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ADDENDUM TO THE HEALTH ASSESSMENT DOCUMENT FOR CHROMIUM

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OVERVIEW AND INTERPRETIVE SUMMARY AND CONCLUSION

Approximately 175 new references were reviewed for consideration in this addendum to the 1984 Health Assessment Document for Chromium. Many of the references were published since the completion of the 1984 HAD; others were not included in the 1984 document. The purpose of this addendum was to address several technical issues which remained still unresolved after the last document. In addressing these issues, the material previously used for the 1984 document was reviewed and cited, when appropriate. As such, this current report cannot stand alone; it is simply an addendum to the 1984 HAD which addresses the following issues:

- Oxidation states and persistence of these states in the environment.
- Sampling and analytical methodology to differentiate these oxidation states and amounts at the submicrogram level.
- Degree of exposure to chromium in the environment - acute and chronic.
- Effects from environmentally relevant levels and the respiratory tract irritation, obstructive lung disease and pneumoconiosis.

These issues are addressed in this section of the addendum. The remaining material can be used to supplement this discussion.

Chromium Oxidation States and their Persistence in the Environment

The most chemically stable state for chromium is chromium III, which comprises most of the total chromium in the environment. Chromium VI is readily reduced into Cr(III) in the presence of organic material and particularly at lower pH levels to form stable Cr(III) complexes. Under certain conditions, Cr(III) will oxidize the Cr(VI). The important variable in this reaction is the presence of manganese oxide, which is reduced as

Cr(III) is oxidized. Recent theoretical work of Rai (1986), Bartelett (1986) and others have focused on reaction-rate kinetics for environmental chromium, but the relative abundances of chromium valence states in the ambient environment are still not well characterized. The oxidation state of chromium in the ambient air most likely depends on the proximity to sources that emit one form over the other, or mixtures of both. Since Cr(III) is found naturally in the earth's crust, in areas that are not source dominated, most of the airborne chromium is probably of the trivalent state. Additional research is needed to develop quantitative data and mathematical descriptions for predicting the chemical attenuation of chromium in the environment. For now, however, the available data indicate that under "typical" environmental conditions (unless there are nearby sources of Cr(VI)), which would include a slightly acidic environment, chromium exists primarily as Cr(III). Also, from limited research, it appears that Cr(VI) exists primarily in the fine particle phase, where for some source specific locations it accounted for about 35% of the total mass and 85% of the mass below 10 μm.

Sampling and Analytical Methodology for Each Oxidation State at Relatively Low Levels

Several methods are available to measure total chromium at the ppb level. Routine monitoring methods to speciate chromium oxidation states (Cr(III) and Cr(VI)) at ambient air levels (less the 1 ppb) are not available. Several research methods are under development which may be amenable for routine monitoring of Cr(VI). Some of the more prominent problems with the existing methods include the following:

1) interference in the sampling and collection procedure and of the presence of other atmospheric contaminants;

2) losses during sample pretreatment;

3) oxidation/reduction of the sampling during analysis.

Some comparative studies are presented in the analytical section of this addendum on ways to mitigate these problems, but at the expense of accuracy and sensitivity. In general, the methods used routinely to monitor total chromium in ambient air, such as neutron activation analyses, a non-destructive technique, are accurate and sensitive to relatively low total chromium levels (sub $\mu g/m^3$). Pre-treatment of the sample or using other collection methods to determine oxidation state Cr(III)/Cr(VI) lack the sensitivity to measure these species at the levels found commonly in ambient air.

Degree of Exposure to Chromium in the Environment

Little new information was found on the types of chromium and compounds occurring in the environment. While analytical methods are available for differentiating Cr(III) from Cr(VI) in occupational settings they are not sufficiently sensitive for ambient air monitoring. Accordingly, knowledge about the forms of chromium emitted and the transport, transformation, and persistence of these species is the main tool that can be used to estimate the abundance of each oxidation state in specific environments.

According to source categories, the primary source emissions of hexavalent chromium are the following:

- production of chromium chemicals
- cooling towers
- chrome plating

Based on estimated total chromium emissions and percent hexavalent chromium, chemical production accounts for approximately four-fifths of total Cr(VI) emissions. Theoretically, much of these emissions are transformed into Cr(III) over a protracted period of time.

The most recent data available from EPA's National Air Data Bank, (NADB), for total chromium shows that the highest 24-hour chromium level nationwide was 0.6 $\mu g/m^3$, in Camden, New Jersey. With the use of standard meteorological dispersion factors (U.S. EPA, 1977), the 24-hour reading translates into a 1-hour level of 1.5 $\mu g/m^3$. The maximum annual mean (arithmetic) also in Camden, for 1984 was 0.08. But on average, annual levels nationwide rarely exceed the limit of detection: 0.005 $\mu g/m^3$.

Effects on the Respiratory System from Chromium Exposure

From a review of the research published since the completion of the 1984 HAD on Chromium, together with earlier material, the lowest observable effect levels are from subchronic exposures to concentrations at about 1 $\mu g/m^3$ Cr(VI) (see the Summary Table). Most of these studies have reported on nasal and cutaneous pathology associated with a protracted exposure to Cr(VI) in the workplace. In some cases, however, poor ventilation and direct contact with chromium dust has been suggested as a causative factor. Only one quantitative study was available on changes in pulmonary function measurements. The work by Lindberg and Hedenstierna (1983) indicated that 8-hour exposure to Cr(VI) could cause transient decreases in lung function measurements.

In describing the fibrogenic potential of welding fumes, Stern et al., (1983) noted that the effects from inhaling welding fumes are reversible. Known as welders lung (welders siderosis) metal-rich particles are deposited in the lower respiratory tract and regress with time due to various clearance mechanisms after exposure ceases. For a fraction of welders, the fume deposition is reversible with the formation of fibrous tissue. Stern et al., (1983) investigated the fibrogenic potential of welding fumes through 3600 indexed pathology cases. Twenty-nine cases were indexed as "Arc Welders

SUMMARY OF THE LOWEST OBSERVED EFFECT LEVELS IN HUMANS
FROM EXPOSURES TO AIRBORNE CHROMIUM COMPOUNDS

Concentration of Chromium	Occupation	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Cr = 37 - μg/m³ Cr(VI) = 0.8 - 4 2 μ/m³	Catalyst Plant worker at 2 plants	8 hrs/day, 40 hrs/week for term of employment	69% + 72% of employers reported 1 or more symtoms (cough, nasal sores, skin rashes.)	Zey and Lucas 1985
Cr = LD.004 - 0.429 mg/m³ Cr(VI) = 0.001 - 0.742 mg/m³	Farm machinery painters/ coaters	8 hrs/day, 40 hrs/week for term of employment	For the painter job, 85% of the measurements exceeded the NIOSH recommended exposure limit of 0.001 mg/m³ or Cr(VI). An measurements of the 8-TWA's for total Cr were below the OSHA PEL of 1mg/m³ for metal and insoluble Cr salts.	Bloom and Pequese 1985
Cr = ND-0.2mg/m³ Cr(VI)=0 8-1.8μg/m₃	97 Silicon steel rollers	Up to 10 hrs/day 40 hrs/week for term of employment	Only 1 area sample of Cr(VI) exceeds NIOSH standards. for term of employment (machine grinding operation in the slapboard). Total Cr levels were within the ACGIH and OSHA standards. 41-43% had mucosal symtoms. 43% recurrent cough and 23% chronic bronchitis. Eye and nasal irritation were statistically associated with work in a dustier job. P<0.05)	Stephenson and Cherniak 1984
Cr(VI) <0.001 mg/m³ - 0 020 mg/m³ (0.004 mg/m³ mean value)	Electroplaters	Average duration of employment 9 years, 4 months	Cr(VI) was within acceptable limits yet widespread author believes that direct contact with the Cr(VI) chromate μ/m³ (vs. inhalation) is the cause of nasal and cutaneous pathology	Lucas et al 1975

SUMMARY OF THE LOWEST OBSERV[ED] EFFECT LEVELS IN HUMANS
FROM EXPOSURES TO AIRBOR[NE] CHROMIUM COMPOUNDS

Concentration of Chromium	Occupation	Duration of Exposure	Author's findings/ Statistical Significance	Reference
MMA/ss 0.2mg/m^3 MIG/ss 0.1mg/m^3 (average) (water soluble CR^6)	welders		Cr(VI) exhibits fibrogenic potential	Stern et al 1983
0.005-0.008 mg/m^3 (TLV=0.05 mg/m^3	Spray-painters	Employed 1-26 years	Histological changes in the exposed group are significantlly higher than that of the non-industrial control group ($p<0.01$). Although exposure values were well below TLV, histopathological changes and clinical symptoms had developed.	Hellquist et al 1983
total Cr 0 02 mg/m^3 Cr(VI). 0 0006 mg/m^3	Welders	16.8 average years, working as welder	Significant excess prevalence of cardio-vascular disease and a significant increased prevalance of some res-piratory symtoms (productive cough) among workers.	Johnson and Milius 1980
mean total chrome 0.0071 mg/m^3	Electroplaters		Association between length of employment and develop-ment of increasingly severe nasal pathology is significantly positive ($p = .01$)	Cohen and Kramkowski 1974
0.2 - 20+ μg/m^3	104 workers exposed to chrome plating	Exposure time correlated with age of the subject (r:0.65)	Nasal septal ulceration and perforation seen in 2/3 of subjects exposed to 20 of μg/m^3 or more for a short term. An 8 hour mean exposure above 2μg/m^3 may cause a transient decrease in lung function.	Lindberg and Hedenstierna 1983

Pneumoconiosis" and revealed welding fumes from the tissue analysis. Exposure to manual metal arc (MMA) welding fumes indicated an increased fibrogenic potential in a small number of cases, but was not considered a common factor for the remaining cases. NO_2 was proposed as the common etiological factor.

The pneumoconiotic effects of metal inert gas welding (MIG) stainless steel fumes and MMA mild steel fumes in the lungs of the rat were investigated by Hicks et al., (1984). Using extremely high concentrations (greater than 1000 mg/m^3 for MMA mild steel and 400 mg/m^3 for MIG stainless steel), the investigators found that while both types of particles caused alveolar epithelial thickening, proliferation of granular pneumocytes, and the appearance of foam cells in alveoli, soluble chromium constituents displayed no fibrogenic potential, and acted more as cytotoxic, non-fibrogenic dusts.

Numerous studies have also been reported on sensitization to chromium in which either inhalation or i.v. injection to chromium triggered sever bronchoconstriction. Tests conducted on non-occupationally exposed groups indicate that 1-2% of the population is allergic to chromium. For people with hand excema, 12-14% of the men and 3% of the women were chromate sensitive. Asthma induced by chromium salts has also been reported for chromium workers who exposures exceed 150 $\mu g/m^3$ Cr(VI) (Circla, 1983).

In conclusion, subtle effects on pulmonary function have been observed in chromium workers exposed subchronically to greater than 1 $\mu g/m^3$ Cr(VI). Similar changes have also been reported by others (e.g. Kilburn, 1986) but at chromium exposure that were poorly characterized. More information on the actual exposure to all elements in the setting of these studies would help determine the influence of other air contaminants on the findings and dose-response relationship.

TABLE OF CONTENTS

LIST OF TABLES

1.0 INTRODUCTION

In August 1984, the US EPA's Environmental Criteria and Assessment Office completed an in-depth review of the scientific literature on chromium and its compounds. Published as the Health Assessment Document (HAD) for chromium, it was to serve as the scientific data base for regulatory decision-making of the Agency, and as such, was to represent an interpretive summary of all relevant scientific studies. The HAD considered all sources of chromium in the environment, the likelihood for its exposure to humans, and the possible consequences to man and lower organisms from its absorption. That information was integrated into a format that could serve as the basis for qualitative risk assessments; at the same time, it identified gaps in scientific knowledge that limited accurate health assessment.

Not withstanding the in-depth analysis, peer-review processes, and multiple revisions of the 1984 Chromium HAD, several salient scientific questions still remained unanswered. To address those issues, a new literature review was initiated, key studies were reanalyzed, and the conclusions of the original HAD were reassessed. Approximately 175 additional references on were reviewed for inclusion in the revised HAD. While this additional material and reanalysis of previously reviewed data add significantly to understanding the role of chromium on human health, many of the questions are still not answered completely, but the confidence of the evaluation has increased markedly. In the addendum the following technical issues have been addressed:

- Types and persistence of chromium compounds in the environment.
- Adequacy of the sampling and analytical methods as a means to evaluate the types and amounts in environmental and controlled study exposures.
- Transformation rates of chromium compounds in the environment.

- Exposure parameters associated with the key studies.
- In-depth review of pulmonary effects.
- Dose-response relationships of acute, subchronic, and chronic effects, including chemical and physical properties of the active chromium species that influence deposition, absorption, and other pharmacokinetics.

In this revision, all key references reported in the 1984 document were reviewed again and compared with their description in the HAD. Sometimes no changes were made; sometimes the original descriptions were redone. The purpose of this draft is to serve solely as an addendum to the 1984 HAD on chromium.

2.0 BACKGROUND INFORMATION

2.1 Chemical and Physical Properties

Chromium is one of the most important metals used in industry today. Discovered in 1797 by the French chemist Louis Vanquelin, chromium was a key ingredient in the industrial revolution. Table 2-1 lists its properties.

Although chromium exists in several oxidation states, from -2 to +6, only chromium +3 and +6 (Cr(III) and Cr(VI)) have been studied moderately in organic chemistry research. The action of these two forms on biological systems are poorly characterized. The intermediate oxidation state of chromium +4 and +5 may also have an important role in acting with biological systems, but until recently virtually no biological research was conducted on these species.

Cr(III) state is the most stable form of chromium. In neutral and basic solutions, Cr(III) forms binuclear and polynuclear compounds in which adjacent chromium atoms are linked through hydroxy-(OH) or oxo-(O) bridges. Interestingly, Cr(III) forms stable complexes with amino acids and peptides. Cr(III) also has a strong tendency to form hexacoordinated octahedral complexes with ligands, such as water, ammonia, urea, ethylenediamine, halides, sulfates, and organic acids. These relatively stable complex formations (Cotton and Wilkinson, 1972; Kiilunen et al., 1983) can prevent precipitation of Cr(III) at pH values at which it would otherwise precipitate, and it is unlikely that at normal pH values further oxidation of Cr(III) occurs (Hartford, 1986).

Cr(VI) exists in solution as hydrochromate, chromate, and dichromate ionic species. The proportion of each ion in solution is dependent on pH. In strongly basic and neutral pHs, the chromate form predominates. As the pH is lowered, the hydrochromate concentration increases. At very low pHs, the dichromate species predominates. In the pH ranges encountered in natural water, the predominant forms are hydrochromate ions (63.6%) at pH 6.0 to 6.2

TABLE 2-1

PHYSICAL PROPERTIES OF CHROMIUM

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_b,°C[a]	1610
heat of fusion, kJ/mol	13.4-14.6
latent heat of vaporization at bp_o kJ/mol[b]	320.6
specific heat at 25°C, kJ/(mol-K)°	23.9 (0.46 kj/kg-K)
linear coefficient of thermal expansion at 20°C	6.2×10^{-6}
thermal conductivity at 20°C, W/(m-K)	91
electrical resistivity at 20°C, μΩ-m	0.129
specific magnetic susceptibility at 20°C	3.6×10^{-6}
total emissivity at 100°C nonoxidizing atm	0.08
reflectivity, R	
λ, nm	300 500 1000 4000
%	67 70 63 88
refractive index	
α	1.64-3.28
λ	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	6.1×10^{-28}
elastic modulus, GPa[c]	250
compressibility a, d at 10-60 TPa	70×10^{-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.

Source: EPA 1984b

and chromate ion (95.7%) at pH 7.8 to 8.5. The oxidizing ability of Cr(VI) in aqueous solution is pH dependent. The oxidation potential of Cr(VI) increases at lower pHs. The ability of Cr(VI) to oxidize organic materials and the tendency of the resulting Cr(III) to form stable complexes with available biological ligands afford a reasonable mechanism by which chromium can interact with the normal biochemistry of man.

The physical properties of various chromium oxidation states and of several environmentally significant trivalent and hexavalent chromium compounds are shown in Table 2-2. It should be mentioned that because there is considerable disagreement in the literature concerning the physical parameters given in this Table, these values should be accepted with reservation. The disagreement in the values is possibly due to the reactions of these compounds with other substances, namely the moisture and air at high temperatures, impurities, and structural and compositional changes occurring during the experimental determinations. The composition of typical ferrochromium alloys and chromium metals is given in Table 2-3. General information on the chemistry of chromium can be found in the 1984 document.

2.2 Production, Use and Release to the Environment

Considerable information is available on production, use, and release of chromium into the environment. Much less information is available on the forms of chromium in the environment. While it is assumed that Cr(III) and Cr(IV) comprise most of the the total environmental chromium, the biological importance of the other oxidation states cannot be ruled out completely.

This section is limited to new information not presented in the 1984 HAD.

TABLE 2-2 OXIDATION STATES OF SELECTED CHROMIUM COMPOUNDS AND THEIR MAJOR PHYSICAL PROPERTIES

Oxidation State Compound	Formula	Density (g/cm^3)	Melting Point (^oC)	Boiling Point (^oC)	Solubility
Oxidation State 0					
Chromium carbonyl	$Cr(CO)_6$	1 77	150 (decomposes) (sealed tube)	151 (decomposes)	Slightly soluble in CCl_4, insoluble in H_2O, $(C_2H_5)_2O$, C_2H_3OH, C_6N_6
Dibenzene-Chromium(0)	$(C_6H_6)_2Cr$	1 519	284-285	Sublimes 150 (vacuum)	Insoluble in H_2O; soluble in C_6H_6
Oxidation State + 1					
Big(biphenyl)-Chroumium (I) iodide	$(C_nH_5C_6H_5)_2CrI$	1.617	178	Deccomposes	Soluble in C_2H_5OH, C_5H_3N
Oxidation State + 2					
Chromous acetate	$(Cr_2(C_2H_3O_2)_4 \cdot 2H_2O$	1 79			Slightly soluble in H_2O; soluble in acide
Chromous chloride	$CrCl_2$	2 93	815	1120	Soluble in H_2O to blue solution, absorbs O^2
Chromous amonium sulfate	$CrSO_4$ $(NH_4)_2SO_4 \cdot 6H_2O$				Soluble in H_2O, absorbs O_2
Oxidation State + 3					
Chromic acetate	$Cr(CH_3COO)_3 \cdot H_2O$	NR	NR	NR	Slightly soluble
Chromic chloride	$CrCl_3$	2 76	1150	1300 (sublimes)	insoluble
Chromic chloride, hexahydrate	$(Cr(H_2O)_4Cl_2)Cl \cdot 2H_2O$	1 76	83	NR	58 5 at 25°C
	$(Cr(H_2O)_6)Cl_3$	NR	NR	NR	soluble
Chromic formate, hexahydrate	$(Cr(HCOO)_3) \cdot 6N_2O$	NR	decomposes above 300	NR	soluble
Chromic oxide	Cr_2O_3	5 21	2266	4000	insoluble

TABLE 2-2 OXIDATION STATES OF SELECTED CHROMIUM COMPOUNDS AND THEIR MAJOR PHYSICAL PROPERTIES (CONTINUED)

Oxidation State Compound	Formula	Density (g/cm³)	Melting Point (°C)	Boiling Point (°C)	Solubility
Oxidation State + 3 (Continued)					
Chromic phosphate	$CrPO_4 \cdot 2H_2O$	2.42 (32.5°C)	NR	NR	slightly soluble
hydrated	$CrPO_4 \cdot 6H_2O$	2.121 (14°C)	100	NR	insoluble
Chromic sulfate	$Cr_2(SO_4)_3$	3.012	NR	NR	insoluble
Chromic sulfate, Hydrated	$Cr_2(SO_4)_3 \cdot 15H_2O$	1.867 (17°C)	100	100(-100 H_2O)	soluble
	$Cr_2(SO_4)_3 \cdot 18H_2O$	1.7 (22°C)	100 (-12H 0)	NR	120 at 20°C
Oxidation state +4 Chromium(IV) oxide	CrO_2 Dark-brown or black powder	4.98 (calculated)	Decomposes to Cr_2O_3	Soluble in acids to Cr^{3+} and Cr^{6+}	
Chromium (IV chloride	$CrCl_4$		830		
Oxidation state +5 Barium chromate (V)	$Ba_3(CrO_4)_2$ Black-green crystals			Slightly decomposes in H_2O; soluble in dilute acids to Cr_{3+} and Cr_{6+}	
Oxidation state +6					
Ammonium chromate	$(NH_4)_2 CrO_4$	1.91[illegible]	180 decomposes	NR	40.5 at 30°C
Ammonium dichromate	$NH_4)_2Cr_2O_7$	2.155[illegible]	180 decomposes	NR	30.8 at 15°C
Barium chromate	$BaCrO_4$	4.498[illegible]	decomposes	NR	3.4×10^{-4} at 160°C
Chromium (VI) oxide	CrO_3	2.70[illegible]	197	decomposes	67.45 at 100°C
Lead chromate	$PbCrO_4$	6.12[illegible]	844	decomposes	$5.8 \times 10_{-6}$ at 25°C

TABLE 2-2 OXIDATION STATES OF SELECTED CHROMIUM COMPOUNDS AND THEIR MAJOR PHYSICAL PROPERTIES (CONTINUED)

Oxidation State Compound	Formula	Density (g/cm^3)	Melting Point (^oC)	Boiling Point (^oC)	Solubility
Oxidation state +6 (Continued)					
Mercurous (I) Chromate	Hg_2CrO_4	NR		NR	very slightly soluble
Mercuric (II) chromate	$HgCrO_4$	NR	decomposes	NR	slightly soluble, decomposes
Potassium Chromate	K_2CrO_4	2.732	971	NR	62.9 at 20°C
Potassium dichromate	$K_2Cr_2O_7$	2.676	398	500 decomposes	4.9 at 0°C 102 at 100°C
Sodium chromate	Na_2CrO_4	2.723	792	NR	87.3 at 30°C
Sodium dichromate dihydrate	$Na_2Cr_2O_7 \cdot 2H_2O$	2.348	84.6 (incongruent)	400 decomposes	180 at 20°C

Sources US EPA 1984 a,b

TABLE 2-3

COMPOSITION OF TYPICAL FERROCHROMIUM ALLOYS AND CHROMIUM METAL

Grade	Chromium	Silicon	Carbon	Sulfur[a]	Phosphorus[a]	Other[b]
ferrochromium						
high-carbon	66-70	1-2	5-6.5	0.04	0.03	
high-carbon, high-silicon						
blocking chrome	55-63	8-12	4-6	0.03		
exothermic ferrochrome	41-51	9-14	3.6-6.4	0.03		
foundry ferrochrome	55-63	8-12	4-6			
refined chrome	53-63	2.5[a]	3-5	0.03		
SM ferrochrome	60-65	4-6	4-6			4-6 manganese
charge chromium						
50-55 percent chromium	50-56	3-6	6-8	0.04	0.03	
66-70 percent chromium	66-70	3	6-6.5	0.04	0.03	
low-carbon:						
0.025 percent carbon	67-75	1[b]	0.025[a]	0.025	0.03	
0.05 percent carbon	67-75	1[b]	0.05[a]	0.025	0.03	
Simplex	63-71	2.0[a]	0.01 or 0.025			
ferrochromium-silicon:						
36/40 grade	35-37	39-41	0.05[a]			
40/43 grade	39-41	42-45	0.05[a]			
chromium metal						
electrolytic	99.3[c]	0.01[a]	0.02[a]	0.03		0.5 oxygen[a] 0.05 nitrogen[a]
aluminothermic	99.3[c]	0.15[a]	0.05[a]	0.015	0.01	0.2 oxygen[a] 0.3 aluminum[a]

[a]Maximum value.
[b]Difference between sum of percentages shown and 100 percent is chiefly iron content.
[c]Minimum value.

Source: U.S. EPA 1984b

2.2.1 Production of Chromium Compounds

According to the U.S EPA's 1984 report on chromium emission factors, chromite ore has not been mined commercially in the United States since 1961, when the U. S. Defense Production Act was phased out, eliminating government subsidization of chromite mining activities. The United States owns chromite deposits in Maryland, Montana, North Carolina, California, Wyoming, Washington, Oregon, Texas, and Pennsylvania; however, the low chromium content of these deposits precludes economical mining. In 1982, the U.S. imported 456 Gg (507,000 tons) of chromite, mostly from Albania (0.8 percent), Finland (8.9 percent), Madagascar (8.1 percent), Pakistan (0.6 percent), the Phillipines (13.8 percent), South Africa (54.6 percent), Turkey (6.3 percent), and the U.S.S.R. (6.7 percent).

In 1984 sodium chromate and sodium dichromate U.S. annual production capacity was 204,000 metric tons. Chromic acid annual production capacity totaled 38,000 metric tons (Blanchard, 1986). The industrial processes for the production of chromium metal and compounds were described adequately in the previous document.

2.2.2 Uses of Chromium and Its Compounds

The 1984 Chromium HAD noted that metallurgical and chemical usages constituted 82% of the total United States chromium consumption in 1979. The major chromium chemicals, uses, and the number of production sites are presented in Table 2-4 and 2-5. As noted in the 1984 Chromium HAD, the pattern of chromium consumption in the United States has been consistent over the last 20 years. However the use of chromite and chrome alloys in the refractory industry is beginning to decline as open hearth furnaces are replaced by basic-oxygen furnaces. In the future, growth in chromium usage is expected in the metallurgical and chemical sectors.

TABLE 2-4

MAJOR CHROMIUM USES AND KEY CHROMIUM CHEMICALS INVOLVED

Chromium Chemical Use Area	Key Chromium Chemicals Involved
Paints and Pigments	Chrome Yellow[a] Chrome Orange[a] Chrome Oxide Green Molybdate Orange[a] Chrome Green
Leather Tanning Liquor	Basic Chromium Sulfate
Metal Finishing and Plating	Chromic Acid
Corrosion Inhibitors	Zinc Chromate Zinc Tetroxychromate Strontium Chromate Lithium Chromate
Catalysts	Cadmium Chromate Copper Chromate Magnesium Dichromate Nickel Chromate Copper Chromite
Drilling Muds	Chromium Lignosulfonate
Wood Preservatives	Chrome Copper Arsenate Chrome Zinc Chloride
Textile Mordants and Dyes	Chromic Chromate Chromic Chloride (hydrated) Chromic Fluoride Chromic Lactate

[a]Contains lead chromate.

Source: U.S. EPA 1984b

TABLE 2-5

LIST OF COMMERCIALLY PRODUCED SECONDARY CHROMIUM CHEMICALS AND THEIR GENERAL USES

Chromium Chemical[A]	Number of Production Sites[B]	General Use
Chromic acid (Chromium trioxide)	2	Electroplating
Chromium acetate	6	Printing and dyeing textiles
Chromium acetylacetonate	3	Catalysts, antiknock compounds
Chromium monoboride	1	Unknown
Chromium carbide	1	Metallurgy
Chromium carbonyl	2	Catalysts
Chromium chloride, basic	1	Metal treatment
Chromium chloride	2	Metal treatment
Chromium diboride	1	Unknown
Chromium difluoride	1	Catalysts
Chromium dioxide	1	Magnetic Tape
Chromium 2-ethylexanoate (Chromic octoate)	2	Unknown
Chromium fluoride	1	Mordants, catalysts
Chromium hydroxide	1	Pigments, catalysts
Chromium hydroxy diacetate	1	Unknown
Chromium hydroxy dichloride	1	Unknown
Chromium naphthenate	2	Textile preservative
Chromium nitrate	2	Catalysts, corrosion control
Chromium oleate	2	Unknown
Chromium oxide (Chrome oxide green)	6	Pigments
Chromium phosphate	2	Pigments, catalysts
Chromium potassium sulfate (Chrome alum)	1	Photographic emulsions
Chromium sulfate	2	Catalysts, dyeing, tanning
Chromium sulfate, basic	1	Tanning
Chromium triacetate	1	Unknown
Chromium trifluoride	1	Printing, dyeing, catalysts
Chrome lignosulfate	1	Drilling muds
Potassium chromate	1	Metal treatment
Potassium dichromate	1	Tanning, dyeing, pigments
Lead chromate	5	Pigments
Zinc chromate	3	Corrosion control
Ammonium dichromate	2	Printing, pyrotechnics
Barium chromate	2	Pyrotechnics
Calcium chromate	3	Corrosion control
Cesium chromate	1	Electronics
Copper chromate, basic	1	Wood preservative
Magnesium chromate	1	Refractory, catalysts
Straontium chromate	3	Corrosion control pigment
Iron chromite	2	Refractory

[A]List does not include sodium chromate and sodium dichromate, which are primary chemicals.
[B]Several sites product multiple chromium chemicals.

Source: U.S. EPA 1984b

2.2.3 Releases Into the Environment

Little new information was found on the emission rates of chromium into the environment. Table 2-6 lists sources, emission rates, and estimated percent hexavalent chromium in the U.S. As a source category, the production of chromium chemicals account for approximately 15% of the total chromium emissions. However, when compared with estimated percent of hexavalent chromium emissions, chromium chemical production accounts for 80% of total Cr(VI).

2.3 Environmental Fate, Transport and Concentrations

2.3.1 Air

Chromium occurs in the environment primarily in two oxidation states: Cr(III) and Cr(VI). The forms, and uses were shown in the previous tables. Reactions of chromium in the environment under typical atmospheric conditions, as theorized by Seigneur (1986) and others, revealed that Cr(VI) may be reduced to Cr(III) at a significant rate by vanadium (V_{2+}, V_{3+}, and VO_{2+}), Fe_{2+}, HSO_3^- and As(III). Conversely, the oxidation of Cr(III) to Cr(VI) may only occur in the atmosphere at a significant rate if (1) Cr(III) is emitted as a chromium salt and not Cr_2O_3 and (2) at least 1 percent of Mn in atmospheric aerosols in present as MnO_2. The time required for these reactions to occur in the environment, given all the other species present, is unknown. In studies conducted by Butler et al., (1986) and others, chromium was found to occur in the smaller particle size fractions. Table 2-7 "contains the results of combining six impactor runs from the two kilns at a chemical plant. The size fractions represented were for particle sizes greater than 10 μm, 2-10 μm, and less than 2 μm in mean aerodynamic diameter. Note that although only 38 percent of the total mass was collected in the size range 10 μm and below, 85 percent of the total

TABLE 2-6

SOURCE AND ESTIMATES OF UNITED STATES ATMOSPHERIC CHROMIUM EMISSIONS*

Source Category	Estimated Number of Sources	Chromium Emissions (Metric Tons/Yr)	Estimated Hexavalent Chromium %
Chrome Ore Refining	6	3	<1
Ferrochromium Production	1	03	4.4
Chromium Chemicals Production (Primary and Secondary	37	450-900	99.4
Refractory Production	10	90	<6
Sewage Sludge Incineration	141	25-30	<1
Municipal Refuse Incineration	129	-	-
Speciality/Steel Production	18	2870	<4
Utility Cooling Towers	Many	5	~100
Refining Cooling Towers	Many	-	~100
Cement Production	145	16	-
Chrome Plating	Many	-	~100
Combustion of Coal and Oil	Many		
Boilers		737	<1
Process heaters		556	<1
		4825-5275	

*Sources: Blanchard, 1986; Radian Corporation, 1984. US EPA, 1984b.

TABLE 2-7

CHEMICAL PLANT PARTICLE SIZE RESULTS

Size Fraction mm	Particulate Mass mg	Particulate Mass % of Total	Cr(VI) Extracted mg	Cr(VI) Extracted % of Total	Cr(III) Extracted mg	Cr(III) Extracted % of Total
>10	39.9	62	84.2	15	349	23
2-10	6.6	10	197.8	35	511	35
<2	18.4	28	286.1	50	621	42
Total	64.9		568.1		1481	

Source: Butler et al., (1986).

Cr(VI) was contained in that range. In fact, 50 percent of the Cr(VI) was found in the size fraction below 2 μm, although this fraction was only 28 percent of the total mass collected in the impactors. These data are very similar to results in the initial ferrochrome particulate analysis reported earlier. In that report (Cox et al., 1985), it was determined by scanning electron microscopy that the small (largely submicron) particles and aggregates of the particles contained the bulk of the Cr(VI)."

In general, 24 hour ambient air chromium levels rarely exceed 0.1 $\mu g/m^3$. From EPA's NADB inventory of daily chromium monitoring, only eight observations at 173 sites exceeded 0.1 $\mu g/m^3$ as a 24-hour avarage in 1984. Table 2-8 lists the number of observations exceeding 0.1 $\mu g/m^3$ from 1977 through 1984. In fact, only about 50 24-hour observations out of approximately one-half million, have exceeded 0.3 $\mu g/m^3$ chromium from 1977 to 1984. Table 2-9 shows the 26 sites at which those 50 observations occurred. Table 2-10 lists the most recent information available from EPA's National Aerometric Data Bank. Twenty-four hour values for total chromium, measured by neutron activation analysis, are presented for the thirteen highest sites, from an examination of 173 site records for the year 1984. From these sites, which comprise the nationwide network, the highest observed 24-hour total chromium concentration was 0.6 $\mu g/m^3$ (in Camden, N.J.). Additionally, only seven of the 173 sites exceeded 0.1 $\mu g/m^3$. It should be noted that these monitors are generally not located near sources that emit significant quantities of chromium (Blanchard, 1986).

2.3.2 Soil and Water

Bartlett (1986) investigated the chemistry of chromium in soils and also noted the importance of the presence of manganese oxide. He found that the

TABLE 2-8

NUMBER OF NADB OBSERVATIONS EXCEEDING 0.1 $\mu g/m^3$
TOTAL CHROMIUM ACCORDING TO YEAR*

	1977	1978	1979	1980	1981	1982	1983	1984
Number	28	21	19	17	18	17	29	8

*NADB Chromium Inventory from 1977-1984; total of 2106 yearly maxima.

TABLE 2-9

NADB SITES EXCEEDING 0.3 $\mu g/m^3$ TOTAL CHROMIUM FROM 1977 TO 1983

Site	Year	No. of Samples	Max Obs	Arith Mean
			$\mu g/m^3$	
Stubenville, OH	1977	21	2.0550	0.5251*
	1979	28	0.6839	0.1212*
East Chicago, IL	1977	24	1.0750	0.1170
Pasadena, CA	1977	32	0.5600	0.0400*
Clarion Co., PA	1977	25	0.4052	0.1475*
Greenville, SC	1977	27	0.4031	0.0311
Columbia, SC	1977	11	0.3045	0.0360*
Huntington, WV	1977	6	0.3742	0.0885*
Torrance, CA	1977	29	0.3153	0.0306
Niagara Falls, NY	1979	30	0.5590	0.0389
Baltimore, MD	1979	26	0.4589	0.0935
	1980	6	0.5794	0.2264
	1982	19	0.4310	0.1019
	1983	23	0.4466	0.0854
Cincinnati, OH	1979	28	0.4316	0.0451
Abilene, TX	1980	53	0.9100	0.0400
Camden, NJ	1980	19	0.4037	0.0903
	1981	30	0.3461	0.0603
New Orleans, LA	1981	30	1.0710	0.0436
Corpus Christe, TX	1981	33	0.7300	0.1200
(2 locations)	1981	36	0.3500	0.0700
Brownsville, TX	1981	51	0.3900	0.0300
Wichita, KS	1982	58	0.3500	0.0150
	1983	56	0.4000	0.0420
Kansas City, KS	1983	42	0.4400	0.0320
Shawnee, KS	1983	57	0.3900	0.0260

*Value derived from data that did not meet SAROAD criteria.
Source: Derived from Data Files From 1977-1984.

TABLE 2-10

HIGHEST MEASURED TOTAL CHROMIUM CONCENTRATIONS FOR THE YEAR 1984

	Max Obs	2nd Max	Arit. Mean	Geom. Mean	Geom. Std Dev
			$\mu g/m^3$		(±)
Camden, N.J.	0.6017	0.2190	0.0834	0.0249	.79903
Reading, PA	0.3530	0.1466	0.0618	0.0369	.78416
Dundalk, M.D.	0.3442	0.1386	0.0497	0.0278	.65148
Baltimore, M.D. (1st site: Fire Dept.)	0.3197	0.2271	0.0626	0.0236	.25783
Youngstown, OH	0.1649	0.0163	0.0181	0.0085	.54443
St. Louis Park, MN	0.1594	0.0318	0.0114	0.0064	.02481
Columbus, GA	0.1502	0.0052*	0.0184	0.0071	.75682
Cleveland, OH (2nd site: Broadway Ave.)	0.1183	0.1053	0.0332	0.0221	.57376
Erie, PA	0.0993	0.0466	0.0161	0.0096	.54879
Philadelphia, PA (2nd site: Edgemont & Auburn St.)	0.0839	0.0428	0.0188	0.0108	.78828
Milwaukee, WI (1st site: Greenfield Ave.)	0.0767	0.0416	0.0149	0.0103	.26647
Huntington, WV	0.0717	0.0220	0.0128	0.0075	.37221
Chattanooga, TN (2nd site: E 11th St.)	0.0713	0.0200	0.0134	0.0082	.37701

*Apparent error in the data analysis.

Source: Calculated from the 1984 files of EPA's National Aerometric Data Bank.

key parameter for oxidizing Cr(III) to Cr(VI) was manganese oxide, which becomes reduced as the Cr(III) is oxidized. According to Bartlett, this phenomenon has not been reported previously because dried, stored lab-dirt samples had been studied. In such samples, reducing organics are released and manganese oxides are temporarily reduced or occluded. As such, Bartlett noted that the Federal toxicity test using acetic acid eliminates the possibility of finding Cr(VI) in most soils.

Whether or not Cr(III) present in soil, or added to it, is oxidized depends upon the interaction between the chemical forms of the chromium and of the manganese oxides. If the Cr(III) is "moderately available", the regulating factor appears to be the "freshness" of the manganese oxide surfaces, and this is related to quantities of oxidizable organic substances along with soil temperature, moisture, aeration, and drying. Strongly bound Cr(III) may remain reduced in soils, although small amounts are oxidized a narrowly-defined optimum. Organic forms are more easily oxidized than insoluble oxides. Reduction of Cr(VI) added to soils occurs readily if pH is low and an organic energy source is available. Because soils are not equilibrium systems, reduction of CR(VI) and oxidation of Cr(III) may occur at the same time in the same sample of soil.

To predict maximum elemental concentrations of chromium in groundwaters, Rai (1986), investigated the thermochemical data for chromium bearing solids that form in geologic environments and the mechanistic data for reactions that control the distribution of chormium redox species. The solubilities of freshly precipitated $Cr(OH)_3$ and $Cr_xFe_{1-x}(OH)_3$ were investigated to provide thermochemical data, previously unavailable or unreliable, for equilibrium constants of solubility reactions and for Cr(III) hydrolysis constants. He also investigated the effects of Mn oxides and Fe(II)-containing minerals on Cr(III)/Cr(VI) redox transformations.

His investigation indicated that the oxidation of aqueous Cr(III) by MnO_2 was significantly more rapid than oxidation by dissolved oxygen, which is the only other oxidant likely to transform Cr(III) to Cr(VI). Additional kinetic studies have shown that aqueous Cr(VI) is reduced to Cr(III) by trace amounts of ferrous iron in soil minerals. Concentrations of aqueous Cr(III) that are produced by reduction are consistent with the solubility of $Cr_xFe_{1-x}(OH)_3$. Rai concluded that redox reactions mediated by solid surfaces, which are often ignored, are important in determining the redox status of elements in sediments.

3.0 ANALYTICAL METHODOLOGY

The previous review of analytical methods for the collection and analysis of chromium is supplemented here by additional work evaluating commonly used and new procedures. Carelli (1981) investigated the source of errors of chromium measurements using S-diphenylcarbazide in a chromium and zinc plating plant. He found that the absorbence of the complex Cr(VI)-S-diphenylcarbazide was a function of time if Cr(VI) was extracted from the atmospheric particulate according to Thomsen and Stern's (1979) method. Also, the absorbence depression was found to depend on the Cr(VI) extraction method used and could be essentially complete if Abell and Carlberg's (1974) extractive method was used on these types of samples. Absorbence decrease is stronger if large amounts of Fe(III) are present. Absorbence measurements should be made within 1 minute in the presence of 500 ug of Fe(III) with 0.4 ug of Cr(VI). Only slight interferences were found to occur at higher concentrations of chromate, i.e. 4.0 ug of Cr(VI). The absorbence of alkaline extracts reached a maximum after 2 min and was constant for about 3 min then decreased after 5 min. Cr(VI) acid extraction gives rise to an erroneous determination of the Cr(VI) content of these environmental samples due to an enhancement of the matrix effect which leads to a significant reduction in the measured Cr(VI) content. Cr(VI) additions to alkaline-extracted samples showed only a slight depressive interference, which could be compensated for with the use of the standard addition method. The Thomsen and Stern method was reliable if the standard addition method is applied and if absorbence measurements are made within the time limits suggested.

Blomquist et al., 1983, compared the DPC method (1,5-diphenylcarbohydrazide of Abell and Carlberg) with the carbonate method of (Thomsen and Stern), in manual metal arc welding and chromium plating plants. To prepare samples for analysis by the DPC method, Abell and Carlberg recommended

leaching in 0.5 M sulfuric acid. But this procedure results in a significant reduction of Cr(VI) within 10 min. Studies on the stability of Cr(VI) show that sodium acetate buffer is more suitable for leaching the filters. As pointed out by Abell and Carlberg, to avoid reduction of the Cr(VI), sampling should be performed on polyvinyl chloride filters, but if the polyvinyl chloride filters are stored for several days, the Cr(VI) is more difficult to recover from the filters. The leaching time has to be extended to at least 15 min. The DPC method, based on sampling on polyvinyl chloride filters and sodium acetate buffer leaching, was demonstrated to give the same results as the more laborious carbonate method, for manual metal arc welding analysis. For the sampling and analysis of airborne Cr(VI) in a chromium plating plant, the DPC method and atomic absorption spectrometer analysis are suitable. The use of sodium acetate buffer for leaching the samples also solves the problem of bivalent iron interference.

Naranjit et al., 1979 utilized atomic absorption spectrometry for quantification and anion- and cation-exchange resins for separation. At pH 3-5, there is no loss of Cr(III) as the hydroxide nor reduction of Cr(VI) by Fe(II). It is only under these pH conditions that valid Cr(III)/Cr(VI) data can be obtained for aqueous extracts of welding fumes. Composition of the welding rods can cause a difference in the water-soluble chromium content of the welding fumes. A combination of anion-exchange and cation-exchange systems is necessary to obtain quantitative results in the determination of Cr(III) and Cr(VI) in the aqueous extracts. Extent of oxidation of Cr → Cr(III) → Cr(VI) and, as such, the ratio of Cr(III)/Cr(VI) depend on the method of welding or reduction intensity coefficents of Si and Mn. Also a very-lean flame (air-acetylene) helps avoid interferences by other anionic and cationic species in welding flames for atomic absorption but results in a

5-fold loss of sensitivity. A standard addition method can compensate for these problems.

Slavin (1981) described the figures of merit for graphite furnace atomic absorption. The technique requires more skill than flame AAS. Good analysis with the furnace requires that compensation be provided for light that is scattered by the sample at the same wavelength at which the analyte metal has its characteristic absorption. Analytical errors have been reported because chromium is volatized at different temperatures depending upon the compounds in which it is bound and probably upon large variations in the mass of the residue still present at the moment of atomization. The different temperatures produce a different analytical signal. This error could be decreased significantly be depositing the sample upon a thin pyrolytic graphite plate (platform) placed within the furnace tube. Also, high halide levels will reduce the chromium signal. But, it has been shown that large amounts of halide can be tolerated if the platform is used for the chromium determination. The quality of the graphite and the pyrolytic coating plays an important role in the repeatability of the chromium determination, especially in complex matrices. Pyrolytically coated tubes have been shown to provide greater sensitivity than ordinary graphite tubes. Errors also result from the loss of organic chromium complexes in biological materials during the charring cycle. Charring conditions should be established by experiments on the sample, not on inorganic standards.

Studies by Butler et al., (1986) and Cox et al., (1985) explored methods to determine chromium speciation at various chromium facilities: a ferrochrome smelter, a chemical plant, and a refractory brick plant. In the initial study by Cox and colleagues, the source of chromium chosen was a ferrochrome smelter that processes mixtures of chromium-containing ores and lime ($CaCO_3$) in an electric arc furnace. Both Cr(III)and Cr(VI) species are

present in the dust captured by pollution control devices, in this case a baghouse. Since the baghouse dusts are disposed of in landfills, where leaching mechanisms can extract species into the environment, the dust provides a useful analytical sample to determine the amount and chemical state of chromium potentially available for biological uptake (operationally designated as "bioavailable" chromium). The main goal of the study was to use nondestructive instrumental techniques in concert with conventional wet chemical analysis to establish the fraction of bioavailable chromium present as Cr(VI) An additional objective was the evaluation of various wet chemical techniques to help establish a reliable, routine approach to environmental source monitoring or differentiate chromium species, ultimately to include ambient particle samples.

A bimodal chromium source contribution (small particles enriched in bioavailable Cr(VI) and large chromite-like particles containing primarily insoluble Cr(III) was found by the results of wet chemical analysis performed on size-resolved dust particles. Although particles less than 10 μm in diameter comprise only 28% of the total particle mass, over 75% of the total Cr(VI) came from particles in this size range. Furthermore, 55% of the Cr(VI) detected is concentrated in particles less than 0.7 μm in diameter, which comprise only about 12% of the total particle mass. It is apparent that the small soluble particles and aggregates resulting from the smelting process contain the majority of the Cr(VI).

Approximately half of the total chromium was extractable by acid/base leaching ~~(bioavailable),~~ of which about 40% was Cr(VI). In the follow-up study by Butler and colleagues, samples from a chemical plant and a brick plant were added and the results were verified through non-destructive techniques. Both studies measured chromium concentration at the ppm level

(mg/m^3) and noted the occurrence of Cr(VI) in the small particle size fractions.

Because occupational exposures comprise the primary health studies on chromium, it is important to characterize the types of chromium species present in occupational settings. The most important occupations where health information on chromium exposure is available are from plating and welding. Two primary techniques are used in welding stainless steel: manual metal arc (MMA) and metal inert gas (MIG). MMA welding generates three to four times more fumes per kg of welded stainless steel than MIG welding at the same power, and the total chromium content of MMA welding fumes ranges from 2.4% to 7%. Forty to ninety percent of the total chromium appears in a hexavalent and soluble form. The relative amount of chromium in MIG welding fumes may be much higher, from 4% to 15%, but the chromium is mostly trivalent or metallic chromium forms. The relative solubility of the chromium is 1000 times higher than in MIG welding fumes. A problem associated with studies in welders is that it is difficult attribute the effects observed only to the chromium exposure because of other pollutants present in the fume.

The mass median diameter ranges from 0.3-0.6 μm for MMA welding fumes. The concentrations of Cr, Mn, and Ni in MIG welding fumes are much higher than in MMA welding fumes, and the particles are very crystalline. Crystalline particles are considered to be biologically more active than amorphous particles with the same chemical composition. Other studies such as those of McIlWain and Neumeier (1983) have focused on the amount and type of chromium emitted from different stainless steel electrodes. For the first types of electrode tested, total chrome amounted to 9 percent (wt) of all chemicals emitted, from which Cr(VI) accounted for 5.04% (4.7% was soluble; 0.34% insoluble) and Cr(III) accounted for 4.2% (1.5% acid soluble; 3.1% insoluble).

Rao & Sastri (1982) examined the various methods for the determination of chromium in natural waters. Spectrophotometry, atomic absorption spectrometry, neutron activation analysis, and luminescence are applied extensively, yet all of these methods, except the luminescence methods, require pre-concentration to improve the sensitivity. The major drawback of these methods is that decontamination of chromium is required, particularly for spectrophotometric methods. The only method which has been tried thoroughly for direct determination at low concentration of chromium in natural waters appears to be the chemiluminescence method. This method, however, suffers from a series of interferences.

4.0 COMPOUND DISPOSITION AND PHARMACOKINETICS

4.1 Uptake and Distribution

Chromium is distributed approximately equally among human tissues with the exception of lung, which may contain 2 to 3 times the concentration of other tissues. Body chromium content increases during fetal development to a maximum at birth, then declines steadily with age. Adults contain approximately 5 to 10 mg total body chromium. Cr(III) is poorly absorbed by the body regardless of the route of administration, while Cr(VI) is more readily absorbed. The three principal routes of exposure are through the lungs, gastro-intestinal tract and skin. In the absence of industrial exposure, the primary means of uptake of chromium is absorption from chromium-containing food and water by the gastro-intestinal tract. It has been estimated that 1% of the chromium content of the diet is absorbed. In occupational exposures, the lungs are the primary route of exposure. Based on deposition studies with Cr(III), pulmonary absorption amounts to approximately 5%. The skin is considered a minor route of exposure for both Cr(III) and Cr(VI) compounds. Occupationally exposed workers can have chromium concentrations in lung that are 300-fold higher than non-exposed controls, and concentrations in liver, kidney and adrenal glands that are 2 to 4-fold, 10-fold, and 10 to 50-fold higher, respectively. Studies by Glaser et al., (1985) and Kollmeier et al., (1985) have shown similar distribution and retention parameters.

To understand the kinetics of different welding fumes, Kalliomaki, et al., (1983) investigated the retention and clearance of metal inert gas (MIG) stainless steel welding fumes in rats and the results were compared with the corresponding results for manual metal arc (MMA) stainless steel welding fumes in rats. For MIG welding fumes, the measured retention corresponded well with the estimated amount of inhaled chromium. The clearance was very slow, with a

half-time (T1/2) of approximately 240 days. The estimated value of T1/2 was not very reliable because of the great variations in chromium concentrations within each group. The retention rate for MMA welding fumes was higher, and the clearance was slower than expected, (T1/2=40d), when the high percentage of soluble chromium in the original MMA stainless steel welding fumes (40-90%) was taken into consideration. It has been suggested that water soluble hexavalent chromium compounds may be reduced to trivalent chromium or transformed into an insoluble Cr(VI) compound in humid surroundings like the airways.

In experimental studies with animals, Cr(VI) is taken up much more readily than Cr(III). Following oral administration, approximately 10% of the dose of Cr(VI) is absorbed, while less than 0.5% of the Cr(III) dose is absorbed. Cr(VI) can be reduced to Cr(III) by the gastro-intestinal tract, thereby reducing uptake. Following intratracheal or intravenous exposure, both Cr(III) and Cr(VI) are distributed throughout the body, with the highest concentrations in liver, kidneys and lungs, which are the target organs for toxicity.

In blood, Cr(III) is bound principally to serum proteins, while Cr(VI) is specifically taken up by red blood cells and bound to hemoglobin. Cellular uptake of Cr(III) is very poor, while Cr(VI) probably crosses the membrane by simple diffusion. The intracellular distribution of Cr(III) is different from that of Cr(VI), probably as a result of metabolism. Approximately 10% of the cellular Cr(VI) content is associated with the nucleus, while 50% of the total cellular Cr(III) is nuclear.

4.2 Metabolism

Metabolism of Cr(VI) involves cellular reduction of Cr(VI) by small molecules and enzyme systems, a process which generates reactive intermediates

and Cr(III). The metabolites ultimately bind to cellular constituents and may result in impairment of their normal function in the cell. In vitro, ascorbic acid (vitamin C) and the thiols, glutathione, cysteine, cysteamine, lipoic acid, coenzyme A and coenzyme M reduce Cr(VI) at a significant rate under physiological conditions. Depletion of glutathione in rat liver in vivo results in decreased reduction of Cr(VI) in the liver and increased excretion of Cr(VI) in the bile. The ability of Cr(VI) to damage DNA in primary cultures of chick embryo hepatocytes is decreased by depletion of glutathione and increased by induction of glutathione. Reaction of Cr(VI) with glutathione in vitro results in the formation of Cr(III) and another unidentified radical species. DT-diaphorase has been identified as the major cytosolic enzyme contributing to Cr(VI) reduction.

Components of the electron-transport chains of both mitochondria and the endoplasmic reticulum are capable of metabolizing Cr(VI). The NADPH-dependent Cr(VI) reductase activity of rate liver microsomes has been identified as cytochrome P-450. The microsomal reduction of chromium is exclusively NADPH-dependent, but the main cellular activity can be detected in cytosolic fractions and, as such, can be ascribed to enzyme-catalyzed mechanisms, e.g., the DT-diaphorase activity. A minor contribution is provided by nonenzymatic components, notably by some electron donors and chiefly by GSH. Interestingly, the metabolic Cr(VI) reduction is selectively enhanced not only by enzyme inducers but, in the rat lung, it is also stimulated by the repeated intratracheal administration of high doses of Cr(VI) itself; this is consistent with a local autoinduction of Cr(VI) metabolism. Additional detoxifying mechanisms occur in the human epithelial-lining fluid, i.e. in the extracellular environment of the lower respiratory tract, and especially in pulmonary alveolar macrophages (PAM). The specific activity in these

defensive cells is even higher than in liver or lung cells, similar reductive mechanisms being involved.

Bryson and Goodall (1983) studied the acute and subacute toxicities of several Cr(III) and Cr(VI) compounds in mice and related the toxicities to the pharmacokinetics. The distal median lethal doses (more than 10 days after treatment) averaged (17.9 $\pm$ 1.8) x 10^{-6} g Cr/g body weight regardless of the oxidation state of the chromium compound injected, (Cr(III) sulfate may be an exception), but acute toxicity (3 days) was much greater with Cr(VI) compounds. Acid digests of entire male mice that were administered i.p. one-sixth of the distal LD_{50}, either once or repeatedly at weekly intervals, were analysed to determine the whole body persistence and clearance kinetics of Cr. Mice dosed once with Cr(III) retained 6.5 times more chromium at 21 days than mice treated with Cr(VI). When Cr(III) was given at weekly intervals, mice accumulated 6 times more chromium by 8 weeks than Cr(VI)-treated mice, though only the latter showed symptoms of chronic toxicity. Whole body chromium concentrations continued to rise with further Cr(III) treatments, but slowly declined with Cr(VI). Analyses of fecal and urinary excretion confirmed most of the urinary chromium clearance occurred soon after injection, and that chromium excretion from Cr(VI)-treated animals was much faster in both urine and feces than from mice given Cr(III). The differential storage and clearance kinetics of Cr(III) and Cr(VI) compounds may be significant in experimental chromium carcinogenesis studies and in the toxicology of chromium in workers exposed industrially to potentially carcinogenic Cr-containing dusts or aerosols. Cr(VI) reduction is significantly enhanced in smokers, which mainly depended on an increase in total proteins in smokers' PAM. All the described mechanisms are likely to determine a selection of the possible in vivo targets of Cr. Also in the

lung, which is the only recognized target of Cr(VI) carcinogenicity in humans, the documented defense pathways are expected to constitute a metabolically regulated threshold limiting the potential carcinogenicity of this metal species. According to Bencko (1985), the absorption values derived from the chromium urinary excretion data may be greatly misleading, by neglecting the role played by the digestive tract in the chromium elimination from the organism. For instance, rats given a single parenteral dose of chromium eliminate in their feces about 4% of Cr(III) and 7% of Cr(VI) within the first 24 hours after administration, and also the biliary excretion of the hexavalent chromium is significantly higher than that of Cr(III).

Inhalation experiments with dust made up of water-soluble salts of Cr(VI) have revealed that the Cr(VI) is absorbed from the lungs into the blood stream (primarily into erythrocytes) prior to its reduction to Cr(III). Under these experimental conditions, a major part of inhaled chromium is excreted in the urine. However, in guinea pigs exposed to chromium in the form of fumes produced by shielding-gas welding, which is known to prevent chromium from being oxidized to its hexavalent form, about 99% of chromium was found in the feces and only about 1% in the urine of these animals during the first three days after exposure. The presumption is that the inhaled aerosols particles were here transported by the mucociliary lift into the nasopharynx, swallowed, and then excreted in the feces, which is fully consistent with the correlation between chromium excretion in the feces and the self-cleansing capacity of the lungs. Chromium absorbed from the respiratory or digestive tract in its hexavalent form tends to bind to erythrocytes, which function as its chief transport medium, but in its trivalent form, it is primarily bound to plasma proteins. In the kidneys, about 60% of chromium filtered at the glomerulus is resorbed.

4.3 Excretion

Chromium is normally excreted through the kidneys and urine, with some excretion through the bile and feces; minor routes of excretion include milk, sweat, hair and nails. In oral and intravenous uptake studies, chromium is excreted principally in urine. However, when chromium is administered by inhalation or intratracheal instillation, appreciable excretion can occur in feces. Following intravenous administration, 40% of the injected dose of Cr(III) was excreted in the urine and 5% in the feces, and 40% of the injected dose of Cr(VI) was excreted equally in urine and feces over a 4 day period. In oral administration studies, as much as 80% of the Cr(VI) dose was recovered in urine in 4 days.

Chromium (VI) causes renal tubular necrosis, probably as a result of resorption of chromium by the tubules. With increasing time of exposure or increasing doses of Cr(VI), there is a progressive decrease in tubular resorption and an increase in tubular necrosis. Normal urinary loss of chromium is approximately 0.5 to 2 µg per day, with an average urine concentration of 1 ng/ml. In one study, workers exposed to an air concentration of 50 µg Cr/m^3 had urine chromium concentrations of 10-40 ng/ml. Among these workers, smokers had approximately twice the urinary chromium concentration of non-smokers, perhaps due to an impaired lung clearance capacity.

As noted in the HAD, absorbed chromium is eliminated from the body in a rapid phase representing clearance from the blood and in a slower phase representing clearance from tissues. Urinary excretion is the primary route of elimination accounting for somewhat over 50% of the eliminated Cr, while fecal excretion accounts for only 5% of the elimination from the blood. The remaining chromium is deposited into deep body compartments. Limited work on modeling the absorption and deposition of chromium indicates that adipose

and muscle tissue retains chromium at a moderate level (~ 2 weeks), while the liver and spleen store chromium for up to 12 months. Estimated half-lives for whole body chromium elimination are 22 and 92 days for Cr(VI) and Cr(III), respectively. Clearance rates of Cr(VI) and Cr(III) from the lung are not well characterized for individual species. Kollmeier et al., (1985) and others have noted an age-dependent increase of chromium lung tissue associated with occupational (primarily inhalation) exposures, compared with chromium in the kidney which seemed to decrease with age. As seen in the next section, decreased phagocytic activity from elevated chromium exposures can effect the long-term clearance of chromium from the lungs.

5.0 TOXICOLOGY

A summary of human clinical, animal, and in vitro studies not appearing in the 1984 HAD or revised from that document is presented in Tables 5-2, 5-3, and 5-4. For clarity, some of the studies on respiratory effects are presented in the text.

In addressing the effects on the respiratory system from exposure to chromium exposure to Cr(III) (for which little evidence of toxicity exists) must be separated from that of Cr(VI). Because the fumes produced from the welding of stainless steel contain primarily Cr(VI), occupational studies can help resolve the following respiratory effect issues:

- The degree that low level exposures to Cr(VI) irritate the upper respiratory tract and reduce pulmonary function.
- The role of Cr(III) and (VI) in producing pneumoconiosis or fibrosis.
- The causal relationship between Cr(VI) and the onset of chronic obstructive lung disease.
- The potential of chromium to cause lung cancer. (This issue will be re-examined by U.S. EPA's Cancer Assessment Group.)

Initially, we want to describe the types, constituents, and amounts of welding fumes in occupational settings. The National Institute for Occupational Safety and Health (NIOSH) differentiates between two forms of hexavalent chromium in airborne welding fumes: the water soluble alkali metal and ammonium chromates, and the water insoluble chromates.

Early analytical studies indicated that Cr(VI) must be leached from the fume or dust specimens by alkaline solutions rather than by dilute sulfuric acid to protect Cr(VI) from reduction to Cr(III) by ferrous iron or other reductants which may be present in the samples. The same conclusion was reached in a interlaboratory study by Bhargava et al. (1983).

When Blakely and Zatka (1978) utilized milligram levels of Cr(III) salts digested in 2% NaOH/3% Na_2CO_3 solution for 2 hours near the boiling point, no evidence of Cr(III) oxidation to Cr(VI) by air was observed. Ferguson (1983) reported air oxidation occurred, and mitigated this effect by blanketing the leaching solution with nitrogen or argon gas. While Cr(III) is oxidized easily by air on alkaline fusion, this is not so in alkaline solutions despite the favorable redox potential of chromium and excellent stability of the resulting chromate ion at pH > 7. Using bulk welding fume collected from a 308-16 stainless steel manual electrode, Zatka (1985) found that the air oxidation of Cr(III) can be prevented by hydrolytic destabilization of the hydroxochromate(III) complex by the presence of magnesium hydroxide precipitate. He reported good reproducibility for soluble and insoluble Cr(VI).

Studies on the effects of chromium on defense mechanisms and the immune systems have been reported. Glaser et al., (1985) conducted inhalation exposures of sodium dichromate Cr(VI) in young rats to study the effects on alveolar michrophages and immune functions. Sub-acute (28 days) and sub-chronic (90 days) exposures were conducted 22 hr/day, 7 days/week to 25 and 50 $\mu g/m^3$ Cr(VI) (acute) and to 25, 50, and 200 $\mu g/m^3$ Cr(VI) (sub=chronic) aerosol averaging 0.2 μm in diameter. A dose-related accumulation of chromium occurred in the lungs, kidney, and liver, with the lung having 30-50 times more chromium than the kidney. Similar findings have been reported elsewhere, e.g., Kollmeier et al., (1985). Both exposures caused an increased in phagocytic activity at 50 $\mu g/m^3$ and above, at 200 $\mu g/m^3$, the phagocytic activity of the alveolar macrophages decreased significantly. Also at 200 $\mu g/m^3$, the ability of the lung to clear inhaled iron oxide particles (0.5 μm) was decreased, requiring four times as

long to clear the Fe_2O_3 particles compared with clearance rates in control animals.

In a similar study by Johansson et al., (1986), rabbits were exposed to hexavalent and trivalent chromium aerosols for 4-6 weeks. Trivalent chromium concentrations were 0.6 mg/m^3, the hexavalent concentrations were 0.9 mg/m^3 with particle size averaging about 1 μm in diameter. The number of macrophages washed out from the lungs of rabbits exposed to Cr(VI) was increased significantly, but not in the Cr(III) group. Under electron microscopy, however, macrophages from the Cr(III) group "exhibited striking morphological alterations", such as dark, chromium enriched bodies situated in the lysosomes. Similar, but less marked, changes were seen in the Cr(VI) group (Johansson et al., 1980, reported similar findings in earlier work). Only the Cr(III) group produced functional changes of the macrophages, i.e., whereby metabolic activity (as measured by the reduction of nitroblue tetrazolium) was increased and phagocytic activity was reduced.

Van der Wall (1985) studied the exposure of welders in Dutch industries to total particulate, Cr, nickel and copper fume during the welding of unalloyed stainless and high alloyed steels. He also measured the exposure to NO_2, NO, and ozone. The correlation between the arc time factor and the welding fume concentration in the breathing zone apparently was poor. MMA-welding fumes of stainless steel contain mainly soluble hexavalent chromium. During MIG and MMA welding, the fumes contain chromium which was insoluble in water and not hexavalent. The dust exposure was often higher than 5 mg/m^{-3} in MMA and gas-shielded arc welding. The exposure to chromium was usually higher than 0.05 mg/m^{-3} for total chromium in MMA welding of stainless steel.

Among the gaseous contaminants NO_2, NO, and ozone, only ozone with MIG welding of aluminum gave concentrations in the breathing zone exceeding 0.2 mg/m^{-3} (0.1 ppm).

Respiratory tract irritation has been reported by numerous investigators. While all of the reports agree that Cr(VI) is irritating to the nose and respiratory tract at the levels found in the workplaces of electroplaters and stainless steel welders, the effects from lower-level exposures are less clear. Cohen and Kramkowski (1973) reported that 12 of 37 chrome platers had nasal ulcers or perforations within a year of employment with exposures averaging 7.1 $\mu g/m^3$ total chrome (1.4 to 49.3 $\mu g/m^3$) and 2.9 $\mu g/m^3$ Cr(VI) (0.091 to 9.1 $\mu g/m^3$).

The analytical procedure consisted of the following methodology:

- Membrane filters were wet ashed with distilled nitric acid and hydrolyzed with one normal hydrochloric acid prior to analysis.
- Total chromium concentrations were determined by atomic absorption methodologies.
- Hexavalent chromium concentrations determined by Abell and Carlberg method.
- Chemical "spot test" (adapted from Feigl Method, Feigl, 1946) used to detect the presence of hexavalent chromium on various surfaces

The authors found that 35 of the 37 workers (95%) had pathologic changes in the mucosa and 4 out of 37 had perforation of septal mucosa. Out of the workers who were employed less than 1 year, twelve (57%) had "more severe" nasal pathology. For the workers employed more than 1 year, 94% had "more severe" nasal pathology. Five workers had "chrome bites" or "chrome holes" on the hands.

Cohen and Kramkowski concluded:

> "It is entirely possible that levels of hexavalent chrome between 0.019 and 9.1 $\mu g/m^3$, as measured during this investigation, may produce nasal damage, whereas chromic acid analyzed as total chrome may be innocuous at much greater concentrations (i.e., given that a high proportion of the chromium is in the trivalent state)."

They also noted that an extensive observation showed a profound lack of emphasis on good industrial hygiene practice, thereby implicating direct contact as an important route of exposure.

A subsequent study by Lucas and Kramkowski (1975) examined 11 employees of an industrial chrome-plating facility. The concentration of Cr(VI) ranged from 1-20 $\mu g/m^3$ with a mean value of 4 $\mu g/m^3$ (measured by the Abell and Carlsberg method). Chemical spot tests showed widespread contamination of Cr(VI) on "virtually all surfaces in the hard chrome area." They concluded that the nasal and cutaneous pathology occurred from direct contact with Cr(VI) ions, rather than through airborne exposures.

A study by Reggiani et al., (1983) examined the correlation between functional parameters and level of exposure, as measured by the urinary chromium. Concentrations of chromium in the workplace air were not measured. A total of 44 male workers from 17 plants had the following pulmonary function tests: Vital Capacity (VC), Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV_1), Forced Expiratory Flow FEF_{25-75}. The mean urinary chromium excretion increased slightly with the consumption of tobacco, but the difference was not significant. (Non smokers - light smokers = 7.5 μg Cr/g creatinine; heavy smokers = 9.4 μg). The multivariate analysis showed a significant effect of chromium on spirometric values ($F = 2, 27$; $p < 0.85$). The univariate analysis showed that the effect was significant on FEV, and FEF_{25-75}, but not on VC. No interaction was seen from the combination of smoking and chromium exposure.

To continue the investigation of subtle effects from short term exposures to relative low chromic acid concentrations on the upper airways, Lindberg and Hedenstierna (1983) studied 100 subjects in the chrome plating industry and compared the results with a group of unexposed controls.

Eighty-five male and 19 females comprised the test group; 65 smoked. The median exposure time was 4.5 years (range of 0.1-36 yr). Forty-three subjects were exposed almost exclusively to chromic acid and constituted a "low exposure" (8-hr. mean below 2 μ/m^3; 22 subjects) and "high exposure' group ($2\mu/m^3$ or more; 21 subjects). Their median exposure time was 2.5 year (range of 0.2-23.6 yr). The other 61 subjects were exposed to a mixture of chromic acid (0.2-1.7 $\mu g/m_3$) and other pollutants such as nitric, hydrochloric, and boric acids, as well as caustic soda and nickel and copper salts. The latter group was included to disclose any additive or synergistic effects of chromic acid and other pollutants and was studied with regard to lung function only. For pulmonary function measurements, the reference group was composed of 119 auto mechanics (no car painters or welders) whose lung function had been evaluated by identical techniques, with the same equipment, and by the same technicians. Sixty-seven smoked, and the ages between the two groups were comparable, mid-thirties. Nineteen office employees (13 males, 14 non-smokers) served as controls for the status of nose and throat. Their mean age was 41 yr. (range of 26-63 yr).

Exposure levels were measured with personal air samplers and stationary equipment. Most stationary equipment was positioned close to the baths containing chromic acid, where the highest concentrations were expected. Air concentrations at the various sampling stations were reported as 6-hr mean values.

Measurements with personal air samplers were performed on 84 subjects on 13 different days. For the remaining 20 subjects, exposure was assumed to be similar to that measured for a fellow worker doing identical work in the same area.

To evaluate the variations in exposure on different days, measurements were performed with personal air samplers on 11 subjects at three factories during an entire work week. Air measurements were performed with stationary equipment at five chrome baths during a total of 19 days.

Sampling was done with glass fiber filters that were leached in an alkaline buffer solution at pH 12. After buffering to pH 4, Zephiramin was added and the Zephiramin-Cr(VI) complex was extracted with methyl isobutyl ketone and analyzed by atomic absorption. The limit of detection was 0.2 µg/filter, which corresponded to 0.2 $\mu g/m_3$ during an 8-hour sampling period.

At mean exposures less than $2\mu g/m_3$, only 4 of 19 workers complained of diffuse nasal symptoms. Further analysis showed that no one exposed to concentrations below 1 $\mu g/m_3$ complained of symptoms (N-9). At higher mean air concentrations (i.e., 2 $\mu g/m_3$ or more) half of the workers complained of "constantly running nose,", "a lot to blow out"; also, in some cases an increased frequency of nose bleeding and in a couple of cases pain in the nose or "phlegm in the throat." The mean exposure in this group ranged between 2 and 20 $\mu g/m_3$, but within this range there was no correlation between exposure and the degree of frequency of the subjective symptoms.

A smeary and crusty septal mucosa was found in 11 of 19 workers exposed to less than 2 $\mu g/m_3$, a frequency which was higher than in controls (5/19; $P< .05$). In a few exposed subjects, as well as controls, the mucosa was diagnosed as reddened or swollen. An atrophied nasal mucosa was found in 4 subjects with low exposure to chromic acid. No subject displayed ulcerations

or perforations. No one in the control group showed signs of atrophy, ulcerations, or perforations.

Among the 24 employees subjected to a higher exposure to chromic acid (i.e., a daily mean of 2μg/m_3 or more), approximately one-third had a reddened, smeary, or crusty nasal mucosa, but no further damage was noted. Atrophy was seen in another 8 subjects, a frequency which was significantly different from that for controls (0/19;P < .05). Another 8 subjects had ulcerations in the nasal mucosa and 5 (2 of whom had ulcerations) had perforations of the nasla septum (P< .01). The ulcerations and perforations could not be correlated with mean exposure concentrations within the range of the group (2-20 μg/m_3). However, all 11 with ulceration and/or perforation were temporarily exposed to at least 20 μg/m_3 when working near the baths. The period of employment in chrome plating when the ulcerations were found were 5 months, 8 months, 3 years, 5 years, 7 years and more than 10 years, respectively.

Non-smokers exposed to high average levels of chromic acid (2μg/m_3 or more) experienced a significant decrease in FVC and FEV_1 of approximately 0.2 liters and in FEF_{25-75} of 0.4 liters/sec from Monday morning to Thursday afternoon. Spirometry on Thursday morning did not significantly differ from that on Monday morning, although mean values tended to be slightly lower. Individuals exposed to low levels of chromic acid showed no changes during the week. Subjects exposed to a mixture of acids, including chromic acid in lower doses and metals, had a significant fall in FVC during the week, but no change in the variables. No significant decrease in lung function was seen in the reference group during the week. Among smokers, similar but smaller changes were noted; a statistically significant change was seen only for FVC. The differences observed between the "high," "low," and "mixed" exposure groups of nonsmokers were less apparent in subgroups of smokers.

Differences in lung function between exposed subjects and references were tested after correction for the influence of age and height. This was accomplished by computing multiple linear regression equations. For exposed subjects and references, respectively, spirometric and nitrogen washout variables were thus expressed as functions of age and height. Regression lines for exposed subjects and references were compared by analysis of co-variance (see Table 5-1). The authors concluded that an 8-hr mean exposure exceeding 2 $\mu g/m^3$ may cause a transient decrease in lung function, and that short-term exposure to at least 20 $\mu g/m^3$ may cause septal ulceration and perforation.

Kilburn (1986) attempted to address the nature of respiratory functional impairment from welding metals, including the site and extent of such impairment and the relationship to specific exposure. His approach was to analyze the results of studies of respiratory function in welders together with prevalence of respiratory symptoms and to discuss the inferences which could be made. In previous attempts to address this issue, Kilburn found that some of the difficulty resulted from comparison of welders to other shipyard workers, all of whom have been exposed to asbestos, and the failure to separate the effects of cigarette smoking. Recent development of pulmonary function values on current and ex-smokers in a stratified random sample of the Michigan population makes possible comparisons within smoking categories, that is, allowance for smoking effects in occupationally exposed workers. According to Kilburn, one of the reasons that the effects of welding may have been under appreciated is that Forced Vital Capacity (FVC) and Forced Expiratory Volume in one second (FEV_1) have been measured to the exclusion of Forced Expiratory Flow from 25 to 75 percent expired (FEF_{25-75}) and Forced Expiratory Flow from 75 to 85 percent expired (FEF_{75-85}). It is also evident that in welders, the recording of expiratory flow has been, in some

TABLE 5-1

REGRESSION EQUATIONS FOR LUNG FUNCTION VARIABLES
IN THE EXPOSED AND REFERENCE GROUP

		Number of Subjects	Function	R	RSD
			Nonsmokers		
FVC	Exp	26	Y - 0.104H - 0.013A - 12.08	0.81	0.61
	Ref	52	Y - 0.068H - 0.022A - 6.14	0.62	1.00
FEV_1	Exp	26	Y - 0.054H - 0.036A - 3.66	0.81	0.59
	Ref	52	Y - 0.039H - 0.023A - 2.08	0.55	0.85
FEF_{25-75}	Exp	26	Y - 0.051H - 0.091A* + 16.88	0.74	1.08
	Ref	52	Y - 0.039H - 0.036A* - 1.45	0.42	1.44
CV%	Exp	17	Y - 0.418A + 0.42	0.81	4.87
	Ref	52	Y - 0.315A + 0.88	0.68	4.44
Phase III	Exp	17	Y - 0.026A + 0.17	0.73	0.40
	Ref	52	Y - 0.020A + 0.81	0.21	1.32
			Smokers		
FVC	Exp	48	Y - 0.070H - 0.025A - 5.96	0.65	0.70
	Ref	67	Y - 0.093H - 0.037A - 9.87	0.77	0.66
FEV_1	Exp	48	Y - 0.053H - 0.033A - 3.63	0.75	0.57
	Ref	67	Y - 0.069H - 0.032A - 7.04	0.66	0.70
FEF_{25-75}	Exp	48	Y - 0.034H - 0.063A + 0.89	0.70	0.99
	Ref	67	Y - 0.043H - 0.042A - 2.99	0.41	1.23
CV%	Exp	24	Y - 0.411A + 0.11	0.70	5.86
	Ref	67	Y - 0.313A + 2.89	0.50	4.81
Phase III	Exp	24	Y - 0.032A + 0.29	0.45	0.90
	Ref	67	Y - 0.022A + 0.67	0.36	0.51

NOTE: When statistically significant, height has been included in equations.

A = Age (yr).
H = Height.
RSD = Residual standard deviation.

*Difference between exposed and references significant (P, < .05).

Source: Lindberg et al, 1983.

cases, stopped before completion of expiration, resulting in an incomplete FVC and that this early termination has produced artificially high air flow values together with FEV_1/FEV ratios above 80%. Furthermore, a sensitive technique, which is to observe changes in flow rates across a workshift in each worker has not been applied to welders.

Kilburn's study, which began in 1981 and did not include exposure levels, was designed to determine the baseline pulmonary function of welders compared with a nonshipyard, non-Los Angeles comparison group, and to measure the cross shift changes in respiratory function in those welding aluminum, stainless steel, and mild steel. The study was designed to interview each welder briefly and measure his FVC and flow rates before he went to work on a Monday morning. After a full workshift, each welder returned to the field laboratory for a second measurement of FVC and flow rates together with a diary of welding exposure during the day, including metal used, rods, type of welding and surface coating materials and protective equipment. A respiratory questionnaire and a questionnaire for cross shift symptoms was completed by the welder with the assistance of the field staff to define standard bronchitis, wheezing and shortness of breath. (Questions were those of the British Medical Research Center questionnaire as adopted by DLD-78.) He also inquired about pneumonia, respiratory illnesses, time lost from work, chest pain, pressure or heaviness. The inventory of symptoms experienced during the work shift included feverishness, chills, thirst, fatigue, headaches, muscle aches, metallic taste, hoarseness, sore throat and chest tightness. This constitutes the symptom list for metal fume fever.

Spirograms were recorded on either an Ohio rolling seal spirometer or on Stead-Wells spirometers. These were calibrated repeatedly with a large syringe during the study. Measurements were made with the subject standing,

wearing a nose clip and following the American Thoracic Society criteria for FVC, FEV_1, FEF_{25-75} and FEF_{75-85}.

The welders were equally distributed among those who had never smoked cigarettes, 73, and those who had smoked, 75. The symptoms were compared to the stratified random sample of Michigan men in a smoking specific manner. Cross shift symptoms were compared to 29 hospital employees with a similar age and ethnic and smoking composition, all of which were men.

In nonsmokers, the prevalence of phlegm production was seven fold greater than Michigan men, and it was increased further in ex- and current smokers, 33.9% in the latter. Shortness of breath on climbing two flights (40 steps) was also much increased and was highest in nonsmokers. Wheezing was also increased and showed a very slight smoking gradient for increase from nonsmokers to current smokers. Chest heaviness was the msot frequent symptom and occurred in 38% to 47% of the welders.

For symptoms during welding, cough and sputum were approximately twice as frequent, chest tightness occurred in up to 25% compared to none in controls, and wheezing ranged from 5% to 21% and only 4% in controls. Palpitations and the symptoms of metal fever (fever, muscle ache, metallic tastes) were also greatly increased.

For pulmonary function measurements, the nonsmokers had significant reductions in FVC (4.3%), FEV_1 (9%), FEF_{25-75} (4.4%) and in FEