively transfer the solution to a 1.0 ml volumetric flask. Dilute to 1.0 ml.
- 7.8 Inject 10 ul of the concentrate in triplicate for analysis using the calibrated FAAS system.
- 7.9 Record the analysis results on the strip chart trace with identifying laboratory identification number and dilutions, if any. Record results and calculations in the AAS laboratory workbook. Record the calculated concentration in nanograms/m³ on the laboratory data sheet. The concentration may be calculated as follows:

$$\text{Chromium +6, ng/m}^3 = \frac{\text{Concentration Found, ng/ml}}{\text{Volume Sampled, m}^3} \times \text{Dilution Factor}$$

8. METHOD VALIDATION

- 8.1 The calibration curve from 10 ng/ml to 60 ng/ml was constructed. The results of this procedure are shown in Table I.
- 8.2 Deionized water was spiked with 20 ng, 40 ng, and 50 ng Cr+6. The analysis was performed using this method with the following results:

Spike, ng	Recovered*, ng	% Recovery*	RSD, %*
20	14	70	17
40	37	92	6.5
50	48	96	11

* Results of three spike sample analyses.

8.3 Field spike studies have not yet been performed, results to be submitted at a later date.

TABLE I
Chromium +6 by Flameless Atomic Absorption
Results of Standard Analysis

Concentration (ng/ml)	Average Recovery, ng/ml	RSD**, %
10	8.9	25
20	24.4	6.6
40	39.0	3.2
60 (calibration)	60	7.2

** Relative Standard Deviation, n = 4

Correlation Coefficient: 0.994

Slope: 0.978

Intercept: 1.2 ng/ml

LOD: $(i + 3\sigma) = 2.1 \text{ ng/ml}$ (0.21 ng/m^3 , 10 m^3 sample, but may be higher due to sample media contamination).

HEALTH ASSESSMENT FOR CHROMIUM

Prepared by:

The Epidemiological Studies and Surveillance Section
California Department of Health Services

September 1985

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1. EXECUTIVE SUMMARY

Chromium is a substance that can exist as several different chemical species. The trivalent form (Cr(III)) and the hexavalent form (Cr(VI)) are believed to be the biologically active species, but their health impacts are not identical, in part because Cr(VI) readily penetrates biological membranes while Cr(III) generally does not. Cr(III) is an essential trace element while Cr(VI) compounds are associated with cancer induction.

Exposure to chromium in occupational settings has resulted in nasal septum perforation, respiratory irritation, and skin reactions. However, at current ambient chromium levels, no acute or noncarcinogenic chronic adverse health effects, with the possible exception of adverse reproductive effects, are expected to occur. Chromium has demonstrated adverse reproductive effects, including teratogenesis in animals. However, experimental data are inadequate to assess potential human reproductive risks from ambient exposures

Genotoxicity tests, animal cancer bioassays, and epidemiologic studies provide evidence for a carcinogenic response to chromium exposure. All short-term assays reported show that Cr(VI) compounds possess genotoxic capabilities, while tests of Cr(III) compounds are generally negative or generate positive results at much higher doses than those used in Cr(VI) tests. Animal studies show similar findings with respect to cancer as the outcome, i.e., the evidence for the carcinogenicity of Cr(III) is

weak, but several hexavalent chromium compounds have demonstrated statistically significant increases in cancer incidence rates. No direct inhalation animal studies have resulted in statistically significant increases in tumor incidence. Rather, the evidence from animal studies supports carcinogenesis at the site of contact. Several epidemiologic studies have shown a strong high association between chromium exposure in the workplace and respiratory cancer. However, these studies were not designed, nor in general did their authors attempt, to systematically identify noncarcinogenic adverse health effects or link the increased cancer mortality to a specific form of chromium.

In reviewing the health information on chromium, the International Agency for Research on Cancer (IARC) has concluded that there is sufficient evidence to demonstrate the carcinogenicity of chromium in both animals and humans. The Department of Health Services (DHS) concurs with these findings and believes, at this time, that there are inadequate data to confirm or refute the carcinogenic potential of trivalent chromium. In addition, the DHS has not found compelling evidence demonstrating the existence of a threshold with respect to chromium carcinogenesis.

The staff of DHS recommends adopting the risk assessment performed by the Environmental Protection Agency (EPA), in which a linear nonthreshold model was applied to the epidemiologic study (Mancuso, 1975) judged to be most methodologically sound and to contain the best exposure data to derive dose-response curves for hexavalent chromium. Data from animal studies were judged to be inadequate for quantitative risk assessment by the staff of DHS.

One of the strengths of the DHS risk assessment is its reliance on human airborne exposures, which obviates uncertainty related to extrapolation between species and from noninhalation routes of exposure. In addition, the use of a linear nonthreshold extrapolation model yields risk estimates that are public health protective. Conversely, there are limitations in the epidemiologic data which create uncertainty in the risk assessment. Uncertainty enters the risk assessment by virtue of extrapolating from high occupational exposure levels to low ambient levels, the reliance on imprecise historical exposure levels as the basis for estimating potency, the lack of data differentiating between chromium oxidation states and compound specificity, and the lack of control for potential confounding factors (e.g., cigarette smoking).

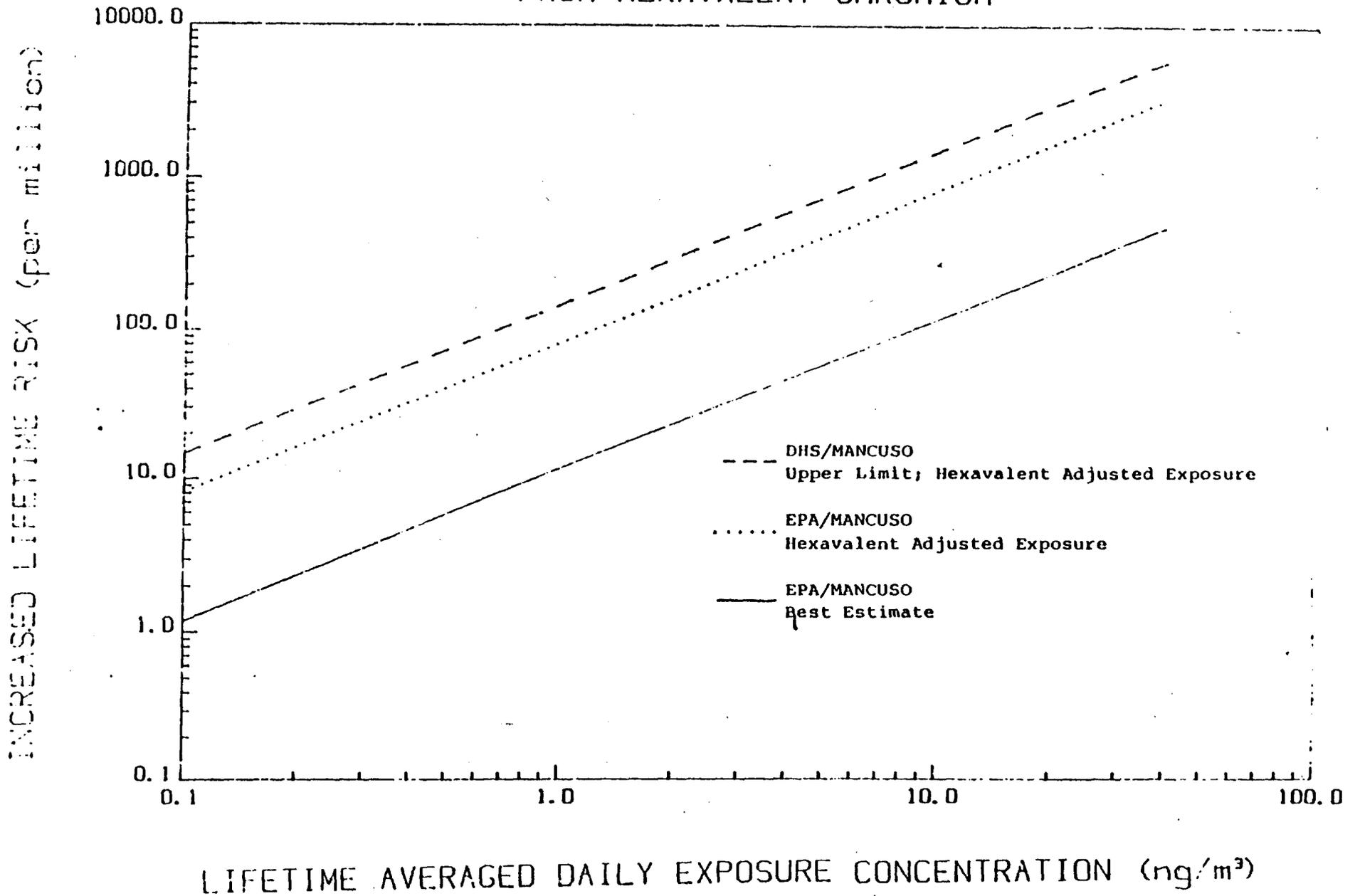
However, making certain assumptions, it is possible to describe dose-response curves for hexavalent chromium. Based on the results derived from application of the linear nonthreshold model and the Mancuso data, the staff of DHS recommends that the Air Resources Board consider the increased lifetime carcinogenic risk from a continuous lifetime exposure to hexavalent chromium as falling in the range of 12 to 146 cancer cases per nanogram hexavalent chromium per cubic meter of air per million people exposed (12-146 cancers/ng/m³/million). This range is illustrated in Figure A, where the solid line represents the curve based on the EPA assessment using total chromium as the exposure, the dotted line is based on the EPA assessment adjusting for the hexavalent chromium fraction of the exposure, and the dashed line was generated by taking the upper limit of the 95% confidence interval for carcinogenic risk due to chromium and

adjusting for the hexavalent fraction of the workplace exposure. There are not, however, sufficient data from this or other epidemiologic studies to estimate the risk of specific hexavalent compounds for airborne exposures.

The risk model and potency estimates can be applied to populations living near point source emitters of hexavalent chromium as well as to the general population. In estimating risks to populations around such "hot spots", however, it should be noted that while the excess theoretical cancer risk among individuals most heavily exposed can be considerable (e.g., .006), the number of people so exposed may be relatively low (e.g., a few thousand people) and therefore the actual number of additional estimated cancer cases will also be relatively low.

Figure A

CANCER RISK FROM HEXAVALENT CHROMIUM



This document presents an evaluation of the health effects resulting from exposure to chromium compounds. The purpose of this undertaking was to determine if exposure to chromium at current ambient levels is likely to produce adverse effects on human health. To achieve this objective, data on the chemistry, toxicology, and epidemiology of chromium were reviewed by the staff of the California Department of Health Services. Salient features of this review are presented and a quantitative risk assessment based on the carcinogenicity of hexavalent chromium is provided.

2. CHEMISTRY

The chemistry of chromium has been reviewed elsewhere (EPA, 1984; Hayes, 1980) and only the relevant chemical properties of this substance will be briefly summarized here, relying on the above secondary sources. The issues of principal chemical concern regarding chromium compounds' toxicity are oxidation state and solubility. It is important to bear in mind that the physical and molecular characteristics of the interaction of chromium compounds with biological systems are not well known. Thus, mechanisms of toxicity are uncertain.

Chromium is a transition element (subgroup VI B of the periodic table) with an atomic weight of 52.01. The most common oxidation states are 0,+2,+3 and +6, although it can occur in all oxidation states from -2 to +6. Trivalent (Cr(III)) and hexavalent (Cr(VI)) compounds have been the most extensively studied in biological systems, and with the exception of relatively unstable species, such as Cr(V), are thought to be the only biologically significant forms of chromium.

Cr(III) is the most stable oxidation state, forming coordination complexes that tend to hydrolyze and chelate in liquids. The coordination complexes are exclusively octahedral, with ligands such as water, urea, sulfates, ammonia and organic acids (EPA, 1984). Stable complexes can thus be formed with amino acids, peptides, proteins, nucleic acids and other macromolecules.

Cr(VI) is virtually always bound to oxygen in ions such as chromates (CrO_4^{-2}) and dichromates ($\text{Cr}_2\text{O}_7^{-2}$). At physiologic pH, the dichromate ion dissociates into the chromate ion. Cr(VI) ions are strong oxidizing agents and are readily reduced to Cr(III) in acid or by organic matter (NAS, 1974). Although chromium is the sixth most abundant element in the earth's crust, Cr(VI) is rarely found in the biosphere because it is so easily oxidized by organic matter (Love, 1983; EPA, 1984).

Certain biological activities of chromium compounds (e.g., carcinogenicity) have been considered to be related to their water solubility. Table 2-1, which lists solubilities of some common chromium compounds, is intended as a reference for subsequent discussions.

Table 2-1. Solubility of Chromium Compounds

<u>Compound</u>	<u>Description of Solubility</u>
Chromite ore (III)*	no information available
Chromium metal (0)	insoluble in water
Barium chromate (VI)	practically insoluble in water (4.4 mg/l at 28°C)
Calcium chromate (VI)	soluble in water (163 g/l at 20°C and 182 g/l at 45°C)
Chromic acetate (III)	soluble in cold water, insoluble in ethanol
Chromic chloride (III)	anhydrous form is insoluble in cold water and slightly soluble in hot water; in its hydrated forms it is very soluble in water (585 g/l) and insoluble in methanol, ethanol, acetone and diethyl ether
Chromic oxide (III)	insoluble in water
Chromic phosphate (III)	slightly soluble in cold water; reacts with most acids and alkali but not with acetic acid
Chromium carbonyl (0)	insoluble in water
Chromium potassium sulfate (III)	soluble in water (243.9 g/l at 25°C)
Chromium sulfate (III)	the heptahydrate is soluble in water (124 g/l at 0°C); the anhydrous salt is slightly soluble in ethanol
Chromium trioxide (VI)	soluble in water (625.3 g/l at 20°C)

Ferrochromium (0)	insoluble in water
Lead chromate (VI)	practically insoluble in water (580 μ g/l at 25 $^{\circ}$ C)
Lead chromate oxide (VI)	insoluble in water
Potassium chromate (VI)	soluble in water (629 g/l at 20 $^{\circ}$ C and 792 g/l at 100 $^{\circ}$ C)
Potassium dichromate (VI)	soluble in water (49 g/l at 0 $^{\circ}$ C and 1020 g/l at 100 $^{\circ}$ C)
Sodium chromate (VI)	soluble in water (873 g/l at 30 $^{\circ}$ C)
Sodium dichromate (VI)	soluble in water (2380 g/l at 0 $^{\circ}$ C)
Strontium chromate (VI)	slightly soluble in water (1.2 g/l at 15 $^{\circ}$ C)
Zinc chromate (VI)	soluble in acids and liquid ammonia; insoluble in cold water and acetone; decomposes in hot water
Zinc chromate hydroxide (VI)	slightly soluble in water

* Oxidation state is noted in parentheses adjacent to the name of each substance.

Source: Adapted from IARC, 1980.

3. PHARMACOKINETICS

The absorption, distribution and excretion of chromium compounds have recently been reviewed elsewhere (EPA, 1984). Therefore, relevant issues are only presented in summary form below.

3.1 Absorption

The extent of absorption of chromium compounds via the respiratory tract, gastrointestinal tract or skin depends on the chemical form. In general, Cr(VI) is better absorbed than Cr(III) because of its facility in crossing cell membranes.

Biological membranes have traditionally been considered permeable to Cr(VI), but not Cr(III) (e.g., IARC, 1980). However, with appropriate heterocyclic aromatic ligands, Cr(III) can also enter cells (Warren et al., 1981). The magnitude of a toxic effect resulting from Cr(VI) exposure may depend in part on whether the reduction of Cr(VI) to stable Cr(III) complexes occurs intra- or extracellularly.

3.1.1 Inhalational Deposition and Absorption

Deposition and retention of inhaled chromium depend on the dose, size and solubility of the substance under investigation. Chromium in ambient air has been reported to contain principally respirable particulates, with a mass median diameter of about 1.5 to 1.9 μm (EPA, 1984).

In this size range particles can reach and be deposited in the deep lung (i.e., respiratory bronchioles and alveoli), though a large percentage may be carried out in the exhaled airstream (Langard, 1982). Soluble particulates will be taken up regardless of deposition site; insoluble compounds need to be deposited in the deep lung in order to be taken up (Langard, 1982). Particles deposited on the ciliated bronchial epithelium will be cleared via the mucociliary escalator and swallowed. Clearance of such particles occurs more quickly than those deposited in the alveoli, which will be cleared to some extent by pulmonary macrophages that migrate to the mucociliary escalator or lymph channels.

In a report on the distribution of chromium in the lungs of 35 randomly selected autopsies conducted in a highly industrialized city, Bartsch et al. (1982) found the greatest quantities in interbronchial lymph nodes (reflecting clearance processes), with the remainder distributed over a gradient increasing towards the lung apices, suggesting a relationship to normal breathing. In other words, the asymmetric pulmonary distribution of chromium was due to inhaled chromium, in contrast to the uniform distribution of constitutive elements in the lung, such as potassium, calcium, copper and zinc. Using particle induced x-ray emission analysis, the concentration of chromium averaged $2.85 \mu\text{g/g}$ dry lung tissue (Bartsch et al., (1982). In itself, this number is of little value, since there was no information on the correlation of chromium content with age distribution, smoking habits (chromium is found in cigarette smoke), possible

occupational exposures, or concentrations of chromium in the lungs of an "unexposed" population.

There is insufficient information to estimate accurately the percentage of chromium absorption from the lungs (EPA, 1984; Langard, 1982). A few rodent experiments involving exposure to chromium dusts or intratracheal instillation of water-soluble chromium compounds indicate that Cr(VI) compounds are absorbed much more quickly than those containing Cr(III), probably because the latter bind to extracellular macromolecules while the former readily penetrate cell membranes. Langard et al. (1978) reported that after short-term (about 6 hours) exposure to zinc chromate dust (mean concentration was 7.35 mg/m^3 , 99% of particles were less than $5 \mu\text{m}$ in diameter), mean blood concentrations in two rats increased from $0.007 \mu\text{g/ml}$ to $0.31 \mu\text{g/ml}$. After several months of repeated exposures mimicking occupational exposure patterns (6-1/2 hr/day, 5 days/week), mean blood chromium values in 12 rats were about $0.5 \mu\text{g/ml}$. Thus, significant absorption of this insoluble chromate occurred relatively quickly: near steady-state values were achieved in a small sample of rats within a few hours' exposure.

Clearance patterns following intratracheal instillation of several water-soluble chromium compounds (sodium chromate (VI), potassium dichromate (VI) and chromic chloride (III)) in guinea pigs were reported by Baetjer et al. (1959). The analytical method could not distinguish Cr(III) from Cr(VI), so that the percentage of Cr(VI) reduced in tissue to Cr(III) could not be ascertained. Ten minutes

post-instillation, 15% of the Cr(VI) was retained in the lungs compared to 69% of the Cr(III). At this time 20% of the administered dose of Cr(VI) was found in the blood and 5% in the liver, spleen and kidney. For Cr(III) only 4% was found in the blood and other tissues. The authors assumed that the remainder had been cleared from the lungs up the trachea and swallowed. At 24 hours post-instillation, only 11% of the Cr(VI), while 45% of the Cr(III) remained in the lungs. Another early study cited by EPA (1984) indicates that, at least for intratracheal instillation, a substantial portion of the administered dose (55% of chromic (III) chloride during the first week after exposure) was found in feces, also suggesting substantial tracheal clearance (Visek et al., 1953). (The latter estimate may be too high, since biliary excretion was not investigated.)

3.1.2 Gastrointestinal Absorption

Chromium compounds are poorly absorbed from the gastrointestinal tract of humans and animals, although Cr(VI) is better absorbed than Cr(III). Most studies have traced the fate of orally administered $^{51}\text{Cr Cl}_3$ (III) and $\text{Na}_2^{51}\text{CrO}_4$ (VI). Based on fecal analysis or on whole body radioactivity, absorption estimates ranged from less than 0.5% for CrCl_3 to about 11% for Na_2CrO_4 in humans and less than 1% to 3% for both salts in rats (EPA, 1984). Others have estimated that up to 3-6% of Cr(VI) may be absorbed by rats (IARC, 1980). Absorption was increased by fasting or duodenal administration (EPA, 1984; Donaldson and Barreras, 1966). The facility with which Cr(VI) crosses cell

membranes is not reflected in a significantly higher absorption in the animal experiments, possibly because acid gastric fluids reduce Cr(VI) to Cr(III) (Donaldson and Barreras, 1966) (See Section 3.2). Furthermore, constituents of gastric juices bind Cr(III), inhibiting absorption (Donaldson and Barreras, 1966). In any case, for purposes of the risk assessment in Section 8, gastrointestinal absorption of chromium swallowed after tracheal clearance is not considered to contribute significantly to total chromium absorption.

3.1.3 Dermal Absorption

Dermal absorption of chromium was recently reviewed (Polak, 1983).

The principal relevant aspects are that:

- (1) Cr(III) binds to skin components, particularly in the epidermis, and thus generally does not penetrate intact skin (but see #4, below). However, all Cr(III) salts tested penetrate skin stripped of the stratum corneum.

- (2) Cr(VI) compounds in aqueous solution readily penetrate intact skin and are systemically absorbed at high concentrations (1%), but do not pass beyond the skin at lower concentrations (0.1 to 0.001%).

- (3) Some Cr(III) salts (e.g., CrCl₃) penetrate intact skin almost as well as Cr(VI) compounds.
- (4) Cr(VI) is reduced to Cr(III) by skin constituents, particularly proteins containing sulfhydryl groups.
- (5) Penetration of Cr(VI) increases with increasing pH of the solution, which correlates with decreasing reactivity as an oxidant, and thus a decreasing probability of Cr(VI) being reduced to Cr(III).

Particulate forms of chromium are unlikely to be absorbable percutaneously unless dissolved. Even in the latter situation it is unlikely, in view of the above findings, that either Cr(III) or Cr(VI) would be systemically absorbed in quantities significant enough to consider for purposes of the risk assessment in Section 8.

3.2 Transport and Distribution

Although most studies of chromium transport, distribution and elimination have been conducted in animals, the general model (at least for Cr(III)) has been confirmed in human subjects using intravenously administered ⁵¹Cr(III), followed by whole-body scintillation scanning and counting and plasma counting (Lim et al., 1983). Cr(III) is transported in the blood bound mainly to transferrin, with uptake by kidney, bone marrow, liver, spleen and soft tissues.

Transferrin is taken up into cells (e.g., reticulocytes) by endocytosis (Light and Morgan, 1982): Cr(III) may thus enter cells bound to this protein, as does iron, the usual occupant of transferrin binding sites. Liver and spleen appear to act as long-term storage depots for chromium, perhaps reflecting patterns of transferrin metabolism. Inhaled Cr(III) would follow a somewhat different distribution pattern, since a large percentage is retained in the lungs (See Section 3.1.1)

The transport and tissue uptake patterns of Cr(VI) are probably similar to those of Cr(III), but, because of different experimental designs, inter-study comparisons are problematic (EPA, 1984). Furthermore, clearance of chromium from whole blood after administration of Cr(VI) is slower than after that of Cr(III), due to facile erythrocytic uptake of the former, followed by intracellular reduction to Cr(III), with binding to erythrocyte proteins, especially hemoglobin. (See Section 3.3, "Metabolism") Unlike Cr(III), Cr(VI) is not significantly bound to plasma proteins (Love, 1983).

3.3 Metabolism

In vitro studies have demonstrated that cell membranes are substantially more permeable to chromate (VI) solutions than to Cr(III), which may result from transport via an anion channel (Kitigawa et al., 1982; Levis et al., 1978). Chromate metabolism has recently been reviewed by Connett and Wetterhahn (1983), whose relevant findings are summarized in the next paragraph.

Absorbed Cr(VI) can react with multiple cellular components, resulting in reduction to Cr(III) by reaction with cellular macromolecules or small molecules, such as cysteine, reduced glutathione, and ascorbic acid. Few purified proteins will reduce chromate at physiologic pH. However, in erythrocytes chromate rapidly oxidizes and binds to hemoglobin; oxidation is potentiated in vitro by the presence of reduced glutathione (Kitigawa et al., 1982). In vitro studies of liver microsome preparations containing cytochrome P-450 and NADPH-dependent cytochrome P-450 reductase indicate that Cr(VI) is reduced, with the formation of a Cr(V) reactive intermediate (Wetterhahn Jenette, 1982; Polnaszek, 1981). There is also substantial Cr(VI) reduction within mitochondria by as-yet-unidentified substances. Reduction of Cr(VI) is not a random process, since most macromolecules and small molecules studied do not appear capable of effecting this process under physiologic conditions (Connett and Wetterhahn, 1983).

Cr(III) resulting from intracellular Cr(VI) reduction is capable of a variety of interactions with cellular constituents, many of which may result in toxicity. Cr(III) can form stable coordination complexes with amino acids and nucleic acids, and can cause intra- and intermolecular cross-linking of proteins and polynucleotides (See Section 5, "Genotoxicity"). Cr(III) may also affect enzyme activity by binding to enzyme protein or to substrate (Levis et al., 1978). About half of intracellular Cr(III) complexes formed are found in the nucleus (Leonard and Lawreys, 1980).

3.4 Elimination

Elimination of chromium was reviewed by EPA (1984) and Langard (1982), from which most of the following summary is adapted.

The major routes of chromium elimination are via the kidneys and gastrointestinal tract (i.e., by biliary excretion). Some is also eliminated in hair, nails, milk and sweat. (Guthrie, 1982,; Leonard and Lawreys, 1980). It is unknown which pathway predominates for the elimination of nutritionally required, ingested trace amounts of Cr(III)(See Section 3.5), since the kinetics of elimination have been studied at higher dose levels.

Clearance from plasma, representing tissue uptake and renal clearance, is rapid, occurring within hours, while elimination from tissues is much slower, with half-times (for Cr(III)) ranging from several days to about 12 months for storage sites (e.g., liver and spleen). Numerous experimental studies in animals indicate that urinary excretion of chromium predominates (>50%), with less than 10% appearing in bile, while a substantial percentage appears to deposit in storage compartments.

Several studies compared elimination of Cr(III) and Cr(VI) administered intravenously, subcutaneously and by gavage. Generally it appears that Cr(VI) is more rapidly excreted than Cr(III) (EPA, 1984). This observation was supported in a recent study examining clearance kinetics of chromium in mice dosed intraperitoneally with

1/6 the LD₅₀ of Cr(III) or Cr(VI) (Bryson and Goodall, 1983). After a single intraperitoneal dose of chromium trichloride (Cr(III)) or potassium dichromate (Cr(VI)), mice were serially sacrificed. At 3 days 87% of Cr(III) was retained, while only 31% of Cr(VI) was; at 7 days these numbers were 73% for Cr(III) and 16% for Cr(VI); and after 3 weeks they were 45% and 7.5%, respectively. (Retention sites were not specified since the method of analysis involved whole body acid digestion.) In a treatment regimen consisting of once-weekly doses of the same substances, Cr(III)-treated mice retained about 9 times as much of the administered doses as those treated with Cr(VI) (totalling approximately 70% of the total injected chromium). Analyses of excreta showed that Cr(VI) was eliminated more rapidly in urine and feces than Cr(III).

The differential excretion and retention of Cr(III) and Cr(VI) probably reflect the greater ability of Cr(III) to form complexes with components of biological systems and of Cr(VI) to cross cell membranes. However, in view of the ready biological reduction of Cr(VI) to Cr(III) both intra- and extracellularly, this distinction in the clearance kinetics of the different oxidation states cannot be complete. In any case, it is clear that exposure to chromium in either oxidation state can result in long (years) residence times in human tissues. For example, Tsuneta et al. (1980) reported that the mean concentration of chromium (not speciated) in the upper lobes of lung cancer patients who were former chromate workers was 72 times greater than that in non-exposed control lungs (36.7 µg/g wet weight compared to 0.51µg/g), even many years after the exposures had ended.

3.5 Chromium as an Essential Nutrient

Although chromium has been recognized as an essential nutrient in animals for more than two decades, the precise nutritional biochemistry has yet to be elucidated. Cr(III) was identified as the active component of a glucose tolerance factor found in brewer's yeast, which could correct an induced deficiency state. The latter is characterized by glucose intolerance (measured by an intravenous glucose tolerance test in animals), glycosuria, hypercholesterolemia, decreased longevity, decreased sperm counts and impaired fertility (Mertz, 1969; Anderson and Polansky, 1981).

Guthrie (1982) reviewed 12 clinical studies on chromium supplementation, reporting that both inorganic Cr(III) (usually as chromium chloride) and chromium administered in brewer's yeast extract significantly ameliorated glucose intolerance and hypercholesterolemia and decreased fasting insulin levels in some subjects, including diabetics, asymptomatic hyperglycemic individuals, and healthy controls. Chromium's nutritional role has not been thoroughly delineated, but appears at least to potentiate insulin activity (Mertz, 1975). The biologically active Cr(III) complex, which also includes nicotinic acid and several amino acids, strongly binds insulin (Guthrie, 1982).

Although there are inadequate data to formulate a recommended dietary allowance for chromium, an adequate and safe intake of 50 to 200 $\mu\text{g}/\text{day}$ for adults has been suggested (NAS, 1980a). Daily intakes for adults in the U.S. are probably less than 200 $\mu\text{g}/\text{day}$, although it is unclear what percentage of Cr(III) intake would be in biologically active forms (Guthrie, 1982). Gastrointestinal absorption of organically bound chromium (as in food) is higher than for inorganic Cr(III), which, as noted in Section 3.1.2, is poorly absorbed from the gastrointestinal tract (NAS, 1980a). The Safe Drinking Water Committee of National Academy of Sciences has reported estimates of the daily intake of chromium by different routes as:

- (a) food: mean 62 $\mu\text{g}/\text{day}$ (range 37-130) from "typical self-selected American diets";
- (b) drinking water: mean 17 $\mu\text{g}/\text{day}$ (range 1-224) assuming consumption of 2 liters/day; and
- (c) air: less than 0.5% of dietary intake in areas where ambient chromium concentrations average 0.015 $\mu\text{g}/\text{m}^3$ and less than 4% in highly polluted areas with an ambient chromium concentration of 0.35 $\mu\text{g}/\text{m}^3$ (NAS, 1980b).

It should be noted that the estimated average daily chromium intakes from food and water refer to Cr(III) and thus are not relevant to the cancer risk assessment for Cr(VI) in section 8.

4. ACUTE AND CHRONIC TOXICITY

4.1 Acute Toxicity

4.1.1 Animal

Because of its poor gastrointestinal absorption and bioavailability, Cr(III) is considered to be relatively nontoxic when orally administered. Oral LD₅₀s in rats are chromic chloride, 1.9 g/kg; chromic nitrate, 3.3 g/kg; and chromic acetate, 11.3 g/kg (EPA, 1984). Intravenous LD₅₀s for various Cr(III) salts in mice are: chromium sulfate, 85 mg/kg; chromic chloride, 400-800 mg/kg and chromic acetate, 2290 mg/kg (IARC, 1980).

Cr(VI) compounds are more toxic than those of Cr(III), regardless of the route of administration. The range of oral LD₅₀s in rats has been reported to be 80 to 114 mg/kg, with death occurring within hours to about 3 days. Symptoms and pathologic findings included cyanosis, gastric ulceration, diarrhea and tail necrosis (EPA, 1984). The principal potentially lethal effect of acute Cr(VI) exposure is renal toxicity, resulting in acute renal failure. Microscopic pathologic changes have been reported in the glomerulus and proximal and distal convoluted tubules in a variety of species, including rats, monkeys, and rabbits, given toxic parenteral doses of Cr(VI), usually as potassium dichromate or sodium chromate. It has been estimated that renal toxicity occurs at a dose level of 1-2 mg Cr(VI)/kg body weight (Tandon, 1982).

Other organs and systems affected by high-dose parenteral administration of both Cr(III) and Cr(VI) include the central nervous system, myocardium and liver (Tandon, 1982).

4.1.2 Human

The estimated range for a lethal dose of ingested Cr(VI), based on reported fatal cases, is between 1.5 and 16 g (IARC, 1980). Reported pathology includes gastrointestinal hemorrhage, intravascular hemolysis and acute renal failure. No such cases have been reported for Cr(III) compounds, which are considerably less toxic by ingestion (see below). As of 1973, no fatalities had been reported due to exposure to airborne Cr(VI) (NIOSH, 1973). Exposure to Cr(VI) aerosols results in mucous membrane irritation and probably bronchospasm, although the latter is not well-documented in the literature (Bidstrup, 1983). Since occupational exposure measurements were not often taken and in the past were not often reliable, no dose-response estimates have been made here, although one would not expect any such effects in the general population from current levels of ambient chromium concentrations. This observation follows a fortiori from the conclusion in Section 4.2.2, infra, that current ambient levels of chromium would not be expected to result in any chronic effects discussed in Section 4.2.

4.2 Chronic Toxicity

Chronic toxic effects (other than genotoxicity, reproductive effects and carcinogenicity) from chromium exposure have been observed in experimental animals and among individuals occupationally exposed. The occurrence of all of the effects listed below is expected to be governed by a threshold, even if the threshold exposure level has not been precisely quantified. In the case of chromium, the difference between current ambient exposure levels and the levels at which chronic toxic effects have occurred (several orders of magnitude) leaves enough of a margin of safety so that none of these effects is expected to occur in the general population.

4.2.1 Animal

Most of the literature on chronic exposure to chromium compounds consists of reports of no observed effect levels ("NOELs") (EPA, 1984). The studies reviewed by EPA are of limited value, however, since few animals were used in each study. All but one of these studies involved ingestion. The one inhalation study reviewed involved intermittent short exposures (10-60 minutes each) over a 4-month period of two cats to chromium (III) carbonate dust at an average concentration of 58.3 mg/m^3 (range 3.3 to 83 mg/m^3) (EPA, 1984). The poor statistical power of this last investigation limits its usefulness for purposes of risk assessment.

Other inhalation experiments using Cr(III) aerosols have shown that chronic effects occur at levels lower than 58.3 mg/m^3 . Three studies cited by Tandon (1982) showed that: (1) inhalation by rats of

chromium (III) oxide or trisubstituted chromium (III) phosphate at a concentration of 42-43 mg/m³ for 5 hr/day for 4 months produced chronic inflammatory changes in the bronchi and lung parenchyma and dystrophic changes in liver and kidney; (2) exposure of rats to chromium ore residue dust at 19 mg/m³ for 1, 3 or 7 days produced swelling and desquamation of alveolar cells, while exposure to lower concentrations (1 or 10 mg/m³) for 3 weeks resulted in alveolar wall thinning and filling of alveoli with dust-laden proteinaceous materials.

There were no Cr(VI) inhalational NOEL studies found. Two rodent inhalational assays produced chronic effects (Steffee and Baetjer, 1965; Nettesheim et al., 1971). Rabbits, guinea pigs, and rats were exposed to mixed chromate (VI) dusts and mists at a mean concentration of 3-4 mg/m for 5 hr/day, 4 days/wk for the animals' lifetimes (Steffee and Baetjer, 1965). Treatment-related effects included nasal septal perforation, alveolar and interstitial inflammation, alveolar hyperplasia, and granuloma formation. No systemic pathology was found. In another experiment, mice were exposed to calcium chromate (VI) dust at a concentration of 13 mg/m³ for 5 hr/day, 5 days/week over their lifetimes (Nettesheim et al., 1971). After six months of exposure, pulmonary effects included epithelial atrophy, necrosis, and hyperplasia, bronchiolar epithelial replacement of alveolar cells, alveolar proteinosis and other pathology. There was decreased weight gain in relation to control animals. Other effects included tracheal and submandibular lymph node hyperplasia, and atrophy of liver and spleen.

The above discussion demonstrates that there are inadequate animal data from which to calculate a chronic inhalational NOEL. DHS staff members therefore believe that, the human experience with chromium compounds should be used for purposes of risk assessment (See Section 4.2.2)

Parenteral administration of various chromium compounds at doses greater than 1 mg/kg to a variety of animal species has resulted in damage to liver, brain, myocardium, and testis, with the effects more severe for Cr(VI) than Cr(III) compounds (Tandon, 1982).

4.2.2 Human

In occupational settings the most commonly reported chronic effects of chromium exposure include contact dermatitis, skin ulcers, irritation and ulceration of the nasal mucosa and perforation of the nasal septum (NIOSH, 1975). Less common are reports of hepatic and renal damage and of pulmonary effects (bronchitis, occupational asthma and bronchospasm)(IARC, 1980; NIOSH, 1975; Bidstrup, 1983).

Chromium is the most common cause of occupational dermatitis and is the second most common skin sensitizer in the general population (Polak, 1983). This condition has an immunologic etiology determined by Cr(VI) penetration of skin, followed by reduction to Cr(III) by sulfur-containing proteins in the dermis. The resulting Cr(III)-protein conjugate is then thought to act as a sensitizing antigenic complex, with Cr(III) as the hapten (Polak, 1983).

Skin ulcers, ulceration of the nasal mucosa and perforation of the nasal septum are corrosive reactions due to the oxidative actions of Cr(VI) and chromic acid (Pedersen, 1982; Burrows, 1983; Bidstrup, 1983). Skin ulcers are believed to occur only where the exposed skin has been damaged (Pedersen, 1982). Similarly, a major factor in nasal ulceration and septal perforation is thought to be a lapse in personal hygiene -- i.e., nose-picking (Bidstrup, 1983). Skin ulcers and nasal perforation often occur in the same individuals (ACGIH, 1982; Burrows, 1983).

Occupational asthma due to sensitization to chromium has occurred in industry, but is uncommon (Bidstrup, 1983). Only recently was an immunologic basis for such asthma confirmed in a case report of an electroplating worker (with a positive inhalational challenge) in whose serum specific IgE antibodies were demonstrated (Novey et al., 1983). Bronchospasm in occupational settings, due to the primary irritant effects of chromium (particularly chromates and chromic acid mist), has occurred, but is not well-documented in the literature (Bidstrup, 1983). It is unknown what levels of pulmonary exposure would be required to induce chromium sensitization.

NIOSH (1975) thoroughly reviewed the health effects from exposure to Cr(VI) compounds. On the basis of this review NIOSH recommended a permissible exposure limit of $25 \mu\text{g}/\text{m}^3$ of Cr(VI) as adequate to protect against noncarcinogenic effects for a 40 hr/wk time-weighted average exposure. Assuming such levels are protective against the

above-noted effects,^{*†} and adjusting for continuous exposure (168 hr/wk), there is still an approximately 3 orders of magnitude difference between this, recommended level and current ambient concentrations. Thus, DHS staff members conclude that none of the chronic effects discussed in this section is likely to occur at current ambient levels of exposure[†]. From this conclusion it can be inferred that no acute toxic effects would be expected either.

*EPA (1984) cited a NIOSH Health Hazard Evaluation of an electroplating plant in which typical symptoms and signs of chromium toxicity occurred at Cr(VI) exposure levels of 1 to 20 $\mu\text{g}/\text{m}^3$. DHS staff has reviewed this NIOSH report, which indicates that the chromium-associated toxicity was due to inadequate work practices rather than airborne chromium.

[†]As noted in the text, there is not enough information to determine a threshold for immunologic sensitization.

5. GENOTOXICITY

Mutagenic and clastogenic effects have been reported almost invariably for Cr(VI), but not Cr(III), compounds. The nature of chromium's genotoxic effects is complex and has been extensively investigated. Chromium's interactions with genetic materials have been reviewed by Leonard and Lawreys (1980), IARC (1980), Heck and Costa (1982), Levis and Bianchi (1982), and EPA (1984).

5.1. Mutagenicity

Cr(VI) has been indisputably demonstrated to induce genotoxic effects in all of the major assay systems, suggesting that the carcinogenicity of this substance (See Section 7) is at least partially explicable on a genotoxic basis. Principal aspects of the genotoxicity of chromium are summarized below.

(1) Bacterial assays

In the standard Ames S. typhimurium test, Cr(VI) compounds induced mutations in tester strains responsive to both base-pair substitution and frameshift mutagens at doses of 10-20 μ g/plate, while Cr(III) compounds were observed to be nontoxic and non-mutagenic at concentrations of up to 20 mg/plate. The mutagenic potency of Cr(VI) compounds could be diminished by addition of liver microsomal S-9 preparations, erythrocyte lysates, ascorbic acid, sodium sulfite, sodium nitrate, and several reducing

metabolites (i.e., GSH, NADH, NADPH), presumably due to extracellular reduction of Cr(VI) to Cr(III) (IARC, 1980; Petrilli and De Flora, 1978). Addition of potassium permanganate, a strong oxidizing agent, to liver microsome and erythrocyte preparations completely blocked the ability of the latter to inhibit Cr(VI)'s mutagenicity (Petrilli and De Flora, 1978). Petrilli and De Flora (1978) observed that rat lung microsome preparations were only very weakly active in reversing Cr(VI) mutagenicity, which is interesting in view of chromium's ability to cause lung cancer in humans (See Section 7).

Similarly, mixing potassium permanganate with Cr(III) compounds resulted in a positive Ames test, which was attributed to extracellular oxidation of Cr(III) to Cr(VI). While most Cr(III) compounds are nonmutagenic in the Ames assay, some containing aromatic ligands cross bacterial cell walls and membranes and are active mutagens in the Ames test and in the E. Coli repair assay (Warren et al., 1981).

In E. Coli assays, experimental results with Cr(VI) were not as consistently positive as those in Ames tester strains. However, several Cr(VI) compounds (including salts of potassium, calcium, lead and sodium as well as stainless steel welding fumes) have been reported as positive in a variety of E. Coli mutagenesis assays. Generally Cr(III) tested negative, although chromic acetate was positive at very high concentrations (16-130 mM) in one E. Coli arg⁻ strain (Heck and Costa, 1982).

(2) Cultured Mammalian Cell Assays

In V79 Chinese hamster cells, soluble potassium dichromate (VI) and slightly soluble zinc chromate (VI) both induced dose-related mutagenesis, while soluble chromic (III) acetate and insoluble lead chromate (VI) (both given at substantially higher doses than $K_2Cr_2O_7$ and $ZnCrO_4$) did not. In the same cell line, potassium chromate and dichromate and welding fumes, but not chromic acetate, caused 6-thioguanine resistance (Levis and Bianchi, 1982). In C3H mouse cells, potassium dichromate and chromium (VI) trioxide induced chromosomal aberrations and 8-azaguanine resistant mutants, while potassium chromate (VI) and chromic (III) sulfate did not. In the L5178Y mouse lymphoma cell TK^{+/-} assay, potassium chromate and dichromate both tested strongly positive (IARC, 1980). In the above assays, all Cr(VI) compounds, with the exception of lead chromate, tested positive. The insolubility and hence low bioavailability of lead chromate may have affected the outcome of this investigation.

5.2 Chromosomal Damage

Numerous studies have demonstrated that chromium compounds, particularly those of Cr(VI), cause clastogenic effects in vitro and in vivo. These studies have been extensively reviewed elsewhere (Leonard and Lawreys, 1980; IARC, 1980; Levis and Bianchi, 1982; EPA, 1984). Relevant conclusions from the review articles are presented in this section.

Every Cr(VI) compound tested in at least 8 different in vitro cell culture systems has produced chromosomal aberrations, most commonly gaps and breaks. Cr(VI) compounds tested included chromium trioxide, potassium chromate and dichromate, sodium chromate and dichromate, lead chromate, calcium chromate, zinc chromate and welding fume particles (EPA, 1984; Levis and Bianchi, 1982). Cell culture sources included human lymphocytes, primary human embryo fibroblasts, primary hamster embryo cells, three hamster cell lines (CHO, DON and V79), primary mouse fetal cells, and a mouse mammary carcinoma line. Cr(III) compounds have also occasionally tested positive for clastogenicity in vitro, but only at doses substantially higher (by one to two orders of magnitude) than those for Cr(VI) compounds tested in similar systems. Such anomalous results may be partially explained by Cr(VI) contamination of Cr(III) compounds and possibly by the action of lysosomal nucleases released through destabilization of lysosomal membranes (IARC, 1980; Levis and Bianchi, 1982).

Consistent with the above observations, sister chromatid exchange (SCE) was induced by every Cr(VI) compound tested (including all of those listed in the previous paragraph) in primary human lymphocyte and fibroblast cultures, 2 hamster cell lines (CHO and DON), and a primary mouse lymphocyte culture. Except where contaminated by Cr(VI) or when mixed at dose levels 300 to 1,000 times higher than those of Cr(VI), Cr(III) compounds were invariably negative in the SCE assays (EPA, 1984).

Observations of chromium's chromosomal effects in vivo have generally confirmed the results of the in vitro experiments. Micronuclei (nuclear fragments due to chromosomal breaks or a delayed anaphase) were found in immature erythrocytes in mice administered potassium chromate (VI) intraperitoneally. However, chromic (III) nitrate and the carcinogen calcium chromate (VI) did not produce significant increases in micronuclei (Levis and Bianchi, 1982).

Chromosomal aberrations have been reported in fish and rats treated with sodium dichromate (EPA, 1984; Levis and Bianchi, 1982). Workers exposed to a variety of Cr(VI) compounds, including sodium chromate, chromium trioxide and others, have had significant increases in chromosomal aberrations in peripheral lymphocytes compared to unexposed controls (IARC, 1980). Similarly, workers exposed to chromium trioxide showed significantly increased number of SCEs and chromosomal aberrations (EPA, 1984). Interestingly, this phenomenon was observed only in the youngest workers, allegedly because these were the least experienced and would thus be more likely to incur significant exposures.

In summary, there is overwhelming evidence that Cr(VI) compounds are capable of causing chromosomal damage. Cr(III) compounds may also be clastogenic, but it is unclear whether this is a real effect or an artifact.

5.3 Transformation

Morphological transformation of mammalian cells is considered to provide a good, short-term method for assessing carcinogenic potential. All Cr(VI) compounds tested have been shown to be capable of cell transformation in several in vitro systems, while, with one exception, Cr(III) (as chromic chloride) has not. Levis and Bianchi (1982) reviewed these experiments and their conclusions are summarized below.

- (1) Potassium chromate (VI) and dichromate (VI) and sodium chromate (VI) transformed mouse and hamster primary cell cultures. Chromic chloride also did so in fetal mouse cells, but not Syrian hamster embryo cells.
- (2) Cr(VI) salts of calcium, lead, zinc, and potassium enhanced viral transformation of hamster cells.
- (3) Cr(VI) (as potassium chromate) enhanced benzo(a)pyrene-induced transformation of hamster embryo cells, whereas Cr(III) (as chromic chloride) did not.
- (4) Cr(VI) (as potassium dichromate or calcium chromate) induced anchorage-independent growth in hamster cells, whereas Cr(III) (as chromic chloride) did not.

(5) Sodium chromate (VI) administered intraperitoneally to pregnant mice resulted in transformation of cell cultures derived from the embryos. Cr(III) was not tested in this system.

Thus, assays for in vitro transformation provide additional qualitative confirmation of the carcinogenic potential of Cr(VI) compounds.

5.4. Mechanisms Proposed for Genetic Toxicity

Cr(VI) compounds are active in every major assay for genotoxicity, while Cr(III) compounds show activity in some systems only at high doses, which has led numerous investigators to propose that Cr(VI) is genetically active, whereas Cr(III) typically is not (Levis and Bianchi, 1982). This hypothesis is clearly correlated with the relative abilities of these oxidation states of chromium to cross biological membranes. As noted earlier, the site of reduction of Cr(VI) to Cr(III) may well be determinative of the extent of genetic toxicity. Extracellular reduction diminishes or abolishes mutagenicity of Cr(VI), while oxidation of Cr(III) has the opposite effect (Petrilli and DeFlora, 1978). Intranuclear reduction of Cr(VI) appears to be the key element in chromium's genotoxicity, resulting in direct oxidation of DNA and/or the formation of stable Cr(III) complexes with nucleophilic sites in DNA (Langard, 1982).

Since Cr(III) compounds possess clear abilities to damage DNA in cell-free systems and, when complexed to certain ligands, in bacterial assays, it is possible that Cr(III) is the ultimate carcinogen

(Fornace et al., 1981; Warren et al., 1981). Interactions of Cr(III) with nucleic acids include binding to cytosine and guanine and to phosphate groups. Unlike Mg (II), which stabilizes DNA through its interactions with phosphate groups, Cr(III)'s effects include inter- and probably intramolecular cross-linking between phosphate moieties, chelation between bases and phosphates, and cross-linking with proteins (Tamino et al., 1981; Levis and Bianchi, 1982).

Experimental evidence from several laboratories supports the notion that intracellular reduction of Cr(VI) to Cr(III) is crucial. Fornace et al. (1981) reported that in several mammalian cell cultures, including bronchial epithelial cells, Cr(VI) (as potassium chromate) produced persistent, dose-dependent protein-DNA cross-linking, measured by alkaline elution. However, in isolated nuclei and in buffered solution with [³H] DNA and bovine serum albumin, Cr(III) (as chromic chloride), but not Cr(VI), induced DNA-protein cross-links. Sirover and Loeb (1976), using a cell-free system, found that Cr(III) decreased the fidelity of DNA synthesis by avian myeloblastosis virus DNA polymerase at a concentration 25 times lower than that of Cr(VI) required to achieve the same result, which may be due to DNA-protein cross-linking (Fornace et al., 1981). Similarly, Tkeshelashvili et al. (1980) reported that Cr(III) (as chromic chloride) was more effective than Cr(VI) (as chromium trioxide) in diminishing the fidelity of DNA synthesis by E. Coli DNA polymerase I.

Using a rat liver microsome/NADPH system, Tsapakos and Wetterhahn (1983) showed that enzymatic reduction of Cr(VI), in the presence of NADPH was required to effect chromium binding to double-stranded DNA. Cr(III) binding was 2 - 3 times lower and was not dependent on the presence of NADPH or microsomes. Binding to single-stranded DNA was substantially higher for both Cr(VI) and Cr(III), with binding of Cr(VI) greater than that of Cr(III). The Cr(VI), microsomes and NADPH bound substantially more protein (bovine serum albumin in this system) to DNA than did Cr(III). Protein and chromium binding to DNA and RNA were linearly correlated. Incubating Cr(VI) with DNA homopolymers showed that binding to poly(G) was favored (by an order of magnitude) over the other homopolynucleotides. This last observation is consistent with the suggestion by Venitt and Levy (1974) that Cr(VI) mutagenicity is due (at least in part) to attack on GC base-pairs, causing GC-->AT transitions in subsequent DNA replication, which is typical of electrophilic mutagens.

Thus, there are at least two pathways in the uptake-reduction model of chromium's genotoxicity. Damage to DNA, with protein cross-linking, is caused most effectively when Cr(VI) is enzymatically reduced in close proximity to DNA (e.g., by the electron transport system cytochrome P-450 complex located in the nuclear membrane). (Tsapakos and Wetterhahn, 1983). This may involve reactive Cr(V) intermediates (Wetterhahn Jennette, 1982; Polnaszek, 1981). Cr(III) produced by other reducing systems may also interact with DNA and

protein, but at a slower rate because of its kinetic stability. Common to both pathways, however, is reduction of Cr(VI) to Cr(III), with cross-linking of macromolecules.

6. REPRODUCTIVE EFFECTS

Potential reproductive effects of chromium have not been investigated epidemiologically. In view of Cr(VI)'s genotoxicity, however, there is reason to believe a priori that it may adversely affect reproduction, unless germ cells or the fetus were resistant to such toxicity. This is clearly not the case, since animal experiments demonstrate adverse effects on male reproductive systems and fetal development.

6.1 Male Reproductive Effects

Both Cr(III) and Cr(VI) are capable of crossing the blood-testis barrier and damaging the testis. Administered intraperitoneally to rabbits at a dose of 2 mg/kg for 3 or 6 weeks, Cr(III) (as chromium nitrate) and Cr(VI) (as potassium dichromate) caused depression of enzyme activity, degenerative histological changes and spermatotoxic effects (i.e., multinucleated germ cells and spermatocyte degeneration in the lumen of the seminiferous tubules) (EPA, 1984). Pagano et al. (1983) showed that Cr(VI) (as sodium chromate) in sea urchins depressed mitotic activity in sperm. Consistent with these observations is the report by Paschin et al. (1981) that potassium dichromate was positive in a dominant lethal mutation assay in mice

given a single dose at 20 mg/kg or daily doses for 21 days at 2.0 mg/kg. Male rats treated with a daily intraperitoneal dose of 1 mg Cr(III)/kg were found to have a mean testicular Cr(III) concentration of 3.2 $\mu\text{g/g}$ tissue, lower than the liver and kidney concentrations of 14.1 $\mu\text{g/g}$ and 8/1 $\mu\text{g/g}$, respectively (Lee, 1983). The lower accumulation in the testis was attributable in part to the protective effect of the blood - testis barrier. Chromium has also been reported to accumulate in the testes of men exposed occupationally, which may be due to reduction of Cr(VI) by testicular microsomes (Levis and Bianchi, 1982). Both Cr(III) and Cr(VI) are thus capable of crossing the blood-testis barrier and of affecting spermatogenesis: the risk to humans cannot be assessed from these data, however.

6.2 Placental Transport

There is direct as well as indirect evidence that chromium can cross placental membranes. As an essential nutrient, chromium (III) must be transported to the developing fetus. Fetal chromium concentrations reportedly increase during gestation, peaking in the neonate, with subsequent declines in various tissues during childhood (Guthrie, 1982).

Cr(III) placental transfer has been examined in several animal studies. In a study using whole-body radioautography, Cr(as chromic (III) chloride) was detected in fetal skin and bone one hour post-injection to the mother, with increasing amounts detectable in

later gestation (Langard, 1982). Similarly, Iijima et al. (1983) reported that concentrations of ^{51}Cr mouse embryos increased at 4-hour intervals after a single intraperitoneal injection of $^{51}\text{CrCl}_3$, to the point where the concentration of radioactivity in the fetus exceeded that in maternal blood. Relatively little inorganic chromium (III) (<0.5% of the administered dose) has been found to cross the placenta. In contrast, when administered in a biologically active form (brewer's yeast) by gavage, twenty to fifty percent of the initial maternal radioactivity was found in the litters (EPA, 1984). In one study comparing transplacental uptake of intravenously administered Cr(III) (as chromic chloride) and Cr(VI) (as sodium dichromate), 0.4% of the dose of Cr(III) and 12% of the dose of Cr(VI) were recovered in embryonic mice (Danielsson et al., 1982). The embryotoxicity and fetotoxicity of these chromium compounds (see below) provides additional, but indirect evidence of chromium's transplacental passage.

6.3 Effects on Fetal Development

Gale (1978) gave single intravenous injections of Cr(VI) (as chromium trioxide) to early gestational (day 8) hamsters at dose levels of 5, 7.5, 10 or 15 mg/kg. Fetuses taken from the treated dams were examined for external, internal and skeletal malformations. There was a dose-dependent increase in the frequency of resorptions and internal and external anomalies. The most common malformation was cleft palate (up to 84% of treated animals in the high-dose group compared to 2% in controls) and the most common internal anomaly was

hydrocephalus (55% of the low-dose group versus 0% in controls). Other fetotoxic effects included delayed ossification and edema. There was maternal toxicity, as evidenced by decreased weight gain and renal tubular necrosis, at dose levels of 7.5 mg/kg and above. On the basis of this experiment, the author concluded that chromium trioxide is embryolethal and teratogenic.

To evaluate the possible contribution of genetic background to chromium teratogenesis, Gale (1982) treated 5 inbred hamster strains and 1 outbred strain with one, 8 mg/kg intravenous injection of chromium trioxide. Similar outcomes (high incidence of resorptions, cleft palate, hydrocephalus) were detected in 3 strains, while the others were noted to be relatively resistant to the embryotoxicity of chromium trioxide.

Cr(III) (as chromic chloride) was shown to be teratogenic in mice given a single intraperitoneal injection on the 7th, 8th or 9th day of gestation (Matsumoto et al., 1976). Doses ranged from 9.76 mg/kg to 24.4 mg/kg. The only statistically significant effect observed in the low-dose group (9.76 mg/kg) was decreased fetal weight. Possible maternal toxicity was not reported. The most common external anomalies were exencephaly, anencephaly and open eyelids. The authors suggested that the more severe cranial anomalies might be due to incomplete neural tube closure. This suggestion received support in later experiments in which pregnant mice treated with a single dose of chromic chloride on day 8 of gestation were serially sacrificed at 4-hour intervals post-injection (Iijima et al, 1983).

Embryos examined histologically had numerous pyknotic neuroepithelial cells in the neural ectoderm at 8 hours post-injection. The authors suggested that Cr(III) has a direct effect on the neural tube, which closes at about 8 1/2 days of gestation. However, an indirect effect on the placental or maternal system cannot be ruled out by this investigation.

EPA (1984) reviewed these and other studies, summarized in Table 6-1. Since the lowest administered dose of Cr(VI) (5mg/kg) noted was teratogenic without significant maternal toxicity, a risk assessment for humans using a safety factor approach cannot be used. A similar rationale applies to the study of Matsumoto et al. (1976), in which (except for fetal weight gain) a no effect level of 9.76 mg/kg for Cr(III) administered intraperitoneally was reported. However, internal malformations were not investigated and it cannot be stated definitively that, from the standpoints of embryoletality and teratogenesis, this dosage is truly a no observed effect level. Furthermore, this represents a single dose exposure while, for purposes of risk assessment, chronic exposure by a more relevant route would be more appropriate. (Single dose studies do, however, illustrate the intrinsic potential of chromium to induce reproductive failure and demonstrate that only one exposure is required to elicit the response.) Thus, the experimental data are inadequate to calculate reproductive risks to humans from ambient exposures to either Cr(VI) or Cr(III).

Table 6-1

Teratogenic and Pototoxic Effects of Chromium

Compound	Route	Species	Dose	Fetal Effects	Maternal Effects	Reference
CrO ₃	i.v.	hamster	5, 7.5, 10, or 15 mg/kg on day 8 of gestation	increased fetal death in 7.5, 10, and 15 mg/kg groups, increased incidence of cleft palate in all groups, hydrocephalus and skeletal defects	depressed weight gain and kidney tubular necrosis at all doses above 5 mg/kg	Gale, 1970
CrO ₃	i.v.	hamster	0 mg/kg on day 7, 8, 9, 10, or 11 of gestation	increased fetal death following administration on day 7, increased incidence of cleft palate following administration on days 7, 8, or 9	weight loss, tubular necrosis of kidneys	Gale and Bunch, 1979
CrCl ₃	i.p.	mouse	9.76, 14.64, 19.52, or 24.4 mg/kg on day 8 of gestation	depression of fetal weights in all Cr treated groups, increase in rate of external abnormalities for groups treated with 14.64, 19.52, or 24.4 mg/kg	not reported	Matsumoto et al., 1976
CrO ₃	i.v.	hamsters (strain LVG)	0 mg/kg on day 8 of gestation	increased incidence of cleft palate	body weight loss	Gale, 1982
		hamsters (strain CB)	0 mg/kg on day 8 of gestation	no effect	no effect	

Table 6-1 (Cont)

Compound	Route	Species	Dose	Fetal Effects	Maternal Effects	Reference
		hamsters (strain LHC)	8 mg/kg on day 8 of gestation	no effect	no effect	
		hamsters (strain LSH)	8 mg/kg on day 8 of gestation	increased incidence of cleft palate	body weight loss	
		hamsters (strain PDH)	8 mg/kg on day 8 of gestation	no effect	no effect	
		hamsters (strain MHA)	8 mg/kg on day 8 of gestation	increased incidence of cleft palate	body weight loss	
CPD ₁	s.c.	mouse	10 or 20 mg/kg on day 7, 8, 9, 10, or 11 of gestation	increase in external malfor- mations in 20 mg/kg group when dosed on day 8, as well as increase fetal death when dosed on day 8 or 11	lethal to 1/3 of dams	Iijima et al., 1979

Table 6-1 (Cont)

Compound	Route	Species	Dose	Fetal Effects	Maternal Effects	Reference
CrCl ₃	i.p.	mouse	9.8 mg/kg on day 0 of gestation	Cr increased gradually and peaked at 24 hr, exceeding maternal blood Cr level.	Maximum blood Cr at 4 hr post-i.p. and gradually decreased	Iijima et al., 1981
CrCl ₃	i.p.	mouse	19.5 mg/kg/day	Pyknotic cells in neuro-epithelium of neural ectoderm in 2 of 5 embryos after 4 hr; in all 5, after 8 hr.	NR	Iijima et al., 1983
CrCl ₃	i.v.	mouse	10 mg/kg on days 13 and 16 of gestation	Fetal Cr(III) was 0.4% of maternal serum Cr 1 hr post-i.v.; high accumulation of Cr in yolk sac placenta. In late gestation, Cr accumulated in calcified areas of fetal skeleton.	NR	Danielsson et al., 1982
		[in vitro]	0 to 15 µg/ml	No overt cytotoxicity at 15 µg/ml in embryonic cell cultures (chick cells).	NA	Danielsson et al., 1982
Na ₂ Cr ₂ O ₇ (Cr(VI))	i.v.	mouse		Fetal Cr(VI) was 12% of maternal serum Cr 1 hr post-i.v. In late gestation, Cr accumulated in calcified areas of fetal skeleton.	NR	Danielsson et al., 1982
Cr(VI)		[in vitro]	0.1 to 0.28 µg/ml	Affected cartilage production at 0.1 µg/ml in embryonic cell cultures (chick cells).	NA	Danielsson et al., 1982

i.v. = Intravenous; i.p. = Intraperitoneal; s.c. = subcutaneous

NR = Not reported; NA = Not applicable

Source: EPA, 1983

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7. CARCINOGENICITY

Epidemiologic studies of cohorts exposed to chromium aerosols occupationally provide clear evidence of carcinogenicity. However, because of mixed exposures and the dearth of reliable exposure data, the relative carcinogenic potencies of different compounds cannot be distinguished on the basis of epidemiologic data alone. However, animal studies involving inhalational exposure to various chromium compounds have been unsuccessful in even confirming the results of these epidemiologic studies, much less resolving issues of identities and potencies of different chromium-containing compounds as respiratory carcinogens. Several chromium compounds have been demonstrated to be carcinogenic when administered to animals by invasive methods. In this section the results of nonhuman studies will be summarized briefly, with greater attention given to the epidemiologic evidence.

7.1 Animal studies

There have been at least eighty reported attempts to induce cancer in rodents by administration of chromium compounds by various routes. These have been reviewed by IARC (1980, 1982), Hayes (1982) and EPA (1984). Appendix I consists of a summary table of studies adapted from EPA (1984). Most early studies have inadequate experimental designs by today's standards. Relevant findings from the above literature reviews are:

- (1) No chromium compound has been unequivocally shown to cause a significantly increased number of neoplasms in experimental animals after

exposure by inhalation. At least 7 experiments involving dusts containing Cr(VI) and/or Cr(III) compounds have been conducted. Although Nettesheim et al. (1971), reported a significantly increased incidence of alveologenic (not bronchogenic) adenomas and adenocarcinomas in mice exposed to calcium chromate dust (13 mg/m^3) over their lifetimes for 5 hr/day, 5 days/wk, this conclusion cannot be confirmed on the basis of the data reported. The authors' statistical methodology was not reported. Fourteen treated animals (6 males and 8 females) developed tumors, whereas only 5 control animals (3 males and 2 females) did. However, the numbers of exposed and control animals were not reported, nor was the distribution of tumor types, so that the claim of a significant increase of treatment-related tumor incidence cannot be validated. IARC (1980) considers that there was no statistically significant increase in this experiment.

The failure of inhalational cancer bioassays to confirm the results of human experience is puzzling and may have no satisfactory explanation. Since respiratory neoplasms have been produced by intratracheal instillation and intrabronchial implantation of Cr(VI)-containing substances, a partial explanation for the negative results in the inhalational studies is that insufficient doses of the carcinogenic materials were deposited and retained in the lung. To some extent this may have been due to deficiencies in experimental methodology. The animal experiments almost all used whole-body inhalation chambers, in which exposures to particulates can be difficult to control. For example, there can be significant losses of particulate materials to the chamber surface due to electrostatic precipitation (Phalen, 1976).

Unlike head- or nose-only exposures, in inhalation chambers animals may be able to avoid exposure by burying their noses in their own or others' fur, which may also be capable of precipitating particulates. An additional impediment to the deposition of particulates in the lungs is the filtration efficiency of rodent nasal turbinates (although for particles $< 2\mu\text{m}$ in diameter--as was the case in the studies cited here--this may not be an important consideration).

It should be noted that similar difficulties in confirming positive results in epidemiologic studies have been encountered with other metal particulates, such as arsenic and cadmium. Thus, it may be that, for metals and other particulates, bioassays involving rodents may not be a good experimental model for inhalational carcinogenesis. For example, pulmonary clearance in rats and mice appears to be more efficient than in humans, so that the latter tend to accumulate a greater burden of particulate materials, as was reported in the study of Baetjer et al. (1959). This phenomenon may be a reflection of significant interspecies anatomic differences: nonciliated respiratory bronchioles are not found in the lungs of rats and mice whereas they are in humans (Tyler, 1983; Phalen and Oldham, 1983).

Recently a cadmium bioassay produced positive results after 24 months of exposure (Takenaka et al., 1983). Tumor development in animals, as in humans, was characterized by a very long latency, so that a significant increase probably would not have been detected in a standard bioassay protocol, which involves termination at 24 months. Such a latency period may also apply to chromium inhalational assays. It is

interesting that in the only chromium inhalational study purporting to find an increase in pulmonary tumors, the mice were exposed until their demise, unlike the other experiments, which involved terminal sacrifices (See Appendix V).

Other considerations that may explain the discrepancy between the results of animal inhalation studies and occupational epidemiologic investigations include the following:

1. Humans may be more susceptible to pulmonary carcinogenesis than rodents.
 2. The occupational cohorts were exposed to other carcinogens and cocarcinogens (e.g., such as those in cigarette smoke), whereas the animals were not.
- (2) No chromium compound has been unequivocally shown to cause a significantly increased number of neoplasms in experimental animals (rats, mice, guinea pigs, and rabbits) after exposure by ingestion. Only three studies of orally administered chromium (III) compounds (as chromic acetate or chromic oxide) were noted by IARC (1980) and EPA (1984), and each of these involved dose levels that produced no overt signs of toxicity, indicating that higher exposure levels could have been tolerated. No ingestion studies using Cr(VI) were reported. In view of the poor gastrointestinal absorption of Cr(III), its nearly nonexistent genotoxicity in systems where cellular membranes are

intact, and the suboptimal dosing used in these bioassays, the negative results are not surprising.

- (3) When administered by methods other than ingestion or inhalation, several Cr(VI) compounds have been shown to be carcinogenic. Since these all have involved injection or implantation of chromium-containing compounds, the lack of correspondence to typical routes of human exposure render these experiments of dubious utility for risk assessment. These bioassays, which are by far the most numerous, provide the basis for the conclusion by IARC (1980, 1982) that there is sufficient evidence for carcinogenicity of calcium chromate, which produces tumors in rats after administration by a variety of routes. Following subcutaneous, intrapleural and/or intramuscular administration in rats, the following substances produced application-site sarcomas: lead chromate (VI), lead chromate oxide (VI), cobalt-chromium alloy, sintered calcium chromate (VI), sintered chromium (VI) trioxide, strontium chromate (VI) and zinc chromate (VI) (IARC, 1980). Lead chromate also reportedly caused systemic (renal) carcinomas after intramuscular application. IARC (1980) concluded that there were inadequate data to evaluate the carcinogenicity of numerous Cr(III) and Cr(VI) compounds, including:

Cr(III)Cr(VI)Cr(0)

chromic acetate	barium chromate	chromium metal
chromic oxide	chromium trioxide	
chromite ore	mixed chromate dust	
chromium carbonyl	potassium chromate	
chromium sulfate	potassium dichromate	
roasted chromite ore	sodium chromate	
	sodium dichromate	
	zinc potassium chromate	
	zinc yellow	

It has been proposed that water solubility of chromates influences their carcinogenicity (NIOSH, 1975). Hueper and Payne (1959) had proposed that chromium carcinogenicity is a function of a compound's biological availability, which would depend on solubility, total dose, and "the proper rate of release of chromium ion from the introduced chromium compound." Compounds of greater solubility would be expected to be rapidly transported away from application or deposition sites and inactivated in erythrocytes (NIOSH, 1975). With respect to pulmonary carcinogenesis, however, solubility may be less important than other factors, such as the size distribution of chromium aerosols, total dose received, and host factors affecting deposition and clearance.

In view of the observation that both soluble and insoluble Cr(VI) compounds are genotoxic and may be implicated in carcinogenesis, it has more recently been suggested that the issue of water solubility has probably been overemphasized (Bidstrup, 1983). In

any case, resolution of the solubility/carcinogenesis issue, although relevant, is not necessary for the purposes of risk assessment.

7.2 Epidemiologic Studies

7.2.1 Introduction

Several reviewers have recently summarized the epidemiologic studies pertaining to chromium (EPA, 1984; IARC, 1980; Hayes, 1982). The purpose of this section is to evaluate key studies with the goal of determining the general health effects associated with chromium exposure and, in particular, whether chromium or certain classes or compounds of chromium are carcinogenic in humans. A summary of some salient features of these studies appears in Table 7-1.

Virtually all epidemiologic studies regarding health effects of chromium were conducted in occupational settings. The studies arose following case reports of lung cancer in workers in the chromium industry dating back to the late 1800s. Based on these reports, in 1936 German authorities recognized lung cancer associated with chromate dust as a possible occupational disease.

7.2.2 Chromate Producing Industry

The most studied sector of the chromium industry has been the chromate producers. Here, chromite ore (Cr(III)) is the raw material and sodium chromate (Cr(VI)) and calcium chromate (Cr(VI)) are the principal intermediate and end products, respectively, of the chromate extraction

Table 7-1. Salient features of Selected Epidemiologic Studies on Chromium

Author	Industry	Design	No. Studied	Exposure	Results	Comments
Mittle & Gregorius, 1968	chromate producing	mortality survey of U.S. plants	about 1000 from 6 plants	mixture; not quantified	all cancer RR ² = 5.3; SS ³ resp ca, RR = 20.7; SS GI ca, RR = 1.0; SS	no cohort defined
Bestler, 1970	chromate producing	case-control in two hospitals (a,b)	290 cases	mixture; not quantified	a) Lung ca, OR = 32; SS b) Lung ca, OR = 23; SS	
Maclean & Cooper, 1971	chromate producing	historical prospective	not stated	mixture .05 - 1.5 mg/m ³ (total Cr)	resp ca, PMR = 10.2% vs 1.2% in control group, SS	pulmonary fibrosis seen in necropsied cases
Maclean, 1975	chromate producing	historical prospective	332	mixture .05 - 1.5 mg/m ³ (total Cr)	demonstrated a dose-response relationship	
Edelstein & Case, 1976	chromate producing	survey	725	hexchromates (Cr(VI)); not quantified	lung ca, RR = 3.6, SS	no cohort defined
Taylor, 1976	chromate producing	historical prospective	1212	mixture; not quantified	resp ca, RR = 0.5, SS	dose response with cumulative years of experience
Hayes et al., 1979	chromate producing	historical prospective	2101	mixture; not quantified	a) lung ca, RR = 2; SS b) lung ca, RR = 2.9; SS (mostly Cr(VI)) c) lung ca, RR = 1.3 (mostly Cr(III))	dose response with duration of exposure

(continued)

Table 7-1 (continued)

AUTHOR	INDUSTRY	DESIGN	NO. STUDIED	EXPOSURE	RESULTS	COMMENTS
Langard & Vigander 1985	chromium pigment	historical prospective	133	Lead & zinc chromates .01 - 1.35 mg/m ³	Lung ca, RR = 4.4, SS	exposure data from 1975-80
Davies 1978, 79, 84	chromium plating	historical prospective	1152 in 3 plants	Lead & zinc chromates	Plant A:Lung ca, RR = 2.2:SS Plant B:Lung ca, RR = 4.4:SS Plant C:Lung ca, RR = 3.2	plant C used lead chromate only
Royle 1975	chrome plating	survey	1238	mostly Cr(VI)	malignant neoplasms;RR=1.9,SS resp ca, RR = 1.8	no cohort defined
Franchini et al. 1983	chrome plating	historical prospective	178	mostly Cr(VI)	Lung ca, RR = 5.0;SS in thick plating department	
Pokrovskaya & Shalygina 1973	ferro-chromium	survey	not stated	mixture; .02-.07 mg/m ³ (estimated Cr(VI))	all ca, RR = 3.3; SS Lung ca, RR = 6.7; SS esophageal ca, RR = 2.0; SS	no cohort defined; few study details given
Axelsson et al. 1980	ferro-chromium	historical prospective	1876	mostly Cr(III),Cr ₂ O ₃ (0) Cr(III)0-2.5mg/m ³ Cr(VI)0-.25mg/m ³	resp ca, RR = 4, SS for subcohort of maintenance workers; 2/4 cases were mesotheliomas	
Langard et al. 1980	ferro-chromium	historical prospective	976	mixture; ³ < 1 mg/m ³ (total chromium)	Lung ca, RR = 2.3 (general population control) Lung ca, RR = 0.5, SS	exposure data from 1975

¹ Mixture implies that both soluble and insoluble and trivalent and hexavalent substances were present.

² RR - Estimated relative risk.

³ SS - statistically significant, $p < 0.01$.

process. Thus, chromium exposure is likely to encompass a mixture of oxidation states, solubilities and specific compounds.

Machle and Gregorius (1948) reported on the mortality of workers in 6 of 7 chromate producing plants in the U.S. Worker cohorts were not defined; instead, life insurance records were reviewed for cause of death for all previous years in which each plant had adequate employment and mortality records. This time period ranged from 4 to 17 years for the different plants. Comparing cancer mortality rates to those of oil refinery workers, statistically significant ($p < 0.05$) increases in the crude rates of cancer at all sites (4.17/1000 chromate vs 0.78/1000 refinery), cancer of the respiratory system (2.9/1000 vs 0.14/1000), and cancer of the digestive tract (0.09/1000 vs 0.05/1000) were found. Though the data were not age-adjusted, the differences persisted when the data were stratified into two groups: age 50 and under and age greater than 50. This suggests that the higher rates observed among chromate workers is not likely to stem from a disproportionate number of older workers in this group.

Limited exposure data were available in this study. The overall range of airborne "chromates" reported by 4 plants was 0.003 -21.0 mg/m^3 , but there was considerable variation by plant and by location within each plant. The authors stated that the incompleteness of these data render them inadequate for further epidemiologic application.

Baetjer (1950) conducted a case-control study of 290 lung cancer patients in two Baltimore hospitals to determine if a relationship existed with employment in the local chromate plant. (The plant in question and the time period covered are part of the Machle and Gregorius study above.)

Controls were age-matched males randomly selected from each hospital's records. Statistically significant ($p < 0.05$) crude odds ratios were found for having lung cancer and exposure to chromium at each hospital. The odds ratios were 32 and 23, respectively.

Mancuso and Hueper (1951) studied the lung cancer-chromium association in employees of the Painesville, Ohio chromate plant. A cohort of workers was defined as consisting of employees who had worked for at least one year during the period 1931-1949. The male population of the county in which the plant was located served as the comparison group. Denominator data were not reported; rather, the results were presented as proportionate mortality ratios (PMR). The PMR for cancer of the respiratory system was 18.2% (6/33) among chromate workers and 1.2% among the general male population. This difference is significant at $p < 0.01$. The authors also stated that about 96% of the workers were exposed predominantly to insoluble chromium (chromite ore Cr(III)), suggesting that insoluble chromium, because of its relatively long pulmonary retention time (see Section 3.4), may have played a causal role in carcinogenesis. However, since all work environments were contaminated with both trivalent and hexavalent chromium, (i.e., both insoluble and soluble chromium) the data are too limited to ascribe the carcinogenic form.

Mancuso (1975) followed up a segment of this population (new employees for the years 1931-37). A major concern of the author was to determine whether an association existed between lung cancer deaths and exposure to chromium of different oxidation states and solubilities. Data from a 1949 industrial hygiene study of the plant were used to derive weighted average

exposures to insoluble, soluble and total chromium which were then applied to the worker cohort. Water-soluble chromium was considered to be hexavalent while insoluble chromium was assumed to be trivalent. The author noted that since the plant's inception in 1931, production had dramatically increased, possibly increasing chromium dust concentrations. This was likely to have continued until 1949, when the company instituted control measures, which markedly reduced the exposure. Thus, the 1949 exposure data probably represent an average exposure for the cohort; that is, the data underestimate exposure from 1931 to 1949 and overestimate it subsequently.

Of the 332 cohort employees, 173 (52%) had died by 1974, including 41 from lung cancer. No comparison to a reference group was made. The age-adjusted data showed an increase in lung cancer rates with increasing exposure to chromium, regardless of solubility (and hence oxidation state). No statistical evaluation of those trends was reported, but the staff of DHS tested the data and found a statistically significant positive trend ($p < 0.001$). Mancuso concluded that the carcinogenic potential of chromium extends to all forms. However, given that employees were exposed to both trivalent and hexavalent compounds and that increases in one form were positively correlated with the other, this conclusion appears unwarranted.

The mortality experience of 723 workers in the bichromate-producing industry in Great Britain was studied by Bidstrup and Case (1956). Lung cancer mortality was significantly higher among workers than would be expected using national death rates: 12 lung cancers were observed versus 3.3 expected ($p = 0.005$). Mortality from other neoplasms or other causes

of death was not elevated. The authors discuss, but do not adjust for, place of residence, social class and smoking habits, noting that differences between the worker cohort and the general population for the factors were minimal and therefore could not account for the 3.6 fold increase in lung cancer mortality that was observed.

Taylor (1966) identified a cohort of 1212 workers from 3 U.S. chromate plants who had worked for at least 3 months during 1937-40. The cohort was followed for 24 years using Social Security records; mortality data were obtained from death certificates. Seventy-one deaths due to cancer of the respiratory system were observed while 8.3 were expected using the U.S. male population for comparison (estimated relative risk = 8.51, $p < 0.001$). A dose-response effect was seen using specific cumulative years of chromate experience as an indicator of "dose" (no exposure data were reported). This effect was also observed for cardiovascular deaths and noncancer respiratory disease.

Hayes et al. (1979) reported on a cohort of 2101 workers who were initially employed between 1945 and 1974 and who worked at least 90 days in a Baltimore chromate plant. The plant was partially rebuilt in 1950-51 and in 1960 in an effort to reduce chromium exposures. In mid-1977 the vital status of 88% of the cohort had been ascertained. Compared to the male population of Baltimore, workers initially employed between 1945 and 1959 experienced a two-fold increase in lung cancer mortality ($p < 0.05$). Employees beginning work after 1959 were deemed to have had insufficient follow-up in view of the presumed long latency period and were not included

in the analysis. Chromium concentrations were not reported, but a dose-response effect was found between duration of employment and mortality (adjusted for age). Also, a history of employment in the departments producing chromic acid and other hexavalent compounds was associated with increased lung cancer (estimated relative risk = 2.9, $p < 0.05$) in contrast to workers with a history of work in the chromite ore Cr(III) processing departments (estimated relative risk = 1.3, $p > 0.05$).

Other groups in the chromium industry have been less extensively studied than chromate producers. However, epidemiologic investigations have been reported for the chromium pigment and plating industries as well as the ferrochromium industry.

7.2.3 Chromium Pigment Industry

Exposures in the chromium pigment industry are mainly to hexavalent compounds, including sodium chromate (soluble), lead chromate (insoluble), and zinc chromate (insoluble).

Langard and Vigander (1983) reported the results of a study of a cohort of 133 employees who began work in Norwegian chromate pigment plants in 1948; the followup period extended through 1980. Workers commencing employment after 1972 were excluded. Early exposure was to both lead and zinc chromates, but production of lead chromate terminated after 1956. Historical exposure levels were not known, but routine measurements between 1975-80 showed chromium levels of 0.01 - 1.35 mg/m^3 . Thirteen cancers were observed in the cohort: 7 were lung cancer. Among 24 workers who had been

exposed more than 3 years, 6 lung cancers were observed versus 0.135 expected based on the Norwegian male population (estimated relative risk = 44, $p < 0.001$).

Davies (1978, 1979, 1984) reported on lung cancer mortality among workers making lead and zinc chromate pigments at 3 English factories. No specific cohorts were defined; instead all non-office male workers completing at least one year's service by June 30, 1975, from as early a date as records permitted were followed. Exposure levels were not reported. Rather, workers were classified into low, medium, and high categories depending on work activity and likely exposure to chromates. Also, the exposure in one of the plants (plant C) was exclusively to lead chromate. For workers on the job for at least one year and for whom plant records were available, no significant increases in lung cancer among the low exposure group were noted in any plant relative to the general male population of England and Wales. However, since there were less than 100 men in this exposure class in any plant, these results should be interpreted cautiously. Also, since cohorts were not defined there may well have been large numbers of recently employed workers for whom the followup period was too short (i.e. - all those starting work after 1960). Statistically elevated increases in lung cancer mortality were found for workers with high or medium exposures in only two plants (plant A estimated relative risk = 21/9.5, $p < 0.001$; plant B estimated relative risk = 11/2.5; $p < 0.001$). Davies interpreted the absence of lung cancer excesses in the 167 workers in Plant C as an indication that lead chromate is not carcinogenic in man. The qualitative nature of the exposure data and the small worker cohort in plant C militate against such a definitive conclusion.

7.2.4 Chrome Plating Industry

Exposures in the chrome plating industry are predominantly to hexavalent chromium compounds, including chromium trioxide, sodium and potassium dichromate, and chromic acid. These compounds are soluble in water.

Royle (1975) studied 1238 past and current plater workers in 54 plants in the United Kingdom. A minimum of 3 months of consecutive employment in a plant was required for entry into the cohort. A reference population consisting of manual workers from non-plating departments of the larger plants and from other industrial plants was the source of individually matched controls for the platers. Matching was based on age, sex, and when last known to be alive. The rate of death due to malignant neoplasms among platers was 3.2/100 (39/1238) versus 1.6/100 (21/1284) in the control group ($p < 0.05$). Mortality rates for cancers of the lung and pleura, gastrointestinal tract, and "other sites" were elevated among platers, but did not reach statistical significance. Increases were also reported for death due to non-neoplastic respiratory disease. No exposure concentration data were reported.

Franchini et al. (1983) reported on the mortality of a cohort of 178 chromeplating workers from 9 plants in Parma, Italy. Workers employed for at least one year between 1951 and 1981 were included. Though airborne chromium concentrations were reported, it is not clear when the measurements were made; there is, however, some indication that the measurements were taken in recent years when the hygienic conditions in the plants had substantially improved. The air levels in the plants engaged in the use of

"thick" plating were 7 mg/m^3 (range 1 - 50) near the plating baths and 3 mg/m^3 (range 0 - 12) in the middle of the room. The authors refer to another industrial hygiene survey of these plants (reporting levels about ten times higher) which indicated air levels would be about one-tenth as great where thinner plating was used.

Stratifying on thick/thin plating and restricting the cohort to those who had a minimum of 10 years of follow-up, there was a significant increase in lung cancer mortality among the thick plating workers: 3 cases were observed versus 0.6 expected, based on the general Italian male population (adjusting for age), ($p < 0.05$). Since only 62 men were in the thin plating subcohort, the lack of an observed response in these workers may be related in part to the small sample size.

7.2.5 Ferrochromium Industry

A limited number of epidemiologic studies have also been published concerning the cancer mortality of workers in the ferrochromium industry. This industry uses both trivalent and hexavalent chromium in the production of steel alloys.

Pokrovskaya and Shabynina (1973, as cited in EPA, 1984) compared the cancer mortality of a group of ferroalloy workers in the Soviet Union to the local population for the time period 1955-69. No specific cohort was defined nor were the numbers of cancer cases, individuals in the comparison groups, and person-years at risk given. Workers in the plant were reported to be exposed to low-solubility chromium compounds with concentrations of

hexavalent chromium exceeding the allowable level of 0.01 mg/m^3 by 2 to 7 times. In addition, some workers were exposed to smelting process fumes for the chromium ore, which included benzo(a)pyrene.

Age-specific cancer mortality ratios (MR) were reported. The ratios for cancers in males aged 50-59 were significantly increased ($p < 0.001$) for all sites (MR = 3.3), lung (MR = 6.67), and esophagus (MR = 2.0). Esophageal cancer mortality was also elevated among 60-69 year old males (MR = 11.3, $p < 0.001$). However, the lack of methodological detail reported as well as the absence of a defined worker cohort leave the results of this study open to question.

Axelsson et al. (1980) investigated the mortality and incidence of tumors among 1932 ferrochromium workers in a Swedish plant. A cohort of 1836 men was defined as all male workers who had worked at the plant for at least one year during 1930-75 and who were alive on January 1, 1951. Expected rates were based on the county in which the plant was located. Exposures in their plant were predominantly to trivalent and metallic chromium, although hexavalent chromium was present in some stages of production. According to the authors, "recent" measurements and discussions with various plant personnel allowed estimation of exposure levels; the range for Cr(0) and Cr(III) was $0 - 2.5 \text{ mg/m}^3$ while that for Cr(VI) was $0 - 0.25 \text{ mg/m}^3$. Of specific work categories, arc-furnace and maintenance employees were most heavily exposed.

The total number of deaths from tumors was less than expected (69 versus 76.7) for the entire cohort but a non-significantly elevated number was

found among maintenance workers (18 vs 13.6). The elevation in maintenance workers was due in part to an increase in mortality from respiratory cancers (3 vs 1.3, $p > 0.05$). This latter finding was paralleled in the incidence data, where 4 respiratory cancers among maintenance workers were observed against one expected ($p = 0.038$). Two of these cases were pleural mesotheliomas and could be related to exposure to asbestos, which was used in the plant. Exposure data for asbestos was not presented.

Langard et al. (1980) studied the incidence of cancer in male workers at a Norwegian ferroalloy plant (chromium and silicon alloys were produced). The cohort studied included all men who had worked at least one year in the period 1928-77, but the analysis focused on 976 workers who started before January 1, 1960. Both overall cancer mortality and incidence were lower than would have been expected based on national data. Lung cancer incidence was elevated; however, 7 cases were found among ferrochromium workers while 3.1 were expected ($p > 0.05$). The authors note that the expected rate may be inflated because the age-corrected lung cancer rate in the population of the county in which the plant is located is only 58% of the incidence in the whole country. Applying 58% to the expected rate results in a significant increase in the incidence ratio ($p < 0.01$). Furthermore, using non-ferrochromium workers as an internal referent population resulted in an 8.5-fold increase in lung cancer incidence ($p = 0.026$).

Exposure data were based on a 1975 industrial hygiene survey of the plant. The total chromium content of dust was "with few exceptions" below 1 mg/m^3 . This level probably underestimates past exposures. Water-soluble chromium

(assumed to be hexavalent) ranged from 11-33% of the total. The presence of high levels of Cr(VI) in previous years was also confirmed by the finding of 2 workers with nasal septum perforations. Exposure to asbestos and low levels of polycyclic aromatic hydrocarbons also occurred, but concentrations were not reported. However, since the 243 ferrosilicon workers studied were similarly exposed yet experienced no lung cancers, the effect of these exposures may be minimal.

7.2.6 Other Epidemiologic Studies

Epidemiologic studies have also been conducted in users of chromium products, particularly welders. Certain welding fumes contain chromium, manganese, nickel, and trace amounts of arsenic and lead. Stern (1983) reviewed the literature and found 22 studies of cancer incidence and welding. Five studies showed statistically significant ($p < 0.05$) increases in the relative risk (range of relative risks: 1.3 - 5). The results in all 22 studies were consistent with a relative risk of 1.3, based on a 95% confidence interval. Because of the mixed exposure to several metals, each of which has demonstrated mutagenicity or is suspected of being a human carcinogen, these studies are not as useful for identifying chromium as a carcinogen and will not be further discussed.

Only one study was found that looked at the carcinogenic potential of chromium in a nonoccupational setting. Axelsson and Rylander (1980) studied lung cancer mortality in communities exposed to chromium emissions from the ferroalloy industry. No statistically significant difference was found for lung cancer mortality rates between communities affected by the

emissions and rural communities having no industrial emissions. Though chromium exposure levels were measured, they were not speciated in terms of chromium oxidation state or specific compounds. Since the ferrochromium industry predominantly uses trivalent chromium, the absence of an effect in this study may be due to exposure to the form of chromium that is not established as a carcinogen. Moreover, any Cr(VI) formed during the processing of Cr(III) could have been subsequently reduced to the trivalent form in the atmosphere (NAS, 1974), which could also account for the lack of increase in lung cancer mortality in the communities. Another possibility to account for the lack of increased lung cancer could be that the chromium was on particles whose size would preclude them from being respired or deposited in the lung.

7.2.7 Summary of Epidemiologic Studies

The health outcomes studied in the published chromium epidemiologic studies are narrow in scope. Based on case reports from the chromium industry, investigators quickly focused on testing the lung cancer hypothesis. Total mortality and mortality from all cancers were also routinely reported and, occasionally, data on cancer for non-respiratory sites were presented. Few authors mentioned any acute effects or other chronic conditions, although nasal perforations were reported as an indication of high hexavalent exposure in several studies. Therefore, the epidemiologic studies are not adequate to evaluate non-carcinogenic effects.

Several different study designs and worker groups were used to study the chromium-lung cancer relationships. The finding of statistically significant associations between worker exposure to chromium and lung cancer on an international basis and from a variety of study designs provides strong evidence to identify chromium as a human carcinogen. However, the studies have not been able to answer all the questions concerning chromium's carcinogenicity for two reasons: control of potential confounding variables and quality of the exposure data.

The major potential confounders are cigarette smoking and exposure to other respiratory carcinogens, such as asbestos and benzo(a)pyrene. Because personal histories typically were not obtained, most authors made the assumption that workers' smoking habits were identical to those of the general population (i.e. the usual comparison group). To the extent this is not true, the observed number of lung cancer cases can be over- or under-estimated. For example, if workers smoked more than their comparison group counterparts, it would not be clear how much of the excess lung cancer observed was due to cigarettes and how much to chromium. Some authors did qualitatively consider the smoking issue and concluded that it did not exert a confounding effect or that smoking could not by itself have accounted for the excesses of the magnitude seen. Staff members of DHS agree with this conclusion: it is not likely that the estimated relative risks, which exceeded 20 in many cases, could be explained solely on the basis of smoking.

Similarly, there cannot be a definitive resolution to the problem of exposure to multiple carcinogens. Since exposure data were generally lacking, quantification of exposure to other carcinogens is tenuous, at

best. The impact of these exposures could reduce or invalidate the chromium-lung cancer relationship. Invalidation does not seem likely, however. For example, asbestos exposure is likely to occur in smelter operations among selected workers (furnace operators and perhaps maintenance workers). The finding of a positive association between chromium exposure and lung cancer in other workers within the same plant and in other chromium industries suggests that chromium has at least an independent role in carcinogenesis.

The second major problem with the epidemiologic studies -- the poor chromium exposure data -- limits the specificity of the cancer-chromium relationship vis-a-vis oxidation state, solubility, and individual compounds. As was indicated earlier, levels of exposure were rarely known. Where exposure levels were given, they were incomplete relative to the period of worker exposure. Further, since employees were exposed to mixtures of chromium-containing materials, the available data are insufficient to differentiate effects based on oxidation state, solubility or specific compounds. The observation by Baetjer (1950) that respiratory cancer was not associated with the mining of chromite ore (trivalent, insoluble) and the findings of lower cancer risks in those industries mainly using trivalent chromium (e.g. ferrochromium) and those with exposure to trivalent and insoluble hexavalent chromium (e.g. Davies, 1984 chrome pigments) suggest that trivalent chromium may not be as carcinogenic as the soluble hexavalent form.

In summary, the epidemiologic data identify chromium as a respiratory system carcinogen, but are insufficient to refine the carcinogenic potential

in terms of individual compounds, the trivalent or hexavalent oxidation state, or differing solubilities. Furthermore, while the findings of some studies suggest chromium is associated with nonrespiratory cancers, the evidence is insufficient to consider this to be of a causal nature.

8 QUANTITATIVE RISK ASSESSMENT

8.1 Introduction

EPA has recently published a health assessment for chromium (EPA, 1984). The report was independently peer-reviewed in public sessions of the Environmental Health Committee of EPA's Science Advisory Board. The quantitative risk assessment of this document has been adopted for this report based on the rationale given below. The assessment focuses on hexavalent chromium, since Cr(VI) compounds have demonstrated both mutagenic and carcinogenic effects while evidence implicating Cr(III) as either a mutagen or carcinogen is weak. The staff of DHS believes this is a reasonable and appropriate interpretation of the health effects data on chromium.

To be protective of public health, a risk assessment should be based on the adverse health effect which arises from the lowest exposure to a substance. Both carcinogenic and non-carcinogenic effects must be considered.

8.2 Noncarcinogenic Risks

Noncarcinogenic effects of hexavalent chromium include skin ulceration and dermatitis, nasal passage irritation and septum perforation, and kidney and liver damage, while Cr(III) has been implicated in causing pulmonary fibrosis (see Section 4.2.2; ACGIH, 1984). These effects have been reported from exposures in occupational settings. As a result, occupational standards have been set at levels presumed not to cause these effects given repeated exposures. The American Conference of Governmental

and Industrial Hygienists (ACGIH) has established the occupational threshold limit value (TLV) for Cr(VI) at 0.05 mg/m^3 while the permissible exposure level (PEL) recommended by NIOSH is 0.025 mg/m^3 (water-soluble, noncarcinogenic Cr(VI)) and 0.001 mg/m^3 (water-insoluble, carcinogenic Cr(VI)). The TLV for Cr(III) is 0.5 mg/m^3 . These occupational standards are not necessarily directly applicable to the general population because of the potential greater susceptibility to disease among the general population. In fact, the ACGIH has cautioned against the general application of TLVs stating that:

These limits are intended for use in the practice of industrial hygiene and should be interpreted and applied only by a person trained in this discipline. They are not intended for use, or for modification for use, (1) as a relative index of hazard or toxicity, (2) in the evaluation or control of community air pollution nuisances, (3) in estimating the toxic potential of continuous, uninterrupted exposures or other extended work periods, (4) as proof or disproof of an existing disease or physical condition... (ACGIH, 1984).

However, temporarily holding these caveats in abeyance, the lowest PEL of 0.025 mg/m^3 can be modified to account for a 24 hour per day and 365 day per year exposure yielding a concentration of about 0.01 mg/m^3 which is "theoretically" protective against nasal irritation, septal perforation, dermatitis, and liver and kidney dysfunction. Further, to be more cautious, an additional conservative safety factor can be applied, e.g., 100, yielding a "population threshold" of 100 ng/m^3 . This level is 5 to 6 times greater than ambient levels. Thus, using this crude and extremely

conservative approach, noncarcinogenic respiratory, renal, hepatic or cutaneous effects would not be expected to appear at ambient levels.

8.3 Carcinogenic Risks

8.3.1 Sources of Data

Typically, bioassays and/or epidemiologic studies are used for quantitative risk assessment of carcinogens. Both sources of data are available for chromium. In general, however, the use of epidemiologic data is preferable since effects in humans are being evaluated, obviating the need for interspecies extrapolation. Moreover, in the case of chromium, the route of exposure in the epidemiologic studies, inhalation, is the route of primary concern to the ARB.

Animal carcinogenicity studies have not been successful in demonstrating a significant increase in tumor incidence following inhalation or ingestion (see Appendix I). This finding holds for both trivalent and hexavalent compounds. However, some studies have shown significant tumor increases at site of contact, particularly for some hexavalent compounds, following subcutaneous injection, intratracheal instillation, or intrabronchial, intrapleural, intramuscular or intratracheal implantation. While supporting the identification of chromium as a potential carcinogen, these latter studies are not used for quantitative risk assessment for reasons described below.

Determination of comparable inhalational dose levels from the above-noted, atypical routes of exposure, that yielded carcinogenic excesses is problematic. In the case of implantation studies, since tumors appear to develop only at the site of contact, the dosage producing the effect (as opposed to the amount of material implanted) is not readily discernible: high local concentrations are likely to appear at the site of exposure and without good absorption data, it is difficult to quantify dosage. For the instillation studies, difficulty arises with respect to relating the delivered dose, to the ambient levels that would have to exist to produce this dose through inhalation, given the anatomy and physiology of the animals' upper respiratory tract. The differential cancer response by route of administration indicates that the dose distribution is affected by the route of exposure. It also points to the need for physiochemical and pharmacokinetic information relating the distribution of chromium in lung tissues after inhalation or intratracheal administration. Such information is not available. Furthermore, the physiologic mechanism of dose distribution by intratracheal administration may depend in a non-linear fashion on the dose levels used in the experiment (EPA, 1984). The study by Steinhoff et al. (1983), in which a weekly dose of sodium dichromate induced a carcinogenic response in rats but failed to do so when one-fifth this dose was given five times per week, supports this contention. Thus, the staff of DHS believes that it is not appropriate to attempt to derive the dose-response curve for an inhalation exposure where the dose parameter is as poorly defined as in the case of the chromium animal studies, particularly when adequate epidemiologic data are available for quantifying the excess risk.

8.3.2 Selection of Chromium Compound(s) For Risk Assessment

As the toxicological data suggest, chromium's health effects are related to the oxidation state, solubility, and the metal elements in the test compounds (e.g. lead, zinc, calcium). In general, trivalent chromium compounds do not show evidence of mutagenicity in short-term genotoxicity tests. Experiments in several animal species further suggest that Cr(III) compounds (e.g. chromic acetate, chromic oxide, chromite ore) are not likely to be carcinogenic. IARC (1980) concluded, however, that these data were inadequate to either confirm or refute the carcinogenicity of trivalent chromium. The staff of DHS agrees with this conclusion.

In contrast, several hexavalent chromium compounds have been shown to cause genotoxic effects in prokaryotic and eukaryotic systems, both in vitro and in vivo. Moreover, studies in rats have demonstrated the carcinogenicity of several Cr(VI) compounds: lead chromate (insoluble), zinc chromate (insoluble), strontium chromate (insoluble), and sintered chromium trioxide (insoluble).

Since these data are not in conflict with the epidemiologic findings, the staff of DHS believes the risk assessment should be based on hexavalent chromium compounds. However, because the DHS assessment will use epidemiologic data to estimate risk, and because these data do not permit differentiation of risk with respect to solubility or compound specificity, the assessment will pertain to the general class of Cr(VI) compounds. The staff of DHS recognizes that, in assuming all hexavalent chromium compounds are equally carcinogenic, the estimated risk per unit dose (potency) may be

underestimated due to the inclusion of potential noncarcinogenic compounds in the cancer potency calculation. The staff also recognizes that the application of this potency factor to a mixed Cr(VI) exposure may overestimate the predicted cancer risk (by assuming exposure to a higher dose of carcinogen than is actually present).

8.3.3 Threshold

A threshold in classical toxicology is a level at or below which a toxic response does not occur. The concept of a threshold is accepted for health effects which are not self-propagating. In theory the threshold represents an absolute level; however, in practice the threshold level is defined where no effect can be detected. The practical threshold is thus a function of technology, i.e., the ability to measure small effects, and of sample size, i.e., the ability to observe a rare event in a given exposed population. Practical thresholds are typically determined by applying a safety factor to the lowest no observed effect level (NOEL) or no observed adverse effect level (NOAEL) among all health effects of concern, as determined from experimental data or observational reports. The safety factor provides an additional degree of protection to account for more susceptible individuals in the genetically heterogenous general population.

Whether carcinogenesis (a self-replicating process that may continue after the exposure has ended) is characterized by a threshold is controversial. Empirically, a threshold level cannot be proven using either animal or human studies (e.g. if there were no effect observed in 25,000 animals, one could not be absolutely assured of a similar outcome in 100,000 animals or

1 million animals). Therefore, the issue of a carcinogenic threshold can only be resolved based on knowledge of the mechanism by which a substance causes cancer. Science has yet to validate proposed mechanisms. It is believed, however, that cancer is a multistage process that can be initiated with an attack by a carcinogen on DNA. The result can ultimately be expressed as a tumor. Theoretically, despite the body's defense mechanisms, the initiating event can be caused by a single molecule of the carcinogen, making the threshold dose indistinguishable, for practical purposes, from zero. This is in contrast to other toxic effects that are believed to occur only after the reserve capacity of the biologic target to withstand and rapidly repair damage has been exceeded.

Some compounds associated with carcinogenic responses do not appear to interact directly with DNA. Although it is possible that these compounds may have thresholds, their mechanisms of action are not well-understood. These compounds are currently treated for purposes of risk assessment as non-threshold substances.

The mechanism by which chromium induces cancer is not known. Levis and Bianchi (1982) have described a possible mechanism which requires exposure to hexavalent chromium because, in contrast to trivalent chromium, Cr(VI) can readily penetrate the cell membrane. However, as noted in Section 5.4, trivalent chromium, formed from either intracellular enzyme-mediated reduction or by reaction with reducing agents, may be the ultimate carcinogen. Thus, it is not known if the "initiating" event is the binding of Cr(III) to DNA, the reduction of Cr(VI) to Cr(III), or some other process. In any

case, the proposed mechanism predicated on the occurrence of a genotoxic event is consistent with the assumption of a nonthreshold process.

One critic of the EPA chromium health assessment document (Hathaway, 1985) interpreted the findings from some short-term genotoxicity studies, metabolic studies, and an animal study as demonstrating the existence of a threshold. The points cited to support this were: 1) Cr(III) appears to be neither mutagenic nor carcinogenic, 2) treatment of Cr(VI) with chemical or biological reducing agents renders Cr(VI) nonmutagenic, 3) treatment of Cr(III) with strong oxidizing agents results in a positive mutagenic response, 4) Cr(VI) is reduced to Cr(III) both extra- and intracellularly, and 5) an unpublished animal study in which a weekly dose of sodium chromate (Cr(VI)) for life yielded a carcinogenic response while one-fifth this dose administered five times per week resulted in no tumors (Steinhoff et al., 1983). In other words, the genotoxicity tests suggest that exogenous Cr(VI) is a carcinogen whereas Cr(III) is not, even if Cr(III) is the valence state with which DNA is ultimately complexed. The implication is that, to the extent that Cr(VI) is reduced extracellularly or even intracellularly prior to reaching the nucleus, the likelihood of a significant genotoxic effect is correspondingly diminished. If the reduction process occurs in a non-linear fashion, a practical threshold may exist. The differential carcinogenic response observed in the animal study also supports the concept of a practical threshold.

The staff of DHS agrees that some of these findings may be consistent with the existence of a metabolic threshold, but do not believe that they constitute compelling proof of a threshold or, in particular, of a threshold

that could be numerically applicable to humans. Other factors need to be considered. For example, possible pharmacokinetic differences between the aforementioned test systems and man limit the direct generalization of these findings to man. Also, even if the reduction of hexavalent chromium were a non-linear process, these metabolic defenses have not convincingly been demonstrated to be completely effective. Furthermore, the demonstration of a dose-rate response (Steinhoff et al., 1983) does not exclude the possibility that a carcinogenic response could have been seen in the low-dose group had a larger population been studied. Alternatively, the dose-rate response observed by Steinhoff could be interpreted as showing that the lifetime-averaged daily dose may not be appropriate for modelling the risk of chromium.

The evidence presented in support of a threshold is inconclusive and perhaps is more suggestive of a nonlinear low-dose response than an absolute threshold. Hathaway (1985) acknowledged these difficulties: "... this evidence does not permit quantification of the threshold or a description of the dose-response at low doses." The staff of DHS concurs with Hathaway on these latter points. Therefore, in accordance in Section 39650 of the Health and Safety Code which stipulates that DHS should be protective of public health, and given that the assumption of low-dose linearity is conservative (i.e., public health protective) the hexavalent chromium risk assessment should be based on a linear non-threshold model.

8.3.4 Extrapolation Models

Chromium exposures in the occupational epidemiologic studies tended to be in the milligram/m³ range. Ambient exposures to atmospheric chromium are in the nanogram/m³ range, or about one million times lower. Therefore, a model and a procedure are required to estimate effects resulting from exposure to ambient levels, when the only demonstrated response occurred at much higher occupational levels.

Empirically, most extrapolation models fit the observable dose-response data equally well, but can give vastly disparate results in the low-dose, nonverifiable range of concern. However, mutagenic studies with both ionizing radiation and a wide variety of chemicals support a linear, non-threshold, dose-response relationship, particularly for low-dose exposures (EPA, 1984). Epidemiologic studies of radiation-induced leukemia, breast and thyroid cancer, and liver cancer induced by aflatoxins in the diet also support this type of relationship (EPA, 1984). Therefore, the DHS risk assessment will adopt the EPA linear nonthreshold model to estimate low-dose chromium exposure carcinogenic risks, recognizing that such a model, although biologically plausible, has scientific limitations. A linear nonthreshold model is also likely to be health-protective because, for example, the linearity assumption may provide an upper limit to the dose-response.

Two procedures were used by EPA to calculate the potency. The first requires age-specific mortality data and calculates the carcinogenic potency taking competing risks of death into account. (A more detailed description

of this procedure is given in Appendix II.) The lifetime probability of lung cancer given continuous lifetime exposure to dose d is given by:

$$P(L,d) = \int_0^L h(s,d) \exp\left\{-\left[\int_0^s h(y,d)dy + A(s)\right]\right\} ds,$$

where L is the maximum human lifetime, $\exp [-A(s)]$ is the probability of surviving to age (s) without acquiring lung cancer, and $h(t,d)$ is the age-cause-specific mortality after adjusting for the background rate. Once the function $h(t,d)$ is specified, its parameters can be estimated from the epidemiologic data; $A(s)$ is estimated from vital statistics.

The second procedure is less complex and is applicable where age-specific information is not given. The method assumes that the risk among exposed individuals (R_e) is a function of the exposure dose (d) and background cancer rate (R_b):

$$R_e = R_b + Bd,$$

where B is the potency factor. The relative risk (i.e., the ratio of risk between exposed and non-exposed individuals) is therefore:

$$\frac{R_e}{R_b} = \frac{R_b + Bd}{R_b} = RR.$$

Solving for B yields:

$$B = [(RR - 1) \times R_0] / d.$$

Data from epidemiologic studies are used to estimate the relative risk while information concerning dose levels, if available, is typically presented in either an epidemiologic study or in an associated industrial hygiene survey. The background rate of cancer is typically obtained from vital statistics data.

The excess lifetime probability of lung cancer, given a continuous lifetime dose of hexavalent chromium, $P(L,d)$, is then given by:

$$P(L,d) = 1 - \exp(-Bd).$$

8.3.5 Selection of Studies for Quantitative Risk Assessment

Many epidemiologic studies have demonstrated the carcinogenicity of chromium, but few have been able to quantify the exposure, particularly in a manner representative of the experience of exposed individuals. Indeed, only one study (Bourne and Yee, 1950 with reference to Mancuso & Hueper, 1951) addressed the issue of particle size which could be a critical factor in establishing dosage. Since the inhalation exposure was most likely due to chromium dust or aerosol (chromic acid mist), actual worker exposures would probably be restricted to respirable particles that would be retained in the lungs (i.e., less than 5 μm (Task Group on Lung Dynamics, 1966)). Thus, it is possible that the exposure data available to calculate the potency are inflated which has the practical effect of underestimating the potency factor. Similarly, the use of respirators would decrease actual

exposures relative to ambient measurements, resulting in an underestimated potency factor. The extent of respirator usage was not, however, discussed in the epidemiologic studies used for the risk assessment.

Exposure data were reported for the Mancuso (1977), Langard et al.(1980), Axelsson et al. (1980), and Pokrovskaya et al. (1973) studies. The analytic group in the Langard study consisted of a cohort of men who began work some time between 1928 and 1960 but the exposure data were based on an industrial hygiene study conducted in 1975. The authors noted that several changes in production routines occurred during the plant's 50 years of operation and that no data were available on chromium exposure levels for previous years. Since the industrial hygiene of the plant undoubtedly improved during the period the cohort was exposed, the 1975 exposure data are likely to significantly underestimate the cohort's average exposure. These data will then yield a spuriously high potency factor. For this reason the staff of DHS do not believe the Langard et al. study should be used for the hexavalent chromium risk assessment.

The Axelsson et al. study also provides exposure data, but the ill-defined sources for these data and the ambiguity of the health findings in this study render it inappropriate for a quantitative risk assessment. The exposure data are based on "recent measurements and discussions with retired workers and foremen employed in the 1930s" (Axelsson et al., 1980). As such, the accuracy of these exposure data is questionable. More importantly, however, was the finding that the subcohort of maintenance workers, which was the only group found to have a statistically significant elevated respiratory cancer risk, was also exposed to asbestos. Two of the four

respiratory cancers observed were mesotheliomas, a neoplasm generally considered to be almost exclusively associated with prior exposure to asbestiform fibers. With one cancer expected and excluding the mesotheliomas, the observed relative risk (2/1) was not statistically significant. Given the synergistic relationship between cigarette smoking and asbestos exposure (i.e., a 50-fold increase in lung cancer risk among smokers who are also exposed to asbestos) and the absence of smoking data for cohort members, the staff of DHS does not believe that the one extra case of lung cancer observed in the Axelsson study can be reliably attributed to chromium. Therefore, this study will not be included in the DHS cancer risk assessment.

Of the remaining studies, the investigation by Mancuso is most appropriate for use in a quantitative risk assessment. The inadequate reporting of the Pokrovskaya et al. study in terms of cohort definition and details concerning the results renders the validity of study's findings somewhat questionable. Therefore, this risk assessment will focus on the Mancuso study. An estimate of chromium's potency based on the Pokrovskaya et al. study is also presented for comparative purposes only with the understanding that it may be less valid.

8.3.6 Risk Assessment Based on the Mancuso Study

Mancuso (1977, see Appendix III) reported on the cancer mortality of 332 men who began work in the chromate (Cr(VI)) producing industry between 1931

and 1937. Forty-one lung cancer deaths had occurred by 1974. Since age-specific deaths were reported, both the competing risk and crude extrapolation models are used to estimate potency.

The risk assessments are based on data in the table below, (Table 8-1) which includes the exposure, lung cancer mortality given this exposure, and expected lung cancer mortality without chromium exposure for the study cohort. The reported weighted average worker exposures were assumed to be equivalent to the continuous exposure d (in $\mu\text{g}/\text{m}^3$) calculated by:

$$d = \frac{D}{f L_e} \times \frac{8}{24} \times \frac{240}{365} \times 10^3 \mu\text{g}/\text{m}^3$$

where D is the reported exposure (in mg/m^3 -years), L_e is the midrange of the age category, f is the fraction of time exposed to chromium, and $8/24$ and $240/365$ are the fractions of a day and year, respectively, that a worker spent at the plant. It was assumed that $f = .65$ which implies that the cohort exposure to chromium began approximately at age 20.

Exposure data are in units of total chromium and are based on a 1949 industrial hygiene study of the plant (Bourne and Yee, 1950; see Appendix IV). Since exposures occurred between 1931 and 1972 (the life of the

Table 8-1. Combined Age Specific Lung Cancer Death Rates and Total Chromium Exposure (in $\mu\text{g}/\text{m}^3$) for the Mancuso Study (Mancuso, 1975).

Age at Death ^a	Average Lifetime Exposure ($\mu\text{g}/\text{m}^3$) ^b	Deaths ^c	Person years At Risk	Background Rate ^d	Estimated Relative Risk	Exposure Range ($\text{mg}/\text{m}^3 - \text{yr}$)
50	5.66	3	1345	6.05×10^{-4}	3.7	≤ 1.99
50	25.27	6	931	6.05×10^{-4}	10.7	2.0 - 5.99
50	46.83	6	299	6.05×10^{-4}	33.2	6.0 - 7.99
60	4.68	4	1063	1.44×10^{-3}	2.6	≤ 1.99
60	20.79	5	712	1.44×10^{-3}	4.9	2.0 - 5.99
60	39.08	5	211	1.44×10^{-3}	16.5	6.0 - 7.99
70	4.41	2	401	1.57×10^{-3}	3.2	≤ 1.99
70	21.29	4	345	1.57×10^{-3}	7.4	2.0 - 7.99

^aMidpoint of 10-year interval.

^bThese values are calculated by first using the formula given in the text (pg 86) and then taking the person year weighted average for the Mancuso-reported exposure subcategories (which have been combined in this table because of small numbers).

^cOnly 32 deaths are included in the risk assessment. The remaining six were among workers with exposures greater than $8 \text{ mg}/\text{m}^3\text{-year}$ but the exact level is unknown and is unlikely to be identical across all age groups.

^dBackground rate is calculated from 1964 U.S. Vital Statistics. The year 1964 is selected because it was estimated by EPA that a large proportion of lung cancer deaths occurred during that year.

plant), exposures based on 1949 data represent an average exposure. Bourne and Yee indicate that, in view of the improvements in equipment and processes after 1946, it is extremely likely that chromium levels pre-1949 were greater than post-1949 levels, which supports the notion that the 1949 data represent average levels.

A review of the EPA risk assessment (Hathaway, 1985) raised the point that the use of the 1949 exposure data would underestimate the true exposure by 20- to 40-fold. This is based on the cumulative effects of three factors. First, the exposure data represent normal plant operating conditions and not plant upset conditions. Using maintenance workers' exposures, which were five to ten times greater than production worker exposures, as a basis of upset exposure levels, Hathaway indicated that a 2- to 4-fold underestimate had been used by EPA. Since it is not known what percentage of the general workforce was exposed to upset conditions or for how long, Hathaway's estimate cannot be verified. However, other estimates for this effect are consistent with the data. For example, if non-maintenance workers were exposed to five times (based on DHS' calculated average of maximum maintenance worker exposures) their usual exposure for three hours per week (based on Bourne and Yee), their increase in exposure is only 30%: $[37(x) + 3(5x)]/40 = 1.3x$, where x is the exposure estimate based on normal operating conditions.

Second, Hathaway stated that Mancuso had assumed that worker exposure post-1949 was zero. This assumption was based on their finding that Mancuso had not obtained worker job assignments after 1949. Hathaway presumed that the

failure to account for post-1949 exposures might result in a two-fold underestimation of exposure. Third, Hathaway alleged that exposures prior to 1949 could have been five times greater than those measured in the 1949 industrial hygiene survey. Thus, these latter two points account for a ten-fold underestimation of exposure levels. Clearly, exact exposure levels cannot be calculated because the requisite data have not been collected. However, by invoking some crude assumptions, alternatives to Hathaway's estimate of exposure underestimation can be formulated. For example, Mancuso has indicated that although post-1949 work histories were not obtained, only about 25% of the worker cohort could have been exposed beyond 1949 (Mancuso, 1985 personal communication).

Therefore, assuming all cohort members were exposed to 5 times the 1949 levels for an average of 15 years (i.e., the median time between cohort formation and 1949) and additionally, 25% of the cohort was exposed to one-half the 1949 levels (estimated from Bourne et al., 1951) for the remaining 23 years that the plant was in operation, the overall weighted average exposure can be estimated as:

$$.75\left[\frac{(15\text{yrs})(5x)}{15\text{yrs}} + \frac{(0\text{yrs})(.5x)}{15\text{yrs}}\right] + .25\left[\frac{(15\text{yrs})(5x) + (23\text{yrs})(.5x)}{15+23\text{yrs}}\right] = 4.3x$$

where x is the 1949 exposure level.

The total underestimation of exposure may be only 5.6-fold (1.3 x 4.3) and not 20 to 40 fold, i.e., if indeed it has been underestimated at all. With

knowledge of Hathaway's comments, EPA still felt that the exposure data might be underestimated by a factor of two.

Estimation of the hexavalent fraction of the total chromium levels reported by Mancuso can also be calculated from the industrial hygiene survey data. Bourne and Yee reported that the ratios of trivalent chromium to hexavalent chromium concentrations in the airborne dust in nine major departments ranged from 1 to 3, except for two departments where chromite ore (Cr(III)) was extensively used; the Cr(III) to Cr(VI) ratios here were 6 for the lime and ash operation and 52 for the ore preparation. Excluding the ore preparation department, exposure data yield an estimate for hexavalent chromium levels no less than one-seventh the amount reported for total chromium.

8.3.6.1 Potency Based on Competing Risks Model

Applying the competing risks model to the exposure and mortality data from Table 1 and estimating the probability of survival to age t ($\exp[-A(t)]$) from U.S. Vital Statistics yield an estimate for the excess lifetime probability of cancer from exposure to chromium of 1.16×10^{-5} per ng/m^3 . Assuming that the hexavalent chromium fraction alone is carcinogenic yields an excess lifetime risk of 8.12×10^{-5} per ng/m^3 . Alternately, assuming the chromium levels have been underestimated by a factor of 5.6, the excess risk per $\text{ng chromium}/\text{m}^3$ would be 2.07×10^{-6} .

8.3.6.2 Potency Based on "Crude" Model

Estimation of the potency factor, B, using the "crude" model is also based on the data in Table 8-1. The estimated relative risk is calculated by taking the weighted average of the age-exposure-specific relative risks where the number of person-years is the weighting factor. Thus, the cohort average RR equals 7.2. The dose, d, is estimated as the weighted average of the age-exposure specific concentrations also weighting by person-years. The dose estimate is 15.5×10^3 ng/m³. The background rate of lung cancer (R_b) is based on the lung cancer mortality rate for the 1964 U.S. population and is equal to 0.036. Therefore, the potency is calculated as follows:

$$B = [(7.2 - 1) \times 0.036] / (15.5 \times 10^3) = 1.44 \times 10^{-5} / \text{ng/m}^3.$$

Accounting for the estimated hexavalent fraction of the exposure or the possible underestimation of the total exposure yields potency estimation of $10.1 \times 10^{-5} / \text{ng/m}^3$ and $2.57 \times 10^{-6} / \text{ng/m}^3$, respectively.

These risk estimates may be too high if the workers smoked more than the general white male population, which the background rates are based upon. Mancuso provided no data on smoking habits, but it is generally accepted that the proportion of smokers is higher among industrial workers than the general population. EPA explored the impact of differential smoking habits on the risk assessment (EPA, 1984). As an example, if the background rate of lung cancer mortality for the Mancuso cohort is increased by 40% the corresponding potency would be reduced by 25%, or from 1.16×10^{-5} to $8.70 \times 10^{-6} / \text{ng/m}^3$. A 40% increase in background lung cancer mortality could

arise assuming that 80% of the chromate workers are ever-smokers while only 50% of the general white male population are ever-smokers.

EPA concluded that the application of other reasonable assumptions about smoking habits of the cohort compared to the general white male population would not reduce the potency estimate by more than 50%. Therefore, the lowest estimates of potency "adjusting" for smoking and the possible under-estimation of dose (e.g. a factor of 5.6 from the sample DHS calculation) would be 11.2 times lower than those previously given or 1.04×10^{-6} /mg/m³ for the competing risks model and 1.29×10^{-6} /ng/m³ for the crude model.

A summary of potency estimates under different scenarios is presented in Table 8-2.

Table 8-2. Excess Cancer Risks from Continuous Lifetime Exposure to Hexavalent Chromium

	Estimated Excess Lifetime Risk per ng/m ³ per-Million Population	
	Competing Risks Model	Crude Model
<u>Mancuso Data</u>		
Exposure = Total Chromium ¹ (best estimate)	11.6	14.4
a) underestimated exposure by 5.6	2.1	2.6
b) smoking rate higher among workers	5.8	7.2
c) a + b	1.0	1.3
d) 95% UCL ² for best estimate	--	20.9
Exposure = Hexavalent Chromium ³ (best estimate)	81.2	100.8
a) underestimated exposure by 5.6	14.5	18.0
b) smoking rate higher among workers	40.6	50.4
c) a + b	7.3	9.0
d) 95% UCL ² for best estimate	--	148.0
<u>Pokrovskaya et al. Data⁴</u>		
a) high dose estimate	--	82.0
b) low dose estimate	--	180.0
c) geometric mean of a + b	--	97.0

¹Potency calculated based on total chromium levels.

²Upper limit of the 95% confidence interval for estimated relative risk. Estimated available for parameters in competing risks model.

³Concentration of hexavalent chromium assumed to be 1/7 the level of total chromium. See text for further explanation.

⁴Insufficient data provided to calculate confidence limits.

8.3.7 Risk Assessment Based on the Pokrovskaya et al. Study

This is a Russian study that was not published in English and hence, was not directly reviewed by the staff of DHS. The potency estimation below is excerpted from the EPA chromium health evaluation (EPA, 1984). The data reported by the authors are only appropriate for use in the crude model.

POTENCY ESTIMATION BASED ON POKROVSKAYA ET AL. (1973)

Although this study showed a significant increase of lung cancer mortality over the control group, the validity of the data is questionable because the study cohort is not clearly defined. The report indicates that the cancer mortalities over the period 1955-1969 in workers from a ferroalloy plant in the Soviet Union were compared with the population of similar ages in the city where the plant was located, but it fails to indicate the criteria by which workers were included in the cohort. The lung cancer mortality ratios were reported to be 4.4 (not statistically significant) for the age group 30-39 and 6.6 ($p = 0.001$) for the age group 50-59 among male workers. Concentrations of hexavalent chromium were reported to exceed the marginally allowable value (0.01 mg/m^3) by 2 to 7 times on the average. The length of employment was from 7 to 20 year, with an average of 15 years.

Based on the information that the average ambient concentrations of hexavalent chromium exceeded the marginally allowable

value 0.01 mg/m^3 by 2 to 7 times, workers' exposure to hexavalent chromium ranged from 0.02 mg/m^3 to 0.07 mg/m^3 . The lifetime doses corresponding to 0.02 mg/m^3 and 0.07 mg/m^3 are, respectively, as follows:

$$d_1 = 0.02 \times 10^3 \times (8/24) \times (240/365) \times (1/4) = 1.1 \text{ ug/m}^3$$

and

$$d_2 = 0.07 \times 10^3 \times (8/24) \times (240/365) \times (1/4) = 3.8 \text{ ug/m}^3$$

(where the factor of 1/4 represents the 15-year average exposure among the 60-year-old cohort members). If 6.6 is taken to be an estimate of the average relative risk for the cohort, then the carcinogenic potency for hexavalent chromium (Cr(VI)) is calculated to range from:

$$B = (6.6-1) \times 0.036/3.8 = 5.2 \times 10^{-2}/\text{ug/m}^3$$

to

$$B = (6.6-1) \times 0.036/1.1 = 0.18/\text{ug/m}^3.$$

The geometric mean of the two limits is $9.7 \times 10^{-2}/\text{ug/m}^3$. It is about 8 times larger than $1.2 \times 10^{-2}/\text{ug/m}^3$, the potency calculated on the basis of the Mancuso (1977) data.

Converting to ambient levels (i.e. nanograms/m³) yields an estimate of 9.7 x 10⁻⁵/ng/m³. This potency estimate is about 8 times greater than the best estimate derived from the Mancuso data using the competing risks model.

8.3.8 Summary of the Risk Assessment

Both animal and epidemiologic studies have demonstrated that chromium causes cancer. However, for the purpose of quantifying the carcinogenic potential of chromium, no animal study and only one epidemiologic study was found to be appropriate. This conclusion was also reached by the Carcinogen Assessment Group (CAG) of EPA (EPA, 1984).

The cohort of chromate workers studied by Mancuso is the basis of the DHS risk assessment. While providing the best data for a risk assessment, four important issues could not be completely resolved. Thus, the carcinogenic potency contains some degree of uncertainty. The four issues are: (1) speciation of exposure with respect to trivalent and hexavalent chromium, (2) possible underestimation of worker exposures, (3) separation of the effect of chromium from that of cigarette smoking, and (4) potency of specific chromium compounds.

Speciation of chromium was based on the assumption that the trivalent form was insoluble in water whereas the hexavalent form was water soluble. This is not completely accurate since some Cr(VI) compounds are insoluble (e.g. lead chromate) and some Cr(III) compounds are soluble (e.g. chromium potassium sulfate). Therefore, the assumption that hexavalent chromium is one-seventh the amount of total chromium in the plant Mancuso studied, and

hence the carcinogenic potency of hexavalent chromium is seven times greater than that based on the total chromium concentration, should be recognized as a source of uncertainty in the risk assessment.

The assertion that chromium levels have been underestimated must also be viewed cautiously, because it is not based on documented evidence from the plant in question. Thus, while the staff of DHS has provided potency estimates assuming a 5.6-fold underestimation in the exposure levels, the staff does not recommend that such an assumption or any assumption with regard to a possible exposure underestimation be used as the basis for a recommended potency level.

With respect to cigarette smoking, Mancuso did not address the potential confounding effect this may have had on the chromium-lung cancer relationship. Rather, the risk assessment assumes that the chromate workers had the same smoking habits as their general population counterparts. EPA, assuming no synergistic effect between chromium and smoking, estimated that even if the Mancuso cohort smoked more than their comparison group it would be unlikely that the potency factor could have been overestimated by more than a factor of 2. (If there is a synergistic effect, the independent role of chromium would be much less than indicated in this risk assessment. Available data are insufficient to verify or refute the existence of a synergistic relationship.) Again, while the DHS risk assessment has shown the estimated impact of smoking, staff members do not believe that the recommended range of potency levels should be based on possible differential smoking patterns.

The matter of potency for specific chromium compounds cannot be resolved with current epidemiologic data. Exposures tended to be mixed or, where only a single compound was present, exposure levels were not quantified. Thus, the staff of DHS recommends that the carcinogenic potency of different hexavalent chromium substances be considered equivalent.

The above issues notwithstanding, the conclusion of the staff of DHS is that hexavalent chromium is a human carcinogen without a threshold. The estimated excess cancer risk incurred from continuous lifetime exposure to hexavalent chromium is given by the range: $1.16 \times 10^{-5}/\text{ng}/\text{m}^3$ to $14.6 \times 10^{-5}/\text{ng}/\text{m}^3$. The lower limit represents the estimate based on using the average total chromium exposure data in the Mancuso study and the upper bound is based on the upper limit of the 95% confidence interval for the estimate of the relative risk in that epidemiologic study and assuming the concentration of hexavalent chromium was one-seventh that of the total. The staff of DHS does not present a lower confidence limit for potency estimates because the true risk may be considerably below even the lower boundary of the 95% confidence interval limit, yet there is no scientific basis for locating this risk. The upper boundary for the confidence interval is given since it represents a conservative estimate that is unlikely to be exceeded by the actual risk and is thus in accordance with Section 39650 of the Health and Safety Code which stipulates that DHS "shall utilize scientific criteria which are protective of public health consistent with current scientific data."

The risk estimates can also be applied to smaller geographic areas, such as those around point source emitters of chromium. In Part A (section III.C)

data from two point sources located in populated areas were given (this is reprinted below). One area was comprised of a 20 x 20 kilometer area centered on a chromium plating facility. The other area was a 40 x 40 kilometer area centered on a bank of cooling towers.

Plating Facility

<u>Annual Average Chromium Concentration, ng/m³</u>	<u>Population Exposed</u>	<u>Cumulative Population</u>
550	1,960	1,960
450	-0-	1,960
350	-0-	1,960
250	1,925	3,885
150	5,825	9,737
100	-0-	9,737
90	-0-	9,737
80	-0-	9,737
70	8,803	18,540
60	1,945	20,485
50	7,742	28,227
40	14,870	43,097
30	22,982	66,079
20	61,829	127,908
10	452,709	508,617
.05 to 5.0	2,400,000	2,993,262

Cooling Towers

<u>Annual Average Chromium Concentration, ng/m³</u>	<u>Population Exposed</u>	<u>Cumulative Population</u>
5.0	8,886	8,886
4.0	2,993	11,879
3.0	23,942	35,821
2.0	96,565	132,386
1.0	730,336	862,722

Table 8-3 shows the theoretical cancer impact each of these point sources would have on the surrounding population using potency estimates of 1.16×10^{-5} /ng/m³ and 14.6×10^{-5} /ng/m³. For each source these are small subgroups within the population that are exposed to (relatively) high chromium levels and they would be subject to a correspondingly high estimated excess lifetime cancer risk. However, because so few people are exposed, the expected excess number of cancer cases would be small. Conversely, more cases would be predicted among population groups with low exposure because of the large number of people so exposed. It should be noted that the average lifetime risk of lung cancer in the U.S. population is about 8,700 per 100,000 in white males and 4,200 per 100,000 for white females (Seidman et al., 1985). Some of the incremental risks in table 8-3 would be large enough to be detected epidemiologically.

Table 8-3. Theoretical cancer impacts of lifetime exposure to Cr(VI) in populations near high point source emission locations.*

	<u>Plating Facility</u>	<u>Cooling Tower</u>
Range of Exposure**	0.05 - 550 ng/m ³	1 - 5 ng/m ³
Population Exposed	2,993,262	862,722
Population-weighted average exposure	7.55 ng/m ³	1.22 ng/m ³
EXCESS LIFETIME CANCER RISK AND NUMBER OF CASES		
A. <u>Potency = 1.16 x 10⁻⁵/ng/m³</u>		
Overall Population Risk	8.8 x 10 ⁻⁵	1.4 x 10 ⁻⁵
a) No. of cases	262	12
Risk at Highest Exposure	6.4 x 10 ⁻³	5.8 x 10 ⁻⁵
a) No. of cases	13 (pop. 1,960)	< 1 (pop. 8,886)
Risk at Lowest Exposure***	5.8 x 10 ⁻⁵	1.2 x 10 ⁻⁵
a) No. of cases	139 (pop. 2,400,000)	9 (pop. 730,336)

B. <u>Potency = 14.6 x 10⁻⁵/ng/m³</u>		
Overall Population Risk	1.1 x 10 ⁻³	1.8 x 10 ⁻⁴
a) No. of cases	3,299	153
Risk at Highest Exposure	7.7 x 10 ⁻²	7.3 x 10 ⁻⁴
a) No. of cases	151	7
Risk at Lowest Exposure***	7.3 x 10 ⁻⁴	14.6 x 10 ⁻⁵
a) No. of cases	1,752	107

* Based on data provided in Part A, Section III.C "Concentrations Close to Sources."

** For this table, it is assumed all chromium is hexavalent although the reported levels are for total chromium.

***For Plating Facility, the lowest exposure was taken as the upper bound of the range i.e., 5 ng/m³.

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APPENDIX I

Summary of Bioassays
(Source: IARC, 1980)

Table 8. Summary of carcinogenicity studies of chromium and chromium compounds in animals.

Compound	Species	Route and dosage	Findings	Reference
Chromium powder	Mouse	4 i.p. injections of 0.2 ml of a 0.005% solution	1 melanoma in 50 treated animals	Hueper, 1955
	Mouse	6 i.v. injections of 0.05 ml of a 0.005% solution	No tumours	Hueper, 1955
	Mouse	6 intrapleural injections of 0.2 ml of a 0.005% suspension	No tumours in 50 treated mice	Hueper, 1955
	Rat	1 intratracheal injection of 10 mg	No squamous cell carcinomas of the lung in 12 treated rats	Makubb, 1978
	Rat	1 i.m. injection of 2 mg	No local tumours in 20 surviving treated animals	Sunderman et al., 1974
	Rat	6 i.p. injections of 0.1 ml of a 0.05% suspension	No increase in round cell sarcoma incidence compared with controls. 2 leiomyomas in treated animals, none in controls	Hueper, 1955
	Rat	6 i.v. injections of 0.15 ml of a 0.05% suspension	2 rats with pulmonary adenomas. No increase in sarcomas compared with controls	Hueper, 1955
	Rat	6 intrapleural injections of 0.05 ml of a 33.6% (by weight) suspension or 6 intrapleural injections of 0.1 ml of a 0.5% suspension	2 pleural adenomas and 1 angiosarcoma in 50 treated animals and 0/25 controls	Hueper, 1955
Rat	Intramedullary injection into the femur of 46 mg	No injection site tumours in 25 treated animals	Hueper, 1955	

Table 8 (contd)

Compound	Species	Route and dosage	Findings	Reference
Chromium powder (contd)	Rabbit	18 i.v. injections of 0.5 ml/kg bw of a 5% suspension	1 carcinoma of lymph node in 3 treated survivors and 0/4 controls	Hueper, 1955
Unroasted chromite (III) ore	Mouse	Intrapleural injection of 10 mg in 0.5 ml of distilled water	Granulomas	Davis, 1972
	Rat	6 intrapleural injections of 0.05 ml of a 73.4% (by weight) suspension	Injection site sarcoma in 1/25 treated animals	Hueper, 1955
	Rat	Intramedullary injection into the femur of 58 mg	No injection site tumours in 25 treated rats	Hueper, 1955
	Rabbit	12 i.v. injections of 5 ml of a 5% suspension	No tumours	Hueper, 1955
Roasted chromite (III) ore	Mouse	1 m. implantation of 10 mg (equivalent to 0.79 mg chromium)	No implantation site tumours	Pavne, 1960
	Rat	1 m. implantation of 25 mg	Sarcomas at implantation site in 3/31 treated animals and 0 vehicle controls	Hueper, 1958
	Rat	1 m. implantation of 25 mg	Tumours (type unspecified) at implantation site in 1/34 treated animals and 0/32 vehicle controls	Hueper, 1961
	Rat	Intrapleural injection of 0.2 ml of a 0.5% suspension	Tumours (type unspecified) at implantation site in 5/32 treated animals and 0/34 controls	Hueper, 1961

Table 6 (cont'd)

Compound	Species	Route and dosage	Findings	Reference
Roasted chromite (III) ore (cont'd)	Rat	Intratracheal implantation of 25 mg	Lung tumours in 2/4 treated rats vs. 1/13 in controls	Payne 1961
	Rat	Intratracheal implantation of 25 mg (equivalent to 2 mg chromium)	Implantation site tumours in 2/25 treated rats and 0/25 controls	Payne 1961
Mixed chromate (VI) dust	Mouse	Inhalation 4 hrs/day, 5 days/week for 16-58 weeks (total dose chromium inhalation 400-1200 mg/kg)	No tumours in 500 treated animals compared with controls	Steffe et al. 1965
	Mouse	56 intratracheal implantations of dust (equivalent to 0.23 mg chromium trioxide)	No more lung tumours in 500 treated mice than in controls	Steffe et al. 1965
	Mouse	4 intratracheal implantations of 0.25 ml of a 2 or 4% suspension	No increase in lung tumour incidence in 55 treated animals compared with 41 controls	Steffe et al. 1965
	Rat	Inhalation 4-5 hrs/day, 4 days/week for lifespan (chromic oxide concentration of 3.4 mg/m ³)	No significant increase in tumour incidence in 75 treated rats compared with controls	Steffe & Barber 1965

Table 6 (cont'd)

Compound	Species	Route and dosage	Findings	Reference
Mixed chromate dust + potassium dichromate (VI)	Rat	16 intratracheal injections of 0.1 ml of suspension of 0.5% roasted chromate + 0.6% potassium dichromate (equivalent to 0.07 mg chromium/dose)	No significant increase in tumour incidence compared with controls	Steffe & Barber 1965
Mixed chromate (VI) dust + potassium dichromate (VI) + sodium chromate (VI) + pulverized residue dust	Rabbit	Inhalation, 4 days/week for 50 months	No increase in tumour incidence compared with controls	Steffe & Barber 1965
	Guinea-pig	Inhalation, 4 days/week for lifespan	Pulmonary carcinomas in 3/30 treated animals	Steffe & Barber 1965
Barium chromate (VI)	Rat	i.m. implantation of 25 mg	No implantation site tumours in 25 rats	Hueper & Payne 1961
	Rat	i.m. implantation	No implantation site tumours in 34 rats	Hueper 1961
	Rat	Intratracheal implantation	Implantation site tumours in 1/31 treated rats and 0/34 controls	Hueper 1961
Calcium chromate (VI)	Mouse	Inhalation, 13 mg/m ³ 5 hrs/day, 5 days/week for lifespan	Lung adenomas in 14/126 treated animals and 5/126 controls	Serrano et al. 1967
	Mouse	i.m. implantation of 10 mg	Implantation site sarcomas in 2/50 and in 0/50 controls	Payne 1961a
	Mouse	i.s.c. injection of 10 mg	Implantation site sarcomas in 1/13 and in 0/50 controls	Payne 1961a

Table B (contd)

Compound	Species	Route and dosage	Findings	Reference
Calcium chromate (VI) (contd)	Rat	Bronchial implantation	5 squamous cell carcinomas and 10 adenocarcinomas of the lung in 100 treated rats; 0/24 controls	Laskin et al. 1970
	Rat	Bronchial implantation	Increased incidence of bronchial squamous cell carcinomas	Lery & Venitt 1975
	Rat	Inhalation, 2 mg/m ³ , 580 exposures of 5 hrs over 811 days	1 squamous cell carcinoma of lung; 1 of larynx; 1 peritumoral tumour (no. of treated animals unspecified)	Laskin 1972
	Rat	I.m. implantation of 12.5 mg	Malignant tumours at implantation site in 4/3 treated animals	Hueber & Payne 1962
	Rat	20 injections, total dose 19 mg	Injection site sarcomas in 18/24 and 0 in vehicle controls	Fox & Curran 1963
	Rat	12 injections of 4 mg	Injection site sarcomas in 5/45 and 0/22 in vehicle controls	Fursten et al. 1976
	Rat	I.m. implantation of 25 mg	Injection site sarcomas in 3/35 treated animals and 0/32 controls	Hueber & Payne 1962
	Rat	I.m. implantation	Tumours (type unspecified) at implantation site in 9/32 treated animals and 0/32 controls	Hueber 1961
	Rat	Intrapleural implantation of 12.5 mg	Malignant tumours (unspecified) at implantation site in 8/14 treated animals	Hueber & Payne 1962
	Rat	Intrapleural implantation	Tumours (type unspecified) at implantation site in 20/32 treated animals and 0/34 controls	Hueber 1961
	Hamster	Inhalation, 2 mg/m ³ , 589 exposures	1 squamous cell carcinoma and 1 papilloma of larynx (no. of treated animals unspecified)	Laskin et al. 1970

Table B (contd)

Compound	Species	Route and dosage	Findings	Reference
Sintered calcium chromate (VI)	Mouse	I.m. implantation of 10 mg	Implantation site sarcomas in 9/46 treated animals and 0/50 controls	Payne 1960
	Mouse	S.c. injection of 10 mg	No injection site sarcomas	Payne 1960
	Rat	I.m. implantation of 25 mg	Implantation site sarcomas in 8/35 treated animals and 0 controls	Hueber & Payne 1962
	Rat	I.m. implantation	Tumours (type unspecified) at implantation site in 12/34 treated animals and 0/32 controls	Hueber 1961
	Rat	Intrapleural implantation	Tumours (type unspecified) at implantation site in 17/33 treated rats and 0/34 controls	Hueber 1961
Chromic (III) acetate	Mouse	P.o., 5 mg/l drinking water for life	No increase in tumour incidence	Schroeder et al. 1966
	Rat	P.o., 5 mg/l drinking water for life	No increase in tumour incidence	Schroeder et al. 1966
	Rat	8 i.m. implantations of 25 mg each over 24 months	Implantation site sarcoma in 1/75 treated animals	Hueber & Payne 1962
	Rat	I.m. implantation	Implantation site tumours (unspecified) in 1/34 and in 0/32 controls	Hueber 1961
	Rat	8 intrapleural implantations of 25 mg each over 13 months	No implantation site tumours within 3 years in 42 treated animals	Hueber & Payne 1962

Table 8 (contd)

Compound	Species	Route and dosage	Findings	Reference
Chromic (III) acetate (contd)	Rat	Intraperitoneal implantation	Implantation site tumours (type unspecified) in 1/24 and in 0/34 controls	Hueber, 1961
Chromic (III) oxide	Rat	P.o. 1, 2 and 5% in bread on 5 days wk for 2 years	1% dose: 3/60 mammary fibroadenomas 2% dose: 1/60 5% dose: 3/60 control: 1/60 mammary carcinoma, 2/60 fibroadenomas	Wankov & Piskunov, 1971
	Rat	Single intratracheal application of 50 or 20 mg	50 mg dose: 7/34 with tumours (4 with lung sarcomas) 20 mg dose: 6/18 with tumours (5 with lung sarcomas) no controls	Orshkov & Fedorova, 1967
	Rat	Bronchial implantation	No lung tumours in 98 animals	Laskin et al., 1970
	Rat	1 µl injection of 20 mg	Lung sarcomas in 4/20; no controls	Orshkov & Fedorova, 1967
	Rat	2 intratracheal injections of 5 mg	Alveolar cell sarcomas of lung in 3/17 treated animals; no controls	Orshkov & Fedorova, 1967
Chromium carbonyl	Rat	Injection of 2.5 mg into subcutaneous implanted tracheal rings	Squamous cell carcinomas in 2/22 animals; none in 4 vehicle controls	Lane & Moss, 1977
Chromium (III) sulphate	Mouse	24 i.p. injections (total doses: 480, 1200 and 2400 mg/kg bw)	No significant increase of pulmonary adenoma incidence in 60 treated rats compared with 40 vehicle and untreated controls	Stoner et al., 1978
Chromium (VI) trioxide	Rat	Bronchial implantation	No increase in lung tumour incidence in 100 treated rats compared with 24 controls	Laskin et al., 1970

Table 8 (contd)

Compound	Species	Route and dosage	Findings	Reference
Sintered chromium (VI) trioxide	Mouse	1 s.c. injection of 10 mg	No injection site tumours in 52 treated animals	Payne, 1964
	Rat	1 m. implantation of 25 mg	Implantation site sarcomas in 15/35 treated animals and 0/35 controls	Hueber & Payne, 1963
Cobalt-chromium alloy	Rat	1 m. injection of 28 mg	Injection site sarcomas in 7/74 treated rats; other tumours in 7/74	Heath et al., 1971
Lead chromate (VI)	Mouse	4 i.m. injections of 3 mg	2 lymphomas and 3 lung adenocarcinomas in 17 mice necropsied; summary incidences in controls	Furst et al., 1978
	Rat	1 s.c. injection of 30 mg	Injection site sarcomas in 26/40 treated animals and 0/60 vehicle controls	Maitan, 1974; 1975
	Rat	9 i.m. injections of 8 mg	Injection site sarcomas in 21/47 treated rats; 3 renal carcinomas; 0/22 in vehicle controls	Furter et al., 1976
	Rat	1 m. implantation	Tumour (type unspecified) at implantation site in 1/33 treated rats and 0/33 controls	Hueber, 1961
	Rat	Intratracheal implantation	Tumours (type unspecified) at injection site in 3/34 treated rats and 0/24 controls	Hueber, 1961
Lead chromate (VI) oxide	Rat	1 s.c. injection of 30 mg	Injection site sarcomas in 21/40 treated rats and 0/60 vehicle controls	Maitan, 1974; 1975

Table 8 (contd)

Compound	Species	Route and dosage	Findings	Reference
Potassium chromate (VI)	Rat	Bronchial implantation	No increased incidence of lung tumours	Levy & Venitt, 1975
Potassium dichromate (VI)	Rat	Bronchial implantation	No increased incidence of lung tumours	Levy & Venitt, 1975
Sodium chromate (VI)	Rat	Bronchial implantation	No increased incidence of lung tumours	Levy & Venitt, 1975
Sodium dichromate (VI)	Rat	16 i.m. injections of 2 mg	No injection site tumours	Hueper & Payne, 1961
	Rat	I.m. implantation	No implantation site tumours	Hueper, 1961
	Rat	16 intrapleural injections of 2 mg	1 lung adenocarcinoma in 39 treated animals; no injection site tumours in 60 vehicle controls	Hueper & Payne, 1961
	Rat	Intrapleural implantation	No injection-site tumours in 26 treated animals	Hueper, 1961
	Rat	Bronchial implantation	No increase in lung tumours	Levy & Venitt, 1975
Strontium chromate (VI)	Rat	I.m. implantation	Implantation-site tumours in 15/33 treated animals and 0/32 controls	Hueper, 1961
Zinc potassium chromate (VI)	Rat	Bronchial implantation	Increased incidence of bronchial squamous cell carcinomas	Levy & Venitt, 1975
Zinc yellow	Mouse	6 intratracheal injections of 0.03 ml of a 0.2% suspension	No pulmonary carcinomas; pulmonary adenomas in 31/62 treated animals and 7/18 untreated controls	Steffe & Baer, 1955

Table 8 (contd)

Compound	Species	Route and dosage	Findings	Reference
Zinc yellow (contd)	Rat	I.m. implantation	Tumours (type unspecified) at implantation site in 16/34 treated animals and 0/32 controls	Hueper, 1961
	Rat	Intrapleural implantation	Tumours (type unspecified) at implantation site in 22/33 treated animals and 0/34 controls	Hueper, 1961 ^a

^aSee footnote on p. 254.^bIt was not specific whether this compound was zinc chromate, zinc potassium chromate or zinc yellow.

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APPENDIX II

Estimation of Parameters for the Competing Risks Model
(Source: EPA, 1984)

7.2.3.1.2. Choice of Dose-Response Model -- It has been widely recognized (e.g., Doll 1971) that the age-specific incidence curve tends to be linear on doubly logarithmic graphs, or equivalently, the age-specific incidence follows the mathematical form

$$I(T) = bT^{k-1}$$

where b and k are parameters that may be related to other factors such as dose, and T may be one of the following three cases:

1. T is age when cancer is observed,
2. T is the time from the first exposure to observed cancer, or
3. T is the time from exposure to cancer minus the minimum time for a cancer to be clinically recognized.

This model has been shown to arise from the somatic mutation hypothesis of carcinogenesis (Armitage and Doll 1954, Whittemore 1978, Whittemore and Keller 1978). It has also been shown to arise from the epigenetic hypothesis when the reversible cellular change is programmed to occur randomly (Watson 1977). These authors and many others have used this model to interpret and/or estimate potency from human data.

Since the data that could be used for risk estimation are limited, a simple model that fits the data should be used. Therefore, the observed age-specific incidence is assumed to follow the model

$$I(t,d) = B(t) + h(t,d)$$

where $B(t)$ is the background rate at age t and $h(t,d) = Q(d) t^{k-1}$ with $Q(d) = q_1 d + q_2 d^2$, a function of dose d .

Once the parameters q_1 , q_2 , and k are estimated, the lifetime cancer risk associated with an exposure d by age t , taking into account the competing risk, can be calculated by

$$P(t,d) = \int_0^t h(s,d) \exp \left\{ - \left[\int_0^s h(y,d) dy + A(s) \right] \right\} ds$$

where $\exp[-A(s)]$ is the probability of surviving to age s and $h(t,d) = I(t,d) - B(t)$, the age-specific incidence after adjusting the background rate.

7.2.3.1.3. Estimation of the Risk Model -- To estimate the parameters in $h(t,d)$ we assume, as is usually done, that the number of lung cancer deaths, X , at age t , follows the Poisson distribution with the expected value

$$E(X) = N \times (B + Q(d) t^{k-1})$$

where N is the person-year associated with X , B is the background rate at age t , and $Q(d) = q_1 d + q_2 d^2$.

Using the BMDP computer program P3R and the theory relating the maximum likelihood and non-linear least square estimation by Jennrich and Moore (1975), the parameters q_1 , q_2 , and k are estimated by the method of maximum likelihood as $q_1 = 1.11 \times 10^{-7}$, $q_2 = 1.84 \times 10^{-9}$, and $k = 2.915$; the corresponding standard deviations are respectively 7.8×10^{-7} , 1.2×10^{-8} , and 1.7.

Thus, the age-specific cancer death incidence at age t due to chromium exposure $d \text{ ug/m}^3$ is given by

$$h(t,d) = Q(d) t^{1.915}$$

where

$$Q(d) = 1.11 \times 10^{-7} d + 1.84 \times 10^{-9} d^2$$

The model fits the data well, as can be seen from the goodness of fit statistic

$$\chi^2 = \sum (O-E)^2/E = 1.60$$

which has, asymptotically, a chi-square distribution with 5 degrees of freedom under the model specified. The observed and predicted values used in calculating χ^2 are (3, 2.5), (6, 7.2), (6, 5.1), (4, 3.1), (5, 6.7), (5, 4.1), (2, 1.4) and (4, 4.3).

Taking into account the competing risk, the lifetime probability of lung cancer death due to exposure to chromium $d \text{ ug}/\text{m}^3$ is given by

$$P(L,d) = \int_0^L h(t,d) \exp \left\{ -\left[\frac{Q(d)}{2.915} t^{2.915} + A(t) \right] \right\} dt$$

where L is the maximum human lifetime and is mathematically equivalent to infinity, since the probability of surviving beyond L is 0.

At low doses, approximately,

$$P(L,d) = d \times P(L,1)$$

where $P(L,1)$ is the lifetime cancer risk due to exposure to $1 \text{ ug}/\text{m}^3$ of chromium. The unit risk, $P(L,1)$, has been adopted by the CAG as an indicator of the carcinogenic potency of a chemical compound.

7.2.3.1.4. Calculation of the Risk at $1 \text{ ug}/\text{m}^3$ -- To calculate the unit risk, $P(L,1)$, it is necessary to know $\exp[-A(t)]$, the probability of surviving to age t . Since this probability can only be estimated, it is assumed that the survival probability is constant over a 5-year interval, as provided in the U.S. Vital Statistics.

Using this approximation and by integrating the formula $P(L,1)$, we have

$$\begin{aligned} P(L,1) &= \sum \left[\exp(-3.87 \times 10^{-8} t_{i-1}^{2.915}) - \exp(-3.87 \times 10^{-8} t_i^{2.915}) \right] \times P_i \\ &= 1.16 \times 10^{-2} \end{aligned}$$

where (t_{i-1}, t_i) is a 5-year interval and P_i is the probability of survival up

to the age t_{i-1} . P_i is assumed to be a constant over the interval and is estimated from the 1975 U.S. Vital Statistics.

APPENDIX III

Mancuso Study of Workers Exposed to Chromium

CONSIDERATION OF CHROMIUM AS AN INDUSTRIAL CARCINOGEN

T. F. Mancuso, M.D.

*Research Professor, Occupational Health, Graduate School of Public Health,
University of Pittsburgh, Pittsburgh, Pennsylvania 15261*

ABSTRACT

Cohorts of employees (1931-1937) of a chromate plant were followed to 1974. Lung cancer deaths accounted for 62% of the total cancers observed. The clustering of lung cancer deaths occurred after 27-36 years of observation. The lung cancer death rates increased by gradient level of exposure to insoluble (trivalent) chromium, soluble (hexavalent) chromium and to total chromium. The lung cancer risk is primarily related to the total chromium exposure regardless of the form of chromium. Extensive depositions of chromium were found in the lungs many years after exposure to chromium ceased. The identification of the lung cancer risk for insoluble (trivalent) form of chromium among workers broadens extensively the potential risk to other populations exposed to chromium in other industries. It is concluded that all forms of chromium are carcinogenic.

RÉSUMÉ

On a examiné en 1974 des cohortes d'employés d'une usine de chromate nés entre 1931 et 1937. Au total, 62% de la mortalité due au cancer provenait d'un cancer du poumon. La mortalité due à ce cancer se produisait après 27 à 36 ans d'observation. Le taux de mortalité par cancer du poumon variait avec l'exposition au chrome insoluble (trivalent), au chrome soluble (hexavalent) et au chrome total. Le risque de cancer dépend avant tout de l'exposition nette au chrome, quelle que soit sa forme. D'importants dépôts de chrome ont été observés dans les poumons plusieurs années après que l'exposition eut cessé. Le fait que la forme soluble du chrome puisse provoquer un cancer du poumon chez les ouvriers en élargit considérablement le danger aux ouvriers exposés au produit dans d'autres secteurs. Nous concluons que toutes les formes de chrome sont carcinogènes.

INTRODUCTION

The excessive lung cancer death rate identified with workers engaged in the manufacture of chromates has been previously established (Machle 1948;

Mancuso 1949; Bactjer 1950; Public Health Service 1953; Taylor 1966). There has been much speculation, during the past 27 years since the original epidemiological observation, concerning the chemical form of the chromium which may be responsible for the development of the high death rate for cancer of the lung among chromate workers.

In brief, virtually all of the postulations concerning the etiology of lung cancer during the span of years, has centered on the hexavalent form of chromium. The principal exception has been the report by Mancuso and Hueper (1951), who emphasized the importance of the insoluble form of chromium (trivalent) in the development of lung cancer and further concluded that exposure to other not readily soluble chromium compounds (chromium pigments, chromium alloys) also be considered.

The present study is a continuation of the first study initiated in 1948-1949, in which epidemiological, medical, engineering and chemical investigations were carried out (Bourne and Fosdick 1950; Bourne and Yee 1950; Urone *et al.* 1950; Urone and Anders 1950; Mancuso 1951; Mancuso and Hueper 1951; Bourne and Rushin 1951). A sufficient number of years has now elapsed, with a corresponding increase in lung cancer deaths, to provide the basis for further evaluation of the carcinogenic potential of chromium in various forms.

Our present study is concerned with the following major questions:

- 1 What is the span of the latent period and how does this affect observations of lung cancer at different points in time?
- 2 Do successive groups of employees new to a chromium exposure sustain similar high rates for lung cancer?
- 3 Is there any association between lung cancer death rates and exposure to a particular form of chromium, insoluble, soluble or to total chromium?

METHODS

In the early part of 1949 the industrial hygiene engineering study of this chromate plant was conducted. Careful time studies, for the full 8 hours and 40 hour week, were made for each of the occupations of the production workers and together with air sampling, the true exposure in terms of the weighted average of exposure to insoluble, soluble and total chromium (per cubic meter) was calculated for each occupation and for each worker for every department.

All personnel records of the chromate plant since its inception, 1931, were microfilmed. A complete work history was prepared on each worker.

Each job held in each department was identified and the duration of employment in the respective occupations and changes in occupations and departments were recorded. In essence then, for every worker in the plant, we had established the weighted average exposure to the type of chromium and the duration of exposure in each respective job the man had. The duration in time (years and months) for each job held was multiplied with its corresponding weighted average exposure for calculation of the exposure years.

The atmospheric concentrations of chromium in our industrial hygiene study of this plant were expressed in terms of elemental chromium, a departure from the customary industrial hygiene procedure in which concentrations are expressed in terms of chromic acid (Cr_2O_3). This method was adopted at the inception of the study in 1949 to avoid the inference of implicating any specific compounds in subsequent cancer effects.

This means that the concentrations calculated per elemental chromium would be lower, by about one half of the level for that calculated as chromic acid (Cr_2O_3). Therefore, whatever associations are presented in the findings with levels of concentration of chromium, it is in terms of the elemental chromium. In the reports of the chemical analyses, the soluble chromium is essentially hexavalent and the insoluble (in water) is chiefly trivalent.

There is another more apparent point, and that is the comparability of the concentrations of chromium found (insoluble, soluble and total chromium) in the environmental appraisal of the plant in the early part of 1949, with the concentrations in the early years of operation, 1931-1937.

The tremendous progressive increase in production in the succeeding years from zero could have brought about a concomitant increase in the dust concentrations to 1949 that could have exceeded the level of the first years of operation. The company instituted control measures after the 1949 study which markedly reduced the exposure.

Since no precise environmental study had ever been conducted in the early years of operation for this plant and none therefore was available, the 1949 weighted average exposures (insoluble, soluble and total chromium) were applied to all workers employed 1 year or more in the 1931-1937 cohort and the 1938-1948 cohort. (The initial exploration of the 1938-1948 cohort has been started and 9 deaths due to lung cancer and 2 cases of cancer of the sinuses have already been identified.)

The data to be presented are confined to the 1931-1937 cohort with 41 lung cancer deaths. All deaths were uniformly coded by an experienced nosologist according to the 7th Revision of the International Classification of Causes of Death.

The age adjusted mortality rate for the cohorts was calculated by the direct method using as the standard the distribution of person years by age group for the total chromate population.

RESULTS

The chromate plant under study began operations in the 1931-1932 period and we have established a cohort of all employees for the period 1931-1937, which has been followed through 1974.

Table 1 shows the number and distribution of chromate workers by the years of first employment in the chromate plant, arranged into successive cohorts, representing new employees who entered employment in the years designated, according to age at the time of first employment.

There were 332 employees in the combined cohort (1931-1937) in which 173 (over 50%) died by 1974. A higher percentage of deceased occurred in the 1931-1932 cohort, which had the longest period of observation and conversely the lower percentage of deaths occurred in the 1935-1937 cohort with the shortest period of observation.

The number of employees, as cohorts, is indeed exceptionally small (78, 154 and 100) for an epidemiological study. Nevertheless, this approach was

TABLE 1

Number of White Male Employees* in a Chromate Plant According to Age at First Employment, Successive Cohorts and Those Living and Deceased.

Age at First Employment	1931-32 Cohort		1933-34 Cohort		1935-37 Cohort		1931-37 Cohort	
	L	D	L	D	L	D	L	D
< 25	12	2	31	19	44	19	87	40
25-34	12	20	26	26	15	11	53	57
35-44	3	17	13	22	2	5	18	44
45-54	0	10	0	14	1	2	1	26
55-64	0	2	0	3	0	1	0	6
65+	0	0	0	0	0	0	0	0
Total	27	51	70	84	62	38	159	173

*Includes 3 deaths due to war casualty and 1 death without death certificate.

utilized to reflect and detect whether similar observations of a high lung cancer rate would occur among the successive new employees, who entered the same work place and were similarly exposed to the same work processes and air concentrations of chromium. Further, the observation on successive cohorts would reflect and provide some indication whether there had been any change in the nature, extent, or degree of exposure in the work place in the succeeding years, as measured in terms of similar or lesser mortality due to lung cancer. Because of the small numbers of employees in the early cohorts, a few deaths not found have more importance than usual. In this respect, the interpretation which can be made of the 1935-1937 cohort with only 7 lung cancer deaths is markedly limited.

Table 2 shows, for the successive cohorts of new employees arranged according to years of first employment, and the combined cohort (1931-1937), the ratios in percent of cancer of the lung to all deaths and to all cancers.

For the first two cohorts (1931-1932 and 1933-1934) with the longest interval of observation, the percentage of lung cancer among all cancers was 63.6 and 62.5. The 1935-1937 cohort had 58.3% and the combined cohort (1931-1937) had 62.1% lung cancer. It is evident that the lung cancer risk was higher in each of the cohorts of new employees in succeeding time periods. Not shown in the table is one case of lung cancer of a worker employed in 1934, who had a pneumonectomy (1956) and is still living.

Figure 1 shows the latent period for the 1931-1937 cohort and demonstrates the clustering of lung cancer cases at the 27-36 year latent period. This is one illustration of the importance of the long-term follow-up in industrial epidemiological studies.

TABLE 2

Ratios (in percent) of Deaths from Cancer to Total Deaths in a Chromate Producing Plant

	All Causes		All Cancers		Cancer of Lung		
	No.	Percentage	No.	Percentage	No.	Percentage of All Deaths	Percentage of All Cancers
1931-1932 Cohort	51	100.0	22	43.1	14	27.5	63.6
1933-1934 Cohort	84	100.0	32	38.1	20	23.8	62.5
1935-1937 Cohort	38	100.0	12	31.6	7	18.4	58.3
1931-1937 Cohort	173	100.0	66	38.2	41	23.7	62.1

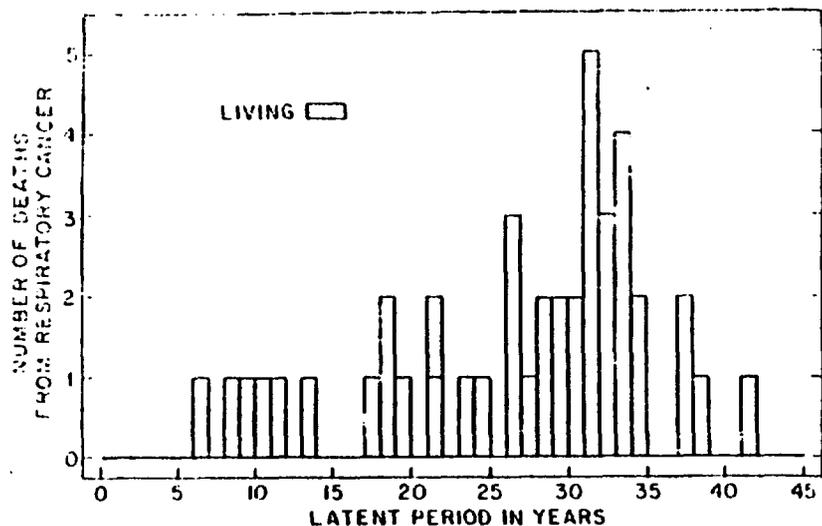


Fig. 1. Latent period for 1931-1937 cohort of new employees in plant manufacturing chromates.

Table 3 demonstrates the influence of the length in years of the period of observation of the successive cohorts, over designated periods of time, on mortality rates due to lung cancer for workers employed five years or more.

For the combined cohort (1931-1937) at less than 15 years period of observation, with a rate of 97.2 there is no reflection of the true magnitude of the excess of lung cancer risk. Yet this period, precisely 14.5 years, was the limited period of observation in the Public Health Service study of a chromite brick plant, (1953). The observation by the PHS of only one lung cancer within that period of 14.5 years has been repeatedly cited in the literature as conclusive evidence that the trivalent form of chromium was not carcinogenic (National Academy Science Review 1974).

We know, of course, that for any industrial carcinogen the magnitude of the risk is reflected over a much greater number of years of observation, because of the latent period required for the development of cancer. Although the occupational cancers may occur early, nevertheless, the largest number of cases appear after a long latent period of many years, as has been observed in asbestos workers and now is shown for chromate plant workers.

TABLE 3

Age Adjusted Mortality Rates* for Cancer of the Lung for Employees in a Chromate Plant Followed According to Designated Years of Observation for Workers Employed 5 years or more.

Years of Observation	Cohort 1931-1932		Cohort 1933-1934		Cohort 1935-1937		Cohort 1931-1937	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate
< 15	3	162.8	2	65.7	1	77.5	6	97.2
< 21	5	271.3	4	131.5	1	77.5	10	161.9
< 27	5	271.3	7	230.1	1	77.5	13	219.5
< 29	6	325.6	9	295.9	1	77.5	16	259.1
< 31	8	434.1	10	328.7	2	154.9	20	323.8
< 33	12	651.1	12	394.5	3	232.4	27	457.2
< 36	12	651.1	16	526.0	6	464.8	34	580.5
< 39	12	651.1	17	558.8				
< 43	13	705.4						

*Per 100,000.

The rates for the combined 1931-1937 cohort show, very clearly, the increasing mortality rate for lung cancer with increasing years of observation. The mortality rate observed for the period of 15 years or less was 97.2 and when the cohort was followed for 39 years, the rate (604.1) was six times greater.

When the years of observation are held constant at 36, the age adjusted mortality rates are: 651.1 for 1931-1932, 526.0 for 1933-1934 and 464.8 for 1935-1937.

Table 4 shows the mortality rate for lung cancer by age at first employment for the successive cohorts. Because the total number of lung cancer deaths was only 7 in the 1935-1937 cohort, comments are confined to the first two cohorts. (We believe our follow-up of the 1935-1937 cohort is incomplete.)

The table demonstrates that for those employed at age 25 or less at the chromate plant for the 1931-1932 and 1933-1934 cohorts, the mortality rate was high, 340.1 and 370.4 respectively. This plant began operations in the 1931-1932 period, so these workers at this young age would represent those without any prior industrial employment, who were exposed for the first time

TABLE 4

Age Adjusted Mortality Rates* for Cancer of the Lung for Employees in a Chromate Plant by Age at First Employment for Successive Cohorts Followed to 1974.

Age at First Employment	Cohort 1931-1932		Cohort 1933-1934		Cohort 1935-1937		Cohort 1931-1937	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate
< 25	2	340.1	7	370.4	3	134.3	12	254.7
25-34	8	721.4	8	438.1	3	336.7	19	496.6
35-44	2	343.6	5	485.0	0	0.0	7	382.7
45-54	2	803.2	0	0.0	0	0.0	2	314.0
55-64	0	0.0	0	0.0	1	10,000.0	1	1,136.4
65 +	0	0.0	0	0.0	0	0.0	0	0.0
All	14	544.5	20	393.8	7	203.4	41	369.7

*Per 100,000.

to the dust of chromium compounds in a plant just starting operations in a rural community. This age group provides a good index of the lung cancer risk due to exposure to chromium compounds.

For those employed at ages 25-34, the rate rose to 721.4 and 438.1 for the first two cohorts. Any further consideration must be deferred until the number of deaths in these respective age groups is enlarged by additional follow-up.

Table 5 shows the age adjusted lung cancer death rates per 100,000 by gradient of insoluble chromium exposures, from less than 0.25 milligrams per cubic meter to over four milligrams. The mortality rate has a "zero" death rate at exposure less than 0.25 milligrams and rises consistently with the increase in levels of exposure, 144.6, 174.6, 327.9, 630.7 and 649.6.

Table 6 shows the age adjusted lung cancer death rate by gradient of soluble chromium exposures. There is a corresponding rise in death rate with the rise in level of exposure. The rates were 80.2, 306.0, 441.5, 462.2 and 998.7.

Table 7 shows the age adjusted lung cancer death rate by total chromium exposure. The mortality rate has "zero" death rate at less than 0.50 milligrams of chromium per cubic meter, with an increase in rate by rise of level of exposure. There was a slight dip at the 2.00-3.99 milligrams per

TABLE 5

Age Adjusted Lung Cancer Death Rates/100,000 by Insoluble Chromium Exposures mg/m³-Years.

Insoluble mg/m ³ -Yrs.	Person Years at Risk	Number of Deaths	Age Adjusted Death Rate
< 0.25	1,399	0	0.0
0.25-0.49	1,499	2	144.6
0.50-0.99	1,708	3	174.6
1.00-1.99	2,039	7	327.9
2.00-3.99	2,409	15	630.7
> 4.00	2,037	14	649.6
Total Chromium	11,091	41	369.7

TABLE 6

Age Adjusted Lung Cancer Death Rates/100,000 by Soluble Chromium Exposure mg/m³-Years.

Soluble mg/m ³ -Yrs.	Person Years at Risk	Number of Deaths	Age Adjusted Death Rate
< 0.25	3,612	3	80.2
0.25-0.49	1,690	5	306.0
0.50-0.99	2,206	10	441.5
1.00-1.99	2,358	11	462.2
> 2.00	1,225	12	998.7
Total Chromium	11,091	41	369.7

cubic meter exposure range. The rates were 0.0, 225.7, 322.7, 255.6, 770.7 and 741.5.

Since the lung cancer death rates are related to the gradient of both the insoluble and soluble chromium, the question was posed whether the relationship was due, principally, to one form of chromium compound, either insoluble (primarily trivalent) or soluble (chiefly hexavalent).

To investigate this, the age adjusted mortality rates were calculated by classifying the workers by the levels of insoluble and by the levels of total chromium exposure. This is shown in Table 8. Within the table, it is seen that

TABLE 7

Age Adjusted Lung Cancer Death Rates/100,000 by Total Chromium Levels.

Total Chromium mg/m ³ -Yr.	Person Years at Risk	Number of Deaths	Age Adjusted Death Rates
< 0.50	2,051	0	0.0
0.50-0.99	1,558	3	225.7
1.00-1.99	1,758	6	322.7
2.00-3.99	2,336	6	255.6
4.00-5.99	1,397	10	770.7
> 6.00	1,991	16	741.5
Total Chromium	11,091	41	369.7

TABLE 8

Age Adjusted Lung Cancer Death Rates/100,000 by Insoluble Chromium and Total Chromium Exposures in mg/m³-Years.

Mg/m ³ -Yrs. Total Insoluble	Total Chromium						All Levels Total Insoluble
	< 0.50	0.50-0.99	1.00-1.99	2.00-3.99	4.00-5.99	> 6.00	
< 0.25	0.0						0.0
0.25-0.49	0.0	309.1					144.6
0.50-0.99		135.2	198.1				174.6
1.00-1.99			451.4	260.4			327.9
2.00-3.99				260.5	904.7	1,732.5	630.7
> 4.00					284.7	683.7	649.6
All Levels Total Chromium	0.0	225.7	322.7	255.6	770.7	741.5	369.7

Blank cells indicate no person years at risk.

for a fixed level of insoluble chromium—example: 0.50-0.99—the lung cancer risk appears to increase as the total chromium increased. In spite of the relatively small numbers of person years at risk and the number of lung cancer deaths in individual cells in the table, this result is consistent for all insoluble levels, except one (1.00-1.99 mg/m³ yr.).

In essence, the data in Tables 5 to 8 are consistent with the lung cancer risk being a function of both the soluble and insoluble chromium; i.e., to total chromium rather than to one class of chromium compound.

In Table 9, which shows the age specific death rates by gradient of exposure to chromium, there is an increase by age group: 528.7 for age 45-54, 685.2 for age 55-64, and 1,088.3 for age 65-74.

Further, although the numbers are small in each cell, there is a pattern of increasing death rates by increasing level of total chromium for each of the age groups.

Comprehensive data on the deposition of chromium in every type of tissue from former chromate workers have been developed and will be presented as a separate report.

Table 10 is confined to the chemical analyses of the lungs and shows, for six deaths due to lung cancer, the level of chromium remaining in the lungs according to the time interval since last exposure to chromium, ranging from 15 months to 16 years and 3 months. It is readily apparent that there is an extensive deposition of chromium in the lungs retained over long periods

TABLE 9

Age Specific Rates Per 100,000 for Cancer of the Lung for Age Groups 45-54, 55-64, and 65-74 by Gradient Exposure to Total Chromium.

Mg/m ³ -Yr.	Age Group 45-54							Total
	< 1.00	1.0-1.99	2.0-3.99	4.0-5.99	6.0-6.99	7.0-7.99	8+	
Deaths	1	2	2	4	3	3	0	15
Person Years	886	459	583	348	159	140	262	2,837
Rate	112.9	435.7	343.1	1,149.4	1,886.8	2,142.9	0.0	528.7
Age Group 55-64								
Deaths	1	3	1	4	2	3	1	15
Person Years	707	356	462	250	113	98	203	2,189
Rate	141.4	842.7	216.5	1,600.0	1,769.9	3,061.2	492.6	685.2
Age Group 65-74								
Deaths	1	1	2	1	1	0	3	9
Person Years	235	166	182	80	42	0	81	827
Rate	425.5	602.4	1,098.9	1,250.0	2,381.0	0.0	3,703.7	1,088.3

TABLE 10

Chemical Analysis by Interval Since Last Exposure to Chromium.

Interval Since Last Exposure	Case No. 1	Case No. 2	Case No. 3	Case No. 4	Case No. 5	Case No. 6
	15 Mos.	3 Yrs. 5 Mos.	8 Yrs. 9 Mos.	10 Yrs.	14 Yrs.	16 Yrs. 3 Mos.
Lung (Pneumonectomy And Biopsy)					Lung W/Tumor	
Right Lung	156.0 155.0		1575.0 975.0	78.7	429.0 514.0	337.0 227.0 117.0
With Tumor Left Lung	312.0 330.0	330.0 380.0 456.0	0.94 450.0 250.0 625.0		63.2 4.1	11.7 46.9 68.5 -114.0 21.4 39.1 57.2 141.0
With Tumor Bronchus			1450.0			

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of time. In control analyses, the lung showed 3.0 micrograms of chromium per 10 grams of tissue.

The table provides adequate confirmation of the hypothesis expressed by Mancuso and Hueper, relative to the retention of chromium, its slow release and the development of lung cancer.

We did find high levels of chromium in the testicle among chromate plant workers, which confirms the animal experimental observation of Hopkins (1965), who found a dramatic uptake of trivalent chromium in the testes. We have also noted a high level of chromium in the adrenal and this may be important in the consideration of the cancer mechanism.

We also have analyzed the chromium content of the lung of a chrome plater at the time of biopsy and found 58 micrograms per 10 grams of tissue. Subsequently, he died of lung cancer.

CONCLUSION

The study demonstrated a high lung cancer risk among new employees entering the same chromate plant and work exposure in successive time periods (1931-1932, 1933-1934, 1935-1937).

Epidemiological evidence is provided that the carcinogenicity of chromium includes the insoluble form of chromium.

The data indicate that the carcinogenic potential extends to all forms of chromium and is directly related to the total amount of chromium taken into the respiratory system.

The national cancer impact of exposure to chromium should be reassessed.

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THE LONG-TERM HEALTH OF TETRAETHYL LEAD WORKERS

T. R. Robinson, M.D., I.M.D.

Plant Medical Director

Ethyl Corporation

P.O. Box 341

*Baton Rouge, Louisiana, 70821, U.S.A.**

ABSTRACT

A mortality study with a 100% 20-year follow-up showed a death rate 26% lower for tetraethyl lead (TEL, an antiknock additive for gasoline) workers than for the general population, with no unusual causes of death. A study of absences from work due to illness among TEL workers with 20 or more years of service showed no statistically significant differences from a matched control group of non-TEL workers, either overall or in disease categories. Other medical data (primarily from periodic medical examinations) on these same workers showed no appreciable differences. The conclusion is drawn that the TEL workers at the facility studied have not suffered detectable impairment of their health as a result of their occupation.

RÉSUMÉ

Une étude de la mortalité due au plomb-tétraéthyle, utilisée comme additif dans l'essence, a permis de suivre pendant 20 ans 100% d'un échantillon. Nous avons trouvé que le taux de mortalité chez les ouvriers en contact avec ce produit était inférieur de 26% à celui de la population générale si l'on exclut les causes normales de décès. L'étude de l'absentéisme pour raisons de maladies chez les ouvriers en contact avec le produit et ayant au moins 20 ans de service n'a pas dégagé de différence significative par rapport à un groupe témoin d'ouvriers d'un autre secteur, que ce soit au niveau de toutes les absences ou de celles dues à une maladie au sens strict. Des données médicales portant sur les mêmes ouvriers et provenant essentiellement d'examen périodiques n'ont pas montré de différences appréciables. Nous concluons donc que les ouvriers en contact avec le plomb tétraéthyle, à l'usine étudiée, n'ont pas souffert de problèmes décelables qu'aurait causé ce produit.

Tetraethyl lead (TEL) has been produced as an antiknock additive for gasoline for about 50 years. The marked potential of the TEL and the

*Present address: Medical Director, Chicago Manufacturing Company, Gamewell, Chicago 30501, U.S.A.

APPENDIX IV

Industrial Hygiene Study of Plant in Mancuso Study

Occupational Cancer in a Chromate Plant —An Environmental Appraisal—

H. G. BOURNE, JR., and H. T. YEE,
Division of Industrial Hygiene, Ohio Department of Health,
Columbus, Ohio

IN 1948, Machle and Gregorius reported¹ the crude death rate for cancer of the lung among workers in seven United States plants engaged in the extraction of chromates from ore as 25 times the normal. They suggest that monochromates may be the compounds responsible.

With the object of adding to the knowledge of the role of chromium compounds in the incidence of respiratory cancer, epidemiological and environmental studies were conducted by the Ohio Department of Health in a single plant manufacturing sodium bichromate from chromite ore. A mortality study by Mancuso² revealed that the proportion of deaths from cancer of the respiratory system to that of all employee deaths in this plant was 14.7 times that in a non-exposed control group. The environmental phase presented here was undertaken to ascertain as far as possible the specific chromium compounds and magnitude of exposure experienced by workers according to their occupation and location.

Although a maximum allowable concentration of chromic acid and chromates was approved³ in 1943, the role of chromium compounds as carcinogenic agents was not suggested in this country until 1948. There is no useful guide at present by which one may compare the carcinogenic hazards associated with exposure to specific concentrations of chromium compounds. Monochromates, as has been suggested, may be the causative agents, yet the evidence is fragmentary and one cannot exclude at the present time elemental chromium (Cr^{0}), trivalent (Cr^{+3}), or bichromate which also has a valence of +6. Therefore, the atmospheric chromium concentrations reported are expressed in terms of chromium ion, a departure from the customary industrial hygiene procedure in which concentrations are expressed in terms of chromic acid (CrO_3). Adopting this method of expression avoids the inference of implicating any specific chromium compounds for cancerous reactions.

The plant in which this study was undertaken has been in operation since 1932. In order to meet price and quality competition, improve-

ments in equipment and processes have been made periodically during the past 18 years, and it is the universal experience of industrial hygiene personnel that greater process efficiency is almost invariably associated with a more healthful working environment. Therefore, there seems little doubt that atmospheric contamination in the past was greater than in early 1949 when the present work was commenced. Later in the same year the company initiated a comprehensive program designed further to improve the manufacturing efficiency and to reduce the exposure of the employees. Thus it is evident that the concentrations which have been recorded do not represent a static condition but only the situation prevailing during the first half of 1949.

The mean latent period for respiratory cancer in the chromate producing industry, according to Machle and the German literature, is approximately 15 years. Thus any present relationship between environmental exposure and incidence of cancer in the plant under study must be predicated on the assumption that the concentrations which are reported are probably the minimum values attained in the past 15 years.

Raw Material

CHROMITE ($FeO \cdot Cr_2O_3$), lime, soda ash and sulfuric acid are the raw materials commonly used for the manufacture of sodium bichromate.⁴ Typical proximate analyses of two South African ores,⁵ the country of origin of the ore used by the plant under study, are shown in Table 1.

Table 2 gives a spectrographic analysis of a sample of ore dust obtained from the ore preparation department.

TABLE 1.
PROXIMATE ANALYSIS TYPICAL SOUTH AFRICAN
CHROMITE ORE

Country	Percentage					
	Cr ₂ O ₃	FeO	Al ₂ O ₃	SiO ₂	MgO	CaO
Rhodesia	51.1	11.4	15.2	4.8	12.7	0.9
Transvaal	45.6	25.8	14.5	1.1	11.9	trace

TABLE 2.
SPECTROGRAPHIC ANALYSIS OF A CHROMITE ORE

Element	Percentage	Element	Percentage
Aluminum	0.1 — 0.01	Magnesium	> 2.0
Calcium	0.1 — 2.0	Manganese	0.01 — 0.001
Cadmium	?	Sodium	< 0.001
Cobalt	0.01 — 0.001	Nickel	0.01 — 0.001
Chromium	>> 2	Phosphorus	0
Copper	< 0.01	Lead	0
Iron	0.1 — 2.0	Silicon	0.1 — 2.0
Potassium	0	Titanium	< 0.01
		Vanadium	0.01 — 0.001

EDITOR'S NOTE: This engineering material, dealing with the environmental background leading to chromium exposures, is to be followed by a report of clinical investigation. This report is not immediately available for examination and publication. While these present engineering data embrace several chromium compounds, it will not necessarily follow that all may act or act equally as carcinogens.]

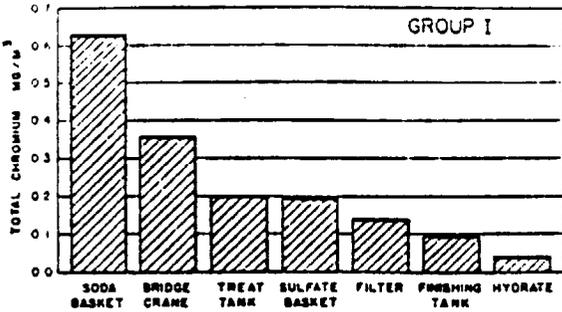


Fig. 2.

Weighted exposure according to occupations having Cr⁺³:Cr⁺⁶ ratio of 1 or less. Sodium bichromate and sulfate centrifuges are known in company nomenclature as soda and sulfate baskets respectively

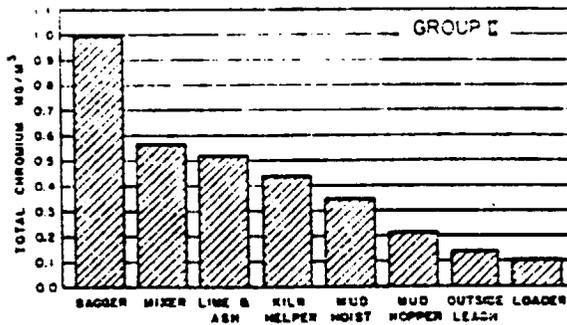


Fig. 3.

Weighted exposure according to occupations having Cr⁺³:Cr⁺⁶ ratio of 1.1 to 4.9

in Fig. 1. The values are based on 121 samples collected by the filter paper technique and analyzed using the polarographic method. The rate of air flow was measured with an orifice-variable area meter.¹⁰

Exposure of Production Workers by Occupations

ON THE basis of company employment classifications, observation of work performed and degree of exposure as estimated by visual observation, the 128 production workers were grouped into 21 occupational classifications. One or more representative individuals of each occupation were then time-studied for eight-hour periods, and the data so obtained were applied by a method described in the literature¹¹ to arrive at a weighted average eight-hour daily exposure. From the weighted exposures the ratio of Cr⁺³:Cr⁺⁶ was also computed for each occupational classification.

On the basis of Cr⁺³:Cr⁺⁶ ratio, the 21 work classifications were sorted into three groups. Group I has a ratio 1.0 or less. It contains the individuals processing sodium monochromate and bichromate liquor and those required to work in close physical proximity to such operations. Their exposure in total chromium is shown in Fig. 2. Group II with a ratio greater than 1 and less than 4.9 (Fig. 3) appears to have a distinctly dual exposure, i.e., sodium monochromate and ore dust; shippers (bagging, loading) are exposed to bichromate and ore. Group III, whose ratio is 4.9 or greater (Fig. 4), comprises occupations primarily exposed to trivalent chromium. It should be pointed out that while the average Cr⁺³:Cr⁺⁶ ratio for all kiln operators is 7, for those whose work location adjoins the filtering department it is 1.4. Therefore, these particular operators might be included in Group II.

Distribution of Maintenance Workers' Time

THE 76 maintenance workers comprised approximately 30% of the total plant personnel, and observation of the conditions under which much of their work was performed indicated a

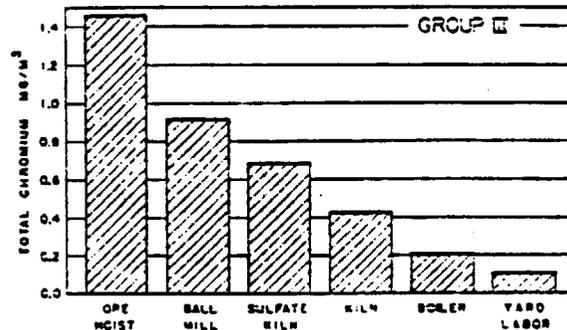


Fig. 4.

Weighted exposure according to occupations having Cr⁺³:Cr⁺⁶ ratio of 5 or more

potentially high degree of exposure. It was deemed necessary, therefore, to time study this group as thoroughly as the production workers.

Obviously, the nature and location of repair work is non-repetitious and must be performed as the occasion demands. A time study similar to that used for production workers could not be properly applied to maintenance personnel; hence a different approach became necessary.

Using the cost of maintenance labor over a year's time as charged to each department by the company accounting office the average man-hours of maintenance expended in each department per day were calculated. Based on the records of the maintenance superintendent and types of process equipment repaired and installed, man-hours maintenance according to crafts were then ascertained for each department. Since time charged to a specific work order might involve work in both the plant and the maintenance

TABLE 4. DISTRIBUTION OF MAINTENANCE TIME BY CRAFTS

Craft	Preparation	Work	Shipping	Other	Total
Welders	1.5	1.5	1.5	1.5	6.0
Electricians	1.5	1.5	1.5	1.5	6.0
Mechanics	1.5	1.5	1.5	1.5	6.0
Painters	1.5	1.5	1.5	1.5	6.0
Boilers	1.5	1.5	1.5	1.5	6.0
Makers	1.5	1.5	1.5	1.5	6.0

building, further adjustments were necessary.

In Table 4 the time distribution of five crafts according to selected departments is shown as an example.

Exposure of Maintenance Workers

UNLIKE production employees, maintenance workers seldom work under normal conditions in a plant. The work necessary to complete their assignments almost invariably results in abnormally high local exposures. The plant under study is no exception since it was observed huge volumes of dust were generated during the repair and cleaning of dust collectors, process equipment or building structure overlaid with an accumulation of dust. It is thus logical to assume the maintenance group receives, in most instances, a greater exposure than production workers.

In Table 5 a minimum and maximum weighted

TABLE 5.
EXPOSURE OF MAINTENANCE EMPLOYEES BY CRAFTS

Craft	Weighted Average 8 Hour Exposure, mg/m ³ Total Cr Cr ⁺³ :Cr ⁺⁶ *		ratio
	Minimum	Maximum	
Handy Men	1.15	1.62	27.8
Millwrights	0.66	3.34	7.5
Maintenance Superintendent	0.55	2.13	4.5
Electricians	0.48	5.67	3.0
Boilermakers	0.44	4.43	2.4
Painters and Riggers	0.42	1.52	4.3
Oilers	0.41	1.94	2.2
Pipefitters	0.28	2.31	2.1
Carpenters	0.27	0.43	3.5
Welders	0.23	2.20	4.8
Machinists	0.07	0.13	6.0
	$\bar{x} = 0.45$	2.32	

average exposure derived from time study and concentrations, as well as Cr⁺³:Cr⁺⁶ ratio, of maintenance employees by crafts are shown. The minimum levels are based on average departmental concentrations measured under normal operating conditions, and the maximum levels are reported on the basis of the highest concentration recorded in each department.

Exposure of Administrative and Technical Personnel

THE administrative and technical staffs together constituted only a small minority of the plant's personnel, accounting for the remaining 21 of the 226 plant employees. With the exception of the plant superintendents and supervisors, this group's work was largely carried out in an office building situated nearby the production buildings, and it is believed their exposure is the result of infiltrated air and contaminated apparel. Grinding and handling

TABLE 6.
EXPOSURE OF ADMINISTRATIVE AND TECHNICAL PERSONNEL

Occupation	Weighted Average 8 Hour Exposure, mg/m ³ Total Cr	Cr ⁺³ :Cr ⁺⁶ ratio
Superintendents	0.18	3.5
Plant Supervisors	0.63	3.2
Office Workers	0.06	5.0
Laboratory Personnel	0.27	17.0

samples in the course of making control analyses undoubtedly account for the higher exposure of laboratory personnel (Table 6).

Conclusions

ALTHOUGH the environmental investigation presented here pertains to a single plant, it is believed that the conclusions that follow may be applied to other plants manufacturing sodium bichromate from chromite ore.

1. Where unit operations are not isolated or adequate dust and mist control established employees may be subjected to a dual exposure, i.e., trivalent chromium (chromite) and hexavalent chromium (chromates). In the plant studied the predominant exposure, based on both magnitude of chromium concentration and number of employees, was to the trivalent compound.

2. In the plant studied, all employees were exposed to measurable amounts of chromium. The lowest concentration which is carcinogenically significant is yet to be determined.

3. Observations during the course of this study convince the authors that the carcinogenic hazard in the chromate producing industry can be controlled successfully by utilizing industrial hygiene engineering methods employed in the safe handling of other toxic chemicals, i.e.:

(a) Undertake through adequate ventilation the control of dust and mist with the ultimate goal of securing the minimum concentration consistent with good engineering practice. Removal of toxic matter from air exhausted to the out-of-doors is essential to prevent a neighborhood public health hazard.

(b) Isolate dust and mist contributory operations, and mechanize where practicable to reduce the number of employees exposed.

(c) Provide under positive pressure uncontaminated air to personal services and process observation rooms or locate such rooms in uncontaminated areas.

(d) Insure good house-keeping by proper building design and adequate janitor services.

(e) Educate employees in personal hygiene and acquaint them with provisions made for their safety.

(f) Supply personal respiratory protective devices approved by the U. S. Bureau of Mines.

4. Establish laboratory facilities and provide technical personnel to measure the concentration of air-borne chromium compounds. Current knowledge of the degree of atmospheric contamination will provide an index of the effectiveness of the control measures as well as directing attention to sources of pollution that have been overlooked.

ACKNOWLEDGMENT: This project was supported by a cancer control grant from the National Cancer Institute, U. S. Public Health Service, CS-437. THOMAS P. MANCUSO, M.D., Project Director.

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That Tired Feeling

THE STATE of being tired is experienced by almost everyone at some time or other. It is a natural feeling at the end of a hard working day, but one that is supplanted with new energy after a refreshing sleep. The fatigue that is always present is the fatigue brought about by a long period of overwork, or late hours with little rest, or meals that do not provide the fuel necessary to maintain the machinery of the body. The maximum of production cannot be obtained from long hours of overwork. Efficiency is lessened to the degree that a worker comes to his job as tired as he left it the night before. The physical fatigue resulting from overwork, either mental or physical, is responsible for the saying "too tired to eat." The body needs fuel, it needs to replenish its stock of energy with energy-producing foods, and this can be done by means of a well-balanced diet. Sugar is needed to combat fatigue. When the blood sugar is depleted, many cases of fatigue and tiredness occur, even to the point of collapse. Numerous conditions stem from fatigue. Again fatigue may stem from various diseases, infection, improper hygiene, too much mental effort, inadequate nutrition. Many accidents can be charged to fatigue. For that tired feeling in the overworked person, a change of hours is recommended. There should be a shorter working day and a brief spell of relaxation, as recreation is important. For exhaustion in a nervous person, it has been found that complete rest in bed aggravates rather than relieves the condition, particularly for chronic nervous exhaustion. Such a person should be encouraged to carry on consistently from day to day, if only in a limited way. In general, however, rest is the best treatment for all types of fatigue. Physical activity should be decreased as much as possible, and such stimulants as coffee, tea and "cokes" should be abandoned or, at least, the use of them curtailed. Consult your doctor. He is the person to investigate the reasons for your fatigue. If a glandular disturbance is responsible, he will detect it. Self-medication won't help. Let your doctor lead you into a balanced social and business way of living. The fatigued person is one who, in his tired state, contributes little to his own enjoyment and nothing to that of any one else. Time passes too quickly to be too tired to enjoy its interest.

—Educational Committee, Illinois State Medical Society, *Health Talk*, November 2, 1950.

APPENDIX V

Comparison of Risk Estimates from Mancuso Study
and Inhalational Bioassays

In earlier documents DHS has attempted to estimate whether cancer risk estimates based on animal bioassays were compatible with those based on the results of epidemiologic investigations. In this instance the animal bioassays from which estimates of dose would be derived - i.e., the inhalation studies, showed no significant response among exposed animals (with the possible exception of the study by Nettesheim et al., 1971. See below.) Thus, in order to compare the results of risk estimates between species, one would have to calculate the lower confidence interval of the slope predicted by the epidemiologic model and compare it with statistical upper confidence limit on one or more of the animal studies. Unfortunately, none of the animal studies was conducted in anticipation of a risk assessment and the data are not reported in a format readily usable toward that end. The inhalational studies are summarized in Table A-V-1.

TABLE A-V-1: CANCER BIOASSAYS FOR
CHROMIUM COMPOUNDS ADMINISTERED BY INHALATION

<u>Study</u>	<u>Compound</u>	<u>MHAD</u> ¹ (<u>µm</u>)	<u>Concentration</u> ² (<u>mg/m³</u>) ³	<u>Duration</u> <u>of</u> <u>Exposure</u>	<u>Animals</u>	<u>Number</u> <u>Exposed</u>	<u>Results</u>
Baetjer et al., 1959	Mixed chromate dust	0.8	0 0.6-1.2	4 hr/day, 5 days/wk for 16-46 wks	Strain A Mice	241	N.S. ³ , although at pulmonary adenomas appeared at younger ages.
Baetjer et al., 1959	Mixed chromate dust	0.8	0 0.6-1.2	4 hr/day, 5 days/wk for 39-58 wks	Swiss Mice	148	N.S. ³ , although pulmonary adenomas appeared at younger ages.
Baetjer et al., 1959	Mixed chromate dust	0.8	0 0.6-1.2	4 hr/day, 5 days/wk for 41-62 wks	C57BL Mice	111	N.S. ³ , although pulmonary adenomas appeared at younger ages.
Baetjer et al., 1959	Mixed chromate dust	0.8	0 0-13	1/2 hr/day for 20 wks	Strain A Mice	36	N.S. ³
Baetjer et al., 1959	Mixed chromate dust	0.8	0 0-13	1/2 hr/day for 43-52 wks	Swiss Mice	25	N.S. ³
Baetjer et al., 1959	Mixed chromate dust	0.8	0 1.2-1.7	4 hr/day, 5 days/wk for up to 151 weeks	Mixed strain rats (Wistar/ McCollum)	100	4 exposed rats de- veloped lymphomas versus one of of 85 control rats (but see below) below)
Staffer and Baetjer, 1965	Mixed chromate dust	0.8	0 1.6-2.1	4 1/2 hr/day, 4 days/wk for	Wistar rats	70	N.S. ³

TABLE A-V-1 (cont'd)

<u>Study</u>	<u>Compound</u>	<u>MHAD</u> ¹ (<u>µm</u>)	<u>Concentration</u> ² (<u>mg/m</u>) ³	<u>Duration</u> <u>of</u> <u>Exposure</u>	<u>Animals</u>	<u>Number</u> <u>Exposed</u>	<u>Results</u>
Steffee and Baetjer, 1965	Mixed chromate dust plus chromate mist	0.8	@ 1.6-2.1	4-5 hr/day, 4 days/wk for 40-50 months	Rabbits	8	N.S. ³
Steffee and Baetjer, 1965	Mixed chromate dust plus chromate mist	0.8	@ 1.6-2.1	4-5 hr/day, 4 days/wk for 40-50 months	Guinea Pigs	50	N.S. ³
Nettesheim et al., 1971	Calcium chromate dust	< 1	@ 4.33	5 hr/day, 5 days/wk for life	C57BL/6 Mice	@272	Authors reported 14 adenomas in exposed versus 5 in control animals. Statistical signi- ficance is indeter- minate (See text).

1. Mean mass aerodynamic diameter

2. Concentration as chromium

3. No significant increase in tumor incidence in exposed versus control animals.

The results of the bioassays conducted by Baetjer et al. (1959) are presented in a variety of ways (including percentage of mice surviving to the end of the experiment with lung tumors, average number of lung tumors in tumor-bearing and all surviving mice, and percentage of tumor-bearing mice with multiple lung tumors), none of which would allow a calculation of the number or percentage of experimental mice at risk that developed lung tumors at a given dose level. For the rats in this experiment, 4 of 100 exposed animals developed lymphosarcomas at various sites, while 1 of 85 control rats did, a difference which is not statistically significant. However, the authors noted that "experiments were not designed to study pathological changes in the tissues other than the lungs." Thus, limiting the findings to pathologic changes in the lungs, there was one lymphosarcoma originating in the lungs of an exposed rat and none in the control animals. Since spontaneously occurring lymphosarcomas are not uncommon in rats, Baetjer et al. (1959) repeated the experiment (reported by Steffee and Baetjer, 1965).

In the second study, Steffee and Baetjer (1965) were unable to replicate their earlier results. Under similar experimental conditions 4 of 78 exposed Wistar rats compared with 4 of 75 controls developed lymphosarcomas involving the lungs. It was not stated whether these were primary tumors or pulmonary metastases. Three exposed rats developed alveologenic adenomas, while two controls did. Steffee and Baetjer (1965) also exposed eight rabbits to chromate dust, none of which developed any pulmonary tumors. Of fifty exposed guinea pigs, three developed alveologenic adenomas, compared with none in control animals, while one of each group had a lymphosarcoma involving the lungs.

Finally, Nettesheim et al. (1971) reported that C57BL/6 mice exposed to calcium chromate for 5 hours/day, 5 days/week for life showed an increased incidence of pulmonary adenomas and adenocarcinomas. This conclusion was based on the authors' observation that fourteen animals exposed to calcium chromate (eight females and six males) developed adenomas, whereas only five control animals did (two females and three males). As noted on page 48 of the main text of this document, the conclusions of Nettesheim et al. cannot be confirmed from the reported data. The authors' statistical methodology was not reported. The denominator--numbers of controls and exposed animals at risk--cannot be precisely ascertained from the published report. The experimental design involved exposure of 1,090 C57BL/6 mice in 2 inhalation chambers (545 mice, 272 males and 273 females/chamber). All the mice in one chamber were infected with influenza virus two weeks prior to the initiation of calcium chromate exposure. Half the mice in each chamber were subjected to 100 R whole-body X radiation four weeks prior to exposure. The gender distribution of the irradiation pre-treatment was not specified: One might guess that roughly equal numbers of males and females were irradiated, but the exact numbers of chromium - exposed animals not subjected to either of these pre-treatments were not reported. Furthermore, at 6, 12, and 18 months into the experiment, 15 mice (pre-treatment status and sex not reported) were removed from each chamber for microbiological testing and histopathological investigation. Three to four percent of the animals that died during the experiment were cannibalized and were thus unavailable for necropsy (distribution between control versus exposed animals and pretreatment status were not given). Thus the numbers of animals exposed only to calcium chromate dust and the periods of exposure can be conjectured but not identified with certainty.

Other difficulties with this bioassay include the following:

1. During the first half of the experiment the mortality rate of the control mice was substantially higher than that of the chromium - exposed mice, attributed by Nettesheim et al. to an epidemic of "urogenital disease" in the former. Until about 70 weeks into the experiment the cumulative mortality of the control mice was about twice that of the treated group, and the cumulative mortality curves (the data were only reported graphically) crossed only after more than 100 weeks of exposure. No data on the cumulative mortality by gender were presented. Although Nettesheim et al. were aware of the non-tumor-related early mortality in the controls, they did not correct for it in the statistical analysis.
2. Both alveologenic adenomas and adenocarcinomas were reported to have occurred. However, the distribution of these tumor types by gender and by exposure status was not reported.

Thus, for purposes of cancer risk assessment, the study of Nettesheim et al. is clearly inadequate. However, to respond to the request of SRP member Dr. Joyce McCann to evaluate the compatibility of risk estimates based on animal inhalation versus human studies, DHS staff members have selected to use this study because (1) the number of exposed animals was larger than in any of the others; (2) there may be an exposure-related increase in tumors; and (3) the animals' exposure lasted until they died, whereas the other above-noted experiments were terminated prior to the demise of all the animals.

To calculate upper confidence intervals for risks from this study, DHS staff members did the following:

(1) Assumed that the number of animals initially at risk in the experimental and the control groups was 250. (1,090 total mice minus 545 infected with influenza, minus $545/2 \approx 273$ subjected to X radiation, minus $45/2 \approx 23$ serially sacrificed during the course of the experiment. Most of the latter were removed prior to the appearance of the first tumor in either group.)

(2) Corrected for early mortality by subtracting from the numbers of animals at risk those that had died prior to the appearance of the first adenoma. (Since the cumulative mortality and the time to first tumor were presented in graphical form only, this correction was of necessity somewhat crude.) Corrected numbers were 164 controls and 222 exposed mice.

(3). Combined tumor incidence for both sexes in each group, since the cumulative mortality data were not displayed by gender. Total numbers of animals with tumors were five controls and fourteen exposed mice.

(4) Calculated average daily dose to be compatible with the human dose units used in the risk assessment as follows: $4.33 \text{ mg/m}^3 \times 5/24 \times 5/7 = .66 \text{ mg/m}^3$, where the latter two numbers correct for the fractional daily and weekly exposures of the animals. Since there are only two dose groups (control = 0 and exposed = $.66 \text{ mg/m}^3$), the dose-response curve is linear and the slope of the curve equals the carcinogenic potency.

(5) Used these values in the linearized multistage model of Crump and Rose, GLOBAL 82, which calculated maximum likelihood estimates and 95% upper confidence intervals on the slope of the dose-response curve.

The maximum likelihood estimate of the slope (q_1) is 0.052 and the upper 95% confidence limit (UCL) on the slope (q_1^*) is $0.11 \text{ (mg/m}^3\text{)}^{-1}$. Converting to nanograms gives a 95% UCL of $1.1 \times 10^{-7} \text{ (ng/m}^3\text{)}^{-1}$. To compare this with the dose-response curve derived from the Mancuso study, the lower confidence limit on the SMR was calculated using method of Liddell (1984).^{*} This yielded a slope of $9.3 \times 10^{-6} \text{ (ng/m}^3\text{)}^{-1}$. Thus, there is a difference of almost two orders of magnitude between the lower confidence limit on the slope of the risk estimate derived from the Mancuso study and the upper confidence limit on that derived from the largest animal study by Kettesheim et al. As noted in the text of part B, this discrepancy may be due to a variety of factors, including differential species sensitivity to carcinogenesis, differences in delivered dose to susceptible tissues, and so forth. It is not possible to provide a compelling explanation for this discrepancy.

* The SMR for lung cancer in the Mancuso study was 7.2, based on 35 observed cases where 4.86 were expected. The potency or slope is $1.44 \times 10^{-5} \text{ (ng/m}^3\text{)}^{-1}$. (See section 8.3.6.2 for calculation.) The lower limit on the SMR obtained by the method of Liddell (1984) was 5.0 and the corresponding potency or slope was $9.3 \times 10^{-6} \text{ (ng/m}^3\text{)}^{-1}$.

PART C - PUBLIC COMMENTS AND RESPONSES

NOTE:

All information which was submitted as supporting documentation for public comments on the draft Report has been forwarded to the Scientific Review Panel. However, in some cases, supporting documents have not been included here because of their length. The cases where this has been done are indicated in the report, and where a summary was provided it has been included. These documents are available upon request from:

Toxic Pollutants Branch
California Air Resources Board
ATTN: Chromium
P. O. Box 2815
Sacramento, CA 95812



ITT CORPORATION

April 29, 1985

Mr. William Loscutoff
California Air Resources Board
P. O. Box 2815
Sacramento, CA 95812

Dear Bill:

Subject: Part B "Health Effects of Chromium" Report

On page 25 of the "Health Effects of Chromium" report, dated February 1985, the EPA Model, or "crude" model is described.

$$B = [(R-1) \times P_0] / d \quad (1)$$

where B = Potency per Unit Dose
R = Relative Risk of Cancer
P = Background Mortality Rate
d = "Lifetime averaged exposure concentration"

Subsequently, P(L,d), the "excess lifetime probabilities of lung cancer for a given dose of chromium" is defined as:

$$P(L,d) = 1 - \exp(-Bxd) \quad (2)$$

If I substitute (1) into (2), I get:

$$P(L,d) = 1 - \exp[-(R-1)P_0] \quad (3)$$

which is independent of dose.

I think something needs to be clarified here. The units of "potency" and dose seem to be different than in standard usage. There is an implicit use of dose in determining R, the relative risk of cancer, since that will be dose-dependent. The problem, however, probably lies in the use of "d" to mean two different things: In the first equation, d and R are

Received
MAY 3 1985
L. W. H. J.

Mr. William Loscutoff
April 29, 1985
Page 2

IT CORPORATION

used to calculate B. The best estimate of B is then used in the second equation to predict an incremental probability due to some observed ambient chromium concentration.

Incidentally, when Bxd in (2) is small, as it will be for airborne chromium, the power series expansion of the negative exponential will lead to:

$$P(L,d) = Bxd \quad (2a)$$

which is linear in dose. This really is the model I think you end up with on page 28.

Feel free to call if there are any questions.

Very truly yours,

Nick

R. Nichols Hazelwood, Ph.D.
Environmental Affairs
Director of Programs

RNH:vh

AIR RESOURCES BOARD

1102 O STREET
BOX 2815
SACRAMENTO, CA 95812



June 18, 1985

R. Nichols Hazelwood, Ph.D.
Environmental Affairs
Director of Programs
IT Corporation
23456 Hawthorne Blvd.
Torrance, CA 90509

Dear Dr. Hazelwood:

Comments on the Draft Chromium Report

Thank you for your comments and suggestions on the Draft Chromium Report. We have referred your comments to the Department of Health Services (DHS) for response. Your comments, their responses, and this letter will be included in Part C of the Report to the Scientific Review Panel. We will send you a copy of that report.

If you have any questions concerning this matter, you may contact Cliff Popejoy at (916) 323-8503.

Sincerely,

A handwritten signature in cursive script that reads 'William V. Loscutoff'.

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

cc: Peter D. Venturini

McCLINTOCK, KIRWAN, BENSHOOF, ROCHEFORT & WESTON
ATTORNEYS AND COUNSELORS AT LAW
611 WEST SIXTH STREET SUITE 2100
LOS ANGELES, CALIFORNIA 90017
TELEPHONE (213) 623-2322

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May 10, 1985

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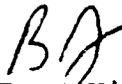
Mr. William Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
1102 Q Street
Sacramento, California 95814

Re: Listing of Chromium as a Toxic Air Contaminant

Dear Bill:

Enclosed are the comments of the Metal Finishing Association of Southern California to the Report to the Scientific Review Panel on Chromium.

Very truly yours,



Betty-Jane Kirwan, P.C.
McCLINTOCK, KIRWAN, BENSHOOF,
ROCHEFORT & WESTON

BJK:vb
Enclosure

MAY 13 1985
3:00

COMMENTS
ON BEHALF OF
THE METAL FINISHING ASSOCIATION OF SOUTHERN CALIFORNIA
ON THE
REPORT TO THE SCIENTIFIC REVIEW PANEL ON CHROMIUM
May 13, 1985

The Metal Finishing Association of Southern California ("MFASC" or "Association") is a nonprofit trade association of companies in the fields of metal finishing, electroplating, powder coatings, enameling, galvanizing, plating and related processes. It has almost 250 members, the vast majority of whom are job shops.¹ These comments are submitted in response to the Report to the Scientific Review Panel on Chromium prepared by the Air Resources Board and the Department of Health Services, dated March 1985. In general, after a careful review of the Report, the MFASC believes that not enough is known concerning the health effects of chromium emissions, in general, and chromium (VI) emission, in particular, to warrant regulation at this time. Unfortunately, the Association cannot offer further comment on the health impact of chromium emissions because it has not conducted independent research on this topic. In the remainder of these comments, we will highlight some confusions and inaccuracies in the Report as it relates to the metal finishing industry with the hope that a more accurate picture of the

¹ This is in contrast with captive corporate metal finishing companies.

industry and its emissions can be developed by a cooperative effort between the ARB and the industry.

Our review of the Report found five problem areas: (1) the Report incorrectly estimates the number of chrome platers; (2) the Report incorrectly assumes all chrome plating is hard chrome; (3) the Report incorrectly assumes that the emissions from the Long Beach Naval Shipyard operations are representative of chrome plating; (4) the Report incorrectly assumes that all chromic acid sold in California is used for chrome plating and generates the same emissions; and (5) the Report incorrectly assumes that all chrome plating operations are uncontrolled. Based on this confusion, the Report incorrectly concludes that the emissions from chrome plating operations in California amount to between 18 and 21 tons per year. We will take up each of these points in order.

The Report estimates that between 1,500 and 1,800 electroplaters operate in California and that if three-fourths are chrome platers there are between 1,100 and 1,300 chrome platers in California. (Report, p. I-2.) The source of the first estimate is a report by Citizens for a Better Environment. Insofar as we are aware, it is not accurate.

As noted above, the MFASC principally represents job shops, which are companies which perform on a piecework basis. It represents very few "captive" shops -- facilities owned by manufacturers facilities which solely service products they manufacture. We estimate that between 50 and 75 percent of the

metal finishers in Southern California are job shops. Of the almost 250 members of the MFASC, only 68 companies (28%) are chrome platers. Assuming, at most, an additional 70 captive shop chrome platers, that would make up to 140 chrome platers in Southern California. We estimate that in Northern California the ratio of chrome platers to electroplaters in general is similar. Based on this information, there are nowhere near 1,100 chrome platers in California. A better estimate is 300. We will attempt before the next submission to develop more detailed information on this topic. This is significant information because the inflated number of California chrome platers is used to estimate in the Report the amount of chromium emissions from the metal finishing industry in this state.

Next, the ARB assumes that all chrome plating is hard chrome. (Report, p. I-5.) By way of background, chrome plating can use either a hard chrome or decorative chrome process. For a hard chrome coating, a part is electroplated with heavy thicknesses of chromium to form a corrosion-resistant and wear-resistant surface. By contrast, decorative chrome is a process by which a part is first plated with nickel and then electroplated with a very thin coating of chromium. Emissions from hard chrome may be significantly greater than from decorative chrome due to the longer time of processing to achieve the heavier deposit. The ARB states, and we agree, that probably three-fourths of chromium use is for hard chrome and one-fourth for decorative chrome. Approximately 46 member companies in the

MFASC (19%) do decorative chrome and 22 (9%) do hard chrome. Eight companies (3%) do both. The likely difference in emissions from these two processes should be acknowledged and taken into account in the emissions calculations.

Further, the Long Beach Naval Shipyard report is used as the basis for establishing an emission factor for chrome plating. (Report, p. I-4.) This likely overestimates emissions significantly. Usually, military facilities do not have the same constraints as does private industry. Additionally, we assume that a shipyard has very large parts which generate substantially more emissions than do typical chrome plated parts. We will be able to comment further on the applicability of this facility once the ARB makes available the Long Beach Naval Shipyard report, which has already been requested.

The Report incorrectly assumes that all chromic acid sold to the metal finishing industry is used for chrome plating. (Report, p. I-4.) A large amount of chromic acid is used for chemical processes, such as dichromating, which is a process whereby a part is treated with cadmium or zinc first and then dipped in a solution of chromium salts to convert the surface metal to a chromate. It is not an electrolysis process. No bubbles are generated, such as in the case of electroplating of chromium, and no emissions are created. It is simply a quick chemical reaction. Secondly, chromic acid is also used to etch parts, both metal and plastic. Similarly, there is not the same type of buildup of bubbles or gas. We estimate that more chromic

acid is used to chemically treat or etch parts than is used in electroplating operations. Thus, the amount of chromic acid sold in California is not directly relevant to the emission report from the Long Beach Naval Shipyard or the emission of chromium into the air.

Finally, the Report calculates the emissions of chromium from the metal finishing industry based on the assumption that all chrome plating is done without air pollution controls. (Report, p. I-5.) Chrome platers located within the South Coast Air Basin -- Los Angeles, Orange, Riverside and San Bernardino Counties -- are required to have air pollution control equipment on all chromium electroplating operations because of concern by the South Coast Air Quality Management District with chromic acid mist. The District's concern rests on the possibility that without controls the sources will create a public nuisance. Chrome electroplating tanks are equipped with mist inhibitors or are controlled by air scrubbers. Air scrubbers are a closed system with virtually no emissions to the atmosphere. We believe that most facilities in the Basin are equipped with such scrubbers. The District checks the efficiency of these units at least once a year. Therefore, use of an emissions factor from the Long Beach Naval Shipyard is misleading.

The information concerning the number of chrome platers and the emissions factors to be applied led the ARB to estimate that the emissions are between 18 and 21 tons per year. As more information is developed, we believe that figure will be

shown to be seriously overstated. The Association looks forward to working with the ARB to develop a more accurate picture of the industry's contribution to the question of the chromium emissions.

AIR RESOURCES BOARD

Q STREET
BOX 2815
SACRAMENTO, CA 95812



July 10, 1985

B. J. Kirwan
McClintock, Kirwan, Benshoof
Rochefort and Weston
611 West Sixth Street, Suite 2100
Los Angeles, CA 90017

Dear Ms. Kirwan:

Comments on the Draft Chromium Report

Thank you for the comments of the Metal Finishes Association of Southern California (MFASC). Your letter and their comments were included in Part C of the draft Report, and changes to draft Part A were made in response to their comments. This letter describes those changes and our responses to the MFASC's comments, and has been forwarded to the Scientific Review Panel as an addendum to Part C.

I am addressing your comments in the same order in which they appeared in your letter.

(1) Number of chrome platers.

Using information from surveys done by the South Coast Air Quality Management District and by the ARB, we have revised the estimate of chrome platers to 400 statewide.

(2) Hard chrome and decorative chrome plating are done in California.

The draft report presented a range of emission estimates; the upper value was based on the assumption that only hard chrome plating is done, and the lower value was based on the assumption that a combination of hard and decorative plating are done. After the draft report was released, we received information from the MFASC on the breakdown of decorative and hard chrome plating in California. Consequently the emission estimate for chrome plating

July 10, 1985

has been revised to reflect this ratio of the numbers of hard and decorative platers in California, and the emission estimate based on the assumption that all plating was hard chrome has been removed from the report.

(3) Long Beach Naval Shipyard plating operations are not representative of private industry.

The Long Beach Naval Shipyard Report used to develop emission factors for chrome plating was based on testing done in 1984, and we believe it is the best available information on chrome plating emissions. A copy of the Naval Shipyard Report was sent to MFASC representatives at their request on May 17, 1985; as of July 5, ARB staff had not received MFASC comments on that report. After the MFASC has reviewed the Naval Shipyard Report, ARB staff would welcome specific information and suggestions to improve emission estimates.

(4) Not all chromic acid sold to the metal finishing industry is used for chrome plating.

The draft report states that "the largest supplier of chromic acid in the United States estimated that 1,500 tons of chromic acid were sold in California in 1984 for chrome plating usage" (draft Report, page I-4). The estimate of chromic acid usage was for chrome plating only and did not include any other uses.

(5) Emission estimates are based on the assumption that all chrome plating is done without air pollution control.

Emissions from chrome plating were calculated based on the assumption that no controls are used on chrome plating operations, because there are no air quality regulations which specifically restrict hexavalent chromium emissions from chrome platers. Any controls in place were designed to control chromic acid mist emissions from a nuisance standpoint, as you pointed out, and were not based on the long-term health effects of hexavalent chromium exposure. The fraction of chrome plating operations which employ emission controls, and the efficiency of those controls, is not known. To provide a range of estimates, we have revised the report to include an estimate based on the theoretical assumption that all chrome platers have controls which are 92 percent efficient. This was the control efficiency of wet scrubbers reported in the Long Beach Naval Shipyard Study. We believe that the efficiency of such controls in industry will be lower than this, but that 92 percent is a technically achievable level of control, and represents a theoretical lower-limit emission estimate. The estimate of emissions based on the no-control assumption has been retained, and represents an upper limit value.

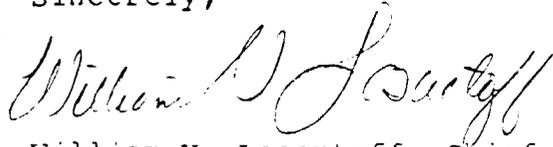
B. J. Kirwan

-3-

July 10, 1985

Thank you again for your comments. If you have questions concerning these responses, please contact Cliff Popejoy at (916) 323-8503.

Sincerely,

A handwritten signature in cursive script that reads "William V. Loscutoff". The signature is written in dark ink and is positioned above the typed name.

William V. Loscutoff, Chief
Toxic Pollutants Branch

Southern California Edison Company

P. O. BOX 800
2244 WALNUT GROVE AVENUE
ROSEMEAD, CALIFORNIA 91770

EDWARD J. FAEDER, Ph.D.
MANAGER OF ENVIRONMENTAL OPERATIONS

TELEPHONE
(818) 302-2009

May 10, 1985

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P. O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

SUBJECT: Report to the Scientific Review Panel on Chromium

Southern California Edison Company has reviewed the document entitled "Report to the Scientific Review Panel on Chromium" (Parts A and B) and would like to submit these brief comments on several important issues which are addressed in this report. These issues include the following:

Exposure Estimates - In the absence of exposure data for hexavalent chromium, a risk assessment cannot be performed at this time and chromium should be reclassified as a "Level 1B" compound since this essential information is not yet available.

Emissions Estimates - Emission estimates from sources which pertain to the electric utility industry have been overestimated due to certain assumptions and methods used in these calculations.

Risk Estimates - The unit risk estimates for hexavalent chromium are being developed from epidemiological studies of widely differing quality. These differences should be reflected in the choice of studies used to develop these risk estimates. We also feel that the boundaries on the estimates developed from these studies should be differentiated from statistical confidence limits since they result from a lack of data rather than the uncertainty inherent in a series of observations.

These issues are described in more detail below.

MAY 15 1985
③

EMISSIONS INVENTORY

Although this is not the final inventory which may be used to develop control strategies for chromium, it is important that emissions estimates are at least reasonably correct. Several errors are evident in the methods used to calculate chromium emissions from electric utility sources such as cooling towers and residual fuel oil combustion.

Fuel Oil Consumption

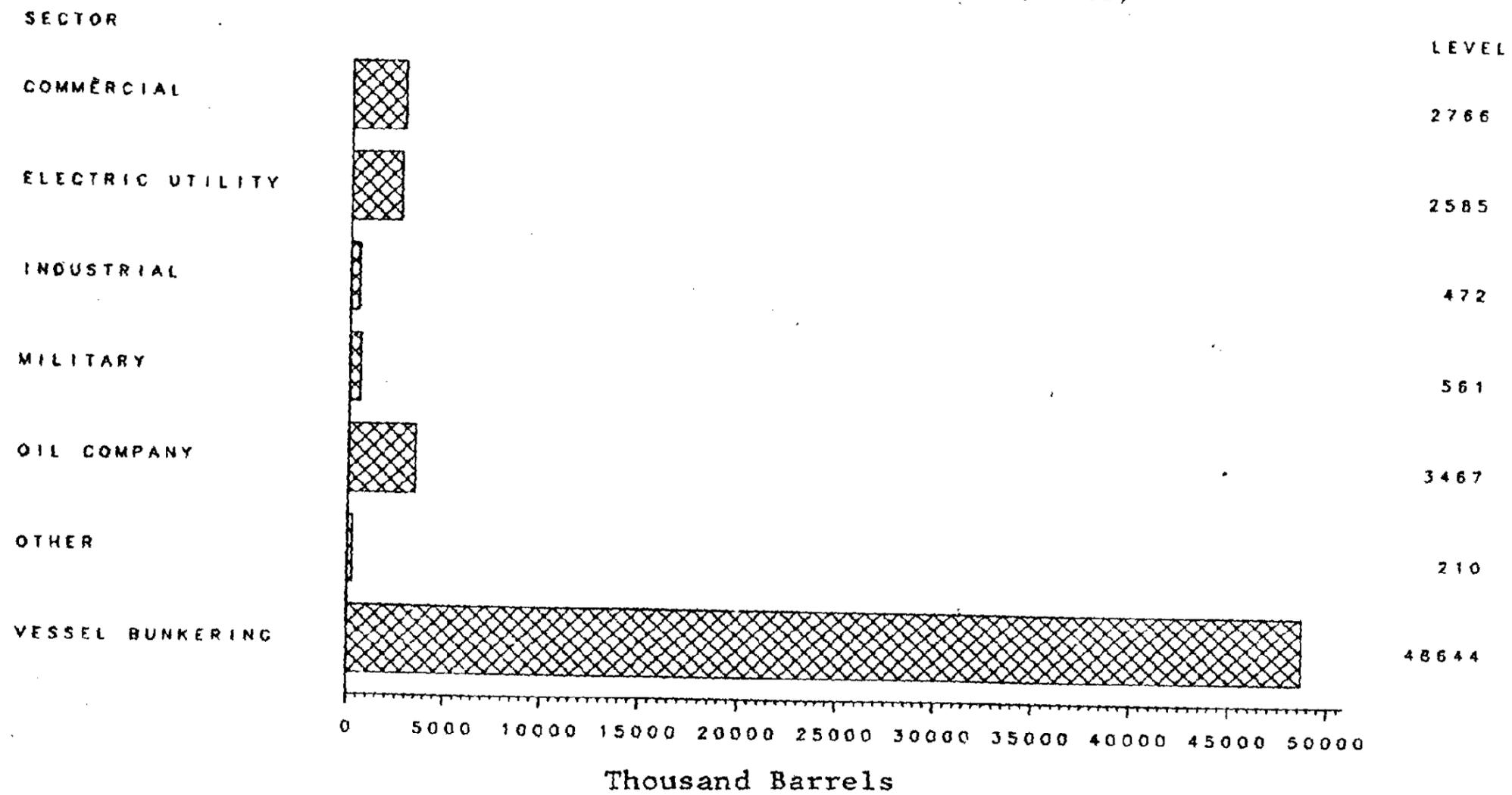
The calculations for residual fuel oil burned within California are inaccurate. The State's petroleum tracking system does not differentiate between oil burned in California and that sold for vessel bunkering which will be burned outside of California. Federal data indicates this is a significant use of residual fuel oil in California (1). This is shown in Figure 1. In the past, ample supplies of high sulfur residual fuel oil in Southern California have tended to drive prices lower, encouraging ships to purchase enough fuel for a round trip (2). Thus while the economic data prepared by the California Energy Commission (and used by the ARB to calculate chromium emissions) indicates that there are marketer receipts for 74 million barrels of residual fuel oil supplied to California in 1983, utilities burned only about 10 million barrels, much of which was purchased in previous years (3). This lack of accounting for vessel bunkering represents a significant overestimate in emissions of chromium from residual fuel oil consumption.

Cooling Tower Emissions

Electric utilities in California are no longer using chromate additives in cooling tower water to the extent they did in the past. SCE has not used these additives since 1982, and other utilities have reduced, or are in the process of completely phasing out, the use of these compounds. The emissions estimates for cooling towers included in the chromium report are, therefore, probably too large, since it was assumed that these compounds are used in approximately 20 percent of the utility industry cooling towers.

The combined effects of these assumptions with regard to residual fuel oil consumption and the use of chromium additives in cooling towers is to overestimate chromium emissions from electric utility sources by a substantial amount. The methods used to calculate these estimates should be reevaluated.

Figure 1. DELIVERIES OF RESIDUAL FUEL OIL BY USE IN CALIFORNIA
 (REFERENCE: PETROLEUM SUPPLY ANNUAL, 1983)



TRACE ELEMENT SPECIATION

The health assessment portion of the chromium document points out the differences in toxicity of various chromium compounds, particularly the difference in carcinogenic potential between trivalent (Cr^{+3}) and hexavalent (Cr^{+6}) chromium. The exposure data essential for conducting a risk assessment relates human population exposure to airborne hexavalent chromium in California. This information is not currently available because: a) there are no validated methods for differentiating between Cr^{+3} and Cr^{+6} at the low concentrations observed in ambient air, and b) given the lack of measurement techniques, the necessary ambient monitoring of Cr^{+6} has not been performed. Speciation techniques have been developed for workroom air (4) and progress has been made in speciating emissions from ferrochrome smelters (5). However, the dusts emitted from these smelters contain several percent chromium by weight. Samples of particulates from ambient air and sources emitting lesser amounts of chromium may contain only microgram per gram quantities. The techniques used on smelter dust might also work at concentrations 1000 times lower, but these techniques must be tested and extensively validated before they can be used in an air quality monitoring program. When these techniques have been validated then the measurements of Cr^{+6} can be made in ambient California air.

RISK ESTIMATES

Earlier risk assessments of toxic air contaminants by DHS have examined different risk estimates, and then made the policy decision to present a "conservative range of estimates" to the risk managers at the ARB. This was not the approach taken with chromium. A table of risk estimates was extracted from the EPA's health assessment document on chromium and these were presented as if they are all equally valid. This treatment of the data is inappropriate, as outlined below.

Comparative Quality of the Studies

All epidemiologic studies have some problems which cause uncertainty in the results. Some studies are considered more reliable because of the size of the study group, the quality of exposure information, and the thoroughness in tracking subjects who leave the work place. The more reliable studies are generally given more weight for developing risk estimates. EPA considered the Mancuso study more reliable than the others and this was reflected in the risk estimate they chose from all those which were calculated. Figure 2 shows the wide range of risk estimates presented by DHS and these can be compared with the estimate chosen by EPA (1.2×10^{-2} per lifetime $\mu\text{g}/\text{m}^3$ exposure). Specifically EPA stated that the studies by Langard (6), Axelsson (7) and Pokrovskaya are "less adequate than the

RANGE OF UNIT RISK ESTIMATES

PRESENTED BY DHS AND EPA

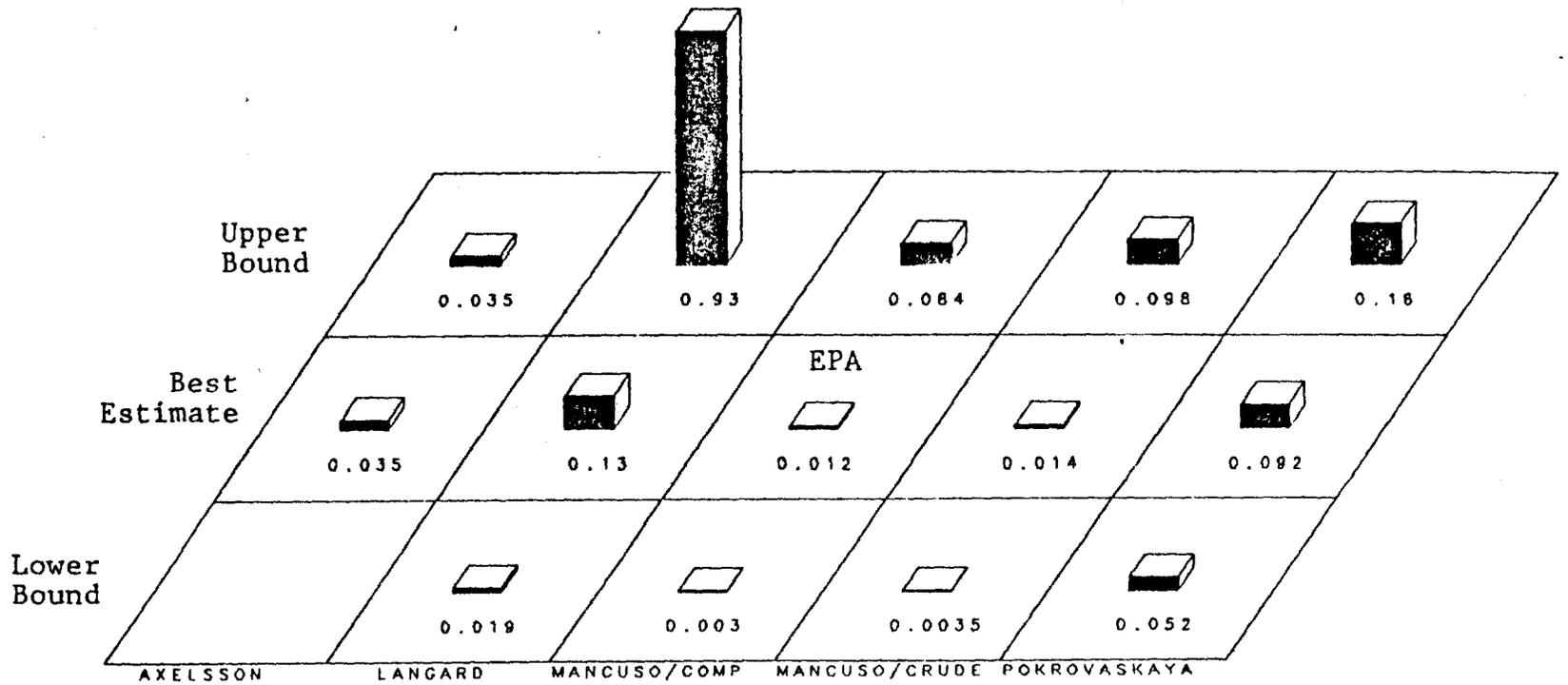


Figure 2. Block Chart of Unit Risk Estimates Derived From Three Studies. (comp= competitive risk, all others= crude model).

Mancuso study for purposes of risk assessment" and that the deficiencies in these studies tend to overestimate the risk. DHS should state why they do not agree with EPA's assessment of the quality of these studies for purposes of developing risk estimates.

The major problem with the Langard (6) and Axelsson (7) studies is the quality of the exposure data. These problems are recognized by the authors. Axelsson et al. state;

"The information on levels of chromium exposure in different parts of the industry was based on approximations, and no measured data existed for the period when a possible occupational cancer could have been induced."

"The estimated exposure data should not be used to construct general dose response relationships or to define threshold values." [emphasis added]

Langard et al. have made similar statements;

"In the present investigation one can only guess at what level the exact chromate concentration has been in previous years."

The EPA Health assessment document on chromium also notes problems with respect to the characterization of the worker cohort in the study by Pokrovaskaya.

While the studies cited above may be useful for purposes of comparison, quantitative risk estimates should be based on the highest quality epidemiologic studies available.

Uncertainty in Risk Estimates

The parameters of interest in toxicological and epidemiological studies, such as exposure and observed responses, are known to vary. This variation can be described in statistical terms, e.g., a mean and the confidence intervals around the mean. These techniques are useful in risk assessment because they can provide an indication of the uncertainty around a risk estimate.

The real parameters of interest may be essentially unknown in some cases. In the Axelsson study, for example, exposure "data" were based on estimates and approximations rather than on actual measurements. One can subjectively estimate a possible range of a variable, but the estimate has little statistical validity and cannot provide the same kind of information as a confidence interval. This type of expert "guess" must be distinguished from statistical confidence limits based upon

multiple observations (such as those presented by DHS for benzene and other toxic air contaminants reviewed to date.)

Another technique for dealing with a lack of data is to use the highest and lowest values of a parameter which were observed to "bound" the analysis. In the Langard study, 89 air measurements of hexavalent chromium were taken to characterize the workplace environment. In deriving upper and lower bounds on risk for hexavalent chromium, both EPA and DHS have assumed that all workers were exposed to either the highest, or conversely, the lowest concentration observed in all of these samples. These calculations provided the lowest and highest estimates on carcinogenic potency respectively. This type of bound or limit must also be distinguished from statistically derived confidence limits. While such estimates may be interesting for comparison, risk estimates which are to be used for risk assessment studies should be based upon the best estimates of individual worker exposure or the best estimates of the overall exposure to the worker population.

Comparison of Risk Estimates With Observed Mortality

One way to judge whether the risk estimates have any bearing on reality is to compare the predicted lung cancer mortality with the observed rates. The annual mortality rate for lung cancer in California is about 40 per 100,000. In a population of 10,000,000 people (such as the South Coast Air Basin) we would expect an annual cancer mortality rate of 4,000 per year. If we used the upper limit of risk presented in the DHS report on chromium, as many as 2,285 cancers would be due to chromium exposures. This is an extraordinarily high estimate of risk and is clearly erroneous in light of the fact that smoking is considered to be responsible for the majority of lung cancer cases.

CONCLUSIONS

SCE recognizes the desire of the ARB to proceed with the review of toxic air contaminants of concern in California in a timely manner. However, it appears that in the case of hexavalent chromium, the fundamental data necessary for conducting a population exposure assessment is not yet available. The risk assessment cannot proceed until methods for the speciation of hexavalent chromium in ambient air have been validated and ambient monitoring data have been obtained. Since the DHS health assessment indicates that hexavalent chromium is the form most likely to be carcinogenic in man, we suggest that hexavalent chromium be listed as a "Level 1B Compound" (a compound for which "significant additional information is pending") until ambient monitoring techniques have been developed and an adequate exposure assessment can be performed. The ARB has conducted a risk assessment assuming that all

airborne chromium is hexavalent. This assumption is inappropriate and should be discontinued.

We also suggest that DHS focus only on those studies with reliable exposure data when calculating risk estimates for hexavalent chromium and that the best estimates of worker exposure to hexavalent chromium (rather than extreme limits) be used for calculating risk estimates.

Methods for calculating emissions estimates from residual oil combustion and cooling tower emissions should also be reviewed for accuracy since they appear to overestimate actual emissions by a significant amount.

Sincerely,

Edward J. Forder

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AIR RESOURCES BOARD

1102 O STREET
D. BOX 2815
SACRAMENTO, CA 95812



June 18, 1985

Edward J. Faeder, Ph.D.
Manager of Environmental Operations
Southern California Edison Company
PO Box 800
Rosemead, CA 91770

Dear Dr. Faeder:

Comments On Draft Chromium Report

Thank you for your comments on the Draft Chromium Report. Your comments on Part B have been referred to the Department of Health Services for response, which, along with your comments and this letter, will be included in Part C of the Report to the Scientific Review Panel on Chromium. We will send you a copy of that report. Our responses follow the same headings you used in your letter.

(Summary of Issues)

EXPOSURE ESTIMATES:

There are data available which have been used to estimate exposure to total and to hexavalent chromium. U.S. EPA National Aerometric Data Bank data for total chromium, were used to assess exposure to total chromium. ARB data on ambient hexavalent and total chromium concentrations were used to estimate excess cancer risk due to ambient hexavalent chromium. We believe that these data establish the presence of chromium and chromium(VI) in the ambient air of California to a degree sufficient to justify listing chromium(VI) as a toxic air contaminant.

EMISSION ESTIMATES:

The emission estimates for sources related to the electric utility industry we made using data from several independent sources. We agree that an improved emission inventory will be necessary in any control development process for chromium(VI). Your specific comments on our emissions estimates are discussed below

FUEL OIL CONSUMPTION:

Since the draft Report on Chromium was released, we realized that the residual oil consumed by vessel bunkering was not taken into account when chromium emissions were estimated. However, there are no available data to estimate how much residual oil was consumed by vessel bunkering in 1983. Therefore we revised our calculations as follows: Residual oil consumption for non-utilities was estimated based on 1981 data in ARB's Emission Data System and the consumption of residual oil by electric utility industry in 1983 was assumed to be 10 million barrels as estimated by SCE. This changes the estimated consumption from 74 million barrels to 49.2 million barrels. The revised calculations result in an emission estimate of 5.1 tons of chromium from residual oil combustion in 1983. In another method, chromium emissions were calculated as a fraction of particulate matter emissions. This approach yielded an estimate of 20 tons of chromium per year. These changes have been reflected in the Report and are discussed in Appendix C of Part A of the Report.

COOLING TOWER EMISSIONS:

We recognize that the electric utility industry in California may not use chromate additives in cooling tower water as extensively as it did in the past. However, chromium emissions from cooling towers were calculated based on the best available data for inventory year 1981 and/or 1979. Lower and upper estimates of 0.23 to 9.2 tons per year were also given in the Report. Therefore, without more specific information on the actual number of cooling towers or concentration of chromium(VI) for all utilities, we think the range given in the Report is the best estimates at this time. We will be trying to get more current and specific information on chromate use in cooling towers in the near future. We, therefore, would like to work with SCE and other utilities to obtain the best information available for future estimates.

TRACE ELEMENT SPECIATION:

We recognize that, because the DHS has indentified dose-response relationships for airborne chromium(VI),

information on hexavalent chromium exposure from ambient air provides the most accurate assessment of the health impact of atmospheric chromium. There are limited data available on ambient concentrations of chromium(VI) in California; we have used these data in revising the overview to include an estimate of the health impact of atmospheric hexavalent chromium. Methods do exist to differentiate between chromium(VI) and total chromium at ambient levels. We recognize that the methods for determining chromium(VI) and total chromium at low concentrations in ambient air have not yet received extensive evaluation. ARB method 106, Procedure for the Sampling and Analysis of Atmospheric Hexavalent Chromium(VI), is based on validated methods for the determination of hexavalent chromium in workplace air, and water and wastewater samples. We have included a copy of Method 106 in Appendix D of Part A. A limited interlaboratory study of this method has shown agreement within 25 percent. Method development of a chromium(VI) analytical method is presently being done by the Inorganic Toxics Analytical Subcommittee of the Toxics Air Monitoring Technical Advisory Committee (TAMTAC) which is comprised of technical representatives of Federal, State, and local air quality and public health agencies.

Chromium(III) is determined by difference between total chromium and chromium(VI). Total chromium measurements used in the exposure assessment were done using a variety of analytical methods, including x-ray fluorescence (XRF) methods similar to ARB method 105: Procedure for the Sampling and Analysis of Total Atmospheric Chromium, Lead, Manganese, and Nickel. We have included a copy of this method in Appendix D of Part A. The ARB's Haagen-Smit Laboratory Division has characterized the accuracy of Method 105 as $\pm 2 \text{ ng/m}^3$, or $\pm 10\text{-}20$ percent at the levels of $10\text{-}20 \text{ ng/m}^3$ of total chromium observed in the ambient air of California.

We believe the available information on atmospheric levels of total and hexavalent chromium in California quantitatively establishes the presence of these species in ambient air to the extent necessary to justify listing chromium(VI) as a toxic air contaminant.

The ARB is working to better characterize ambient levels of chromium(VI) in California. As more temporally and spatially representative data on chromium(VI) concentrations in the state become available, it will be possible to make a more precise estimate of the health impact of ambient chromium(VI).

CONCLUSIONS:

We believe, for the reasons stated above, that sufficient evidence of population exposure to ambient chromium(VI) exists to require evaluation of chromium(VI) as a

June 18, 1985

toxic air contaminant. We also believe based on the health effects information supplied by the DHS and usage and emission estimates, that chromium(VI) should be listed as a toxic air contaminant and treated as a substance having no carcinogenic threshold level.

We have deleted risk estimates based on the assumption that all ambient chromium is hexavalent, and have included revised risk estimates based on measured ambient concentrations of hexavalent chromium. As you requested, we have reviewed the methods used for calculating emission estimates from residual oil combustion and cooling towers as described previously in this letter. Based on information which you provided, we revised the emission estimate for chromium emission from fuel oil consumption.

Again, thank you for your comments. If you have other questions, please contact Cliff Popejoy at (916) 323-8503, of my staff.

Sincerely,



William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

cc: Peter D. Venturini



California Council for Environmental and Economic Balance

1512 - 14th Street, Sacramento, CA 95814 • (916) 443-8252

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May 13, 1985

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

RE: Report to the Scientific Review Panel on Chromium

Dear Mr. Loscutoff:

The California Council for Environmental and Economic Balance (CCEEB) is a nonprofit organization whose board of directors include leaders of business, organized labor, and other public interest groups. CCEEB has reviewed the report by the California Air Resources Board (ARB) and the California Department of Health Services (DHS) to the Scientific Review Panel on chromium dated March 1985, and is presenting the following comments for your consideration.

In summary, the Council believes:

- (1) The risk assessment should be restricted in scope to include only chromium (VI) since this is the only species that has been associated with carcinogenicity in humans and animals.
- (2) A more appropriate range of risk of the cancer potency of chromium (VI) is 8.3×10^{-4} to 1.3×10^{-1} .
- (3) The ARB/DHS should review the studies used to determine the risk associated with chromium (VI) exposure and should focus on those studies with the most valid data when developing risk estimates. The report should more clearly state the quality problems associated with the studies chosen for inclusion in the document and the uncertainties these problems impose on the resultant risk estimates.

We believe a significant deficiency of the report is the lack of distinction between the different chromium species when drawing conclusions on the risk associated with exposure to chromium. In Part A of the report (Overview,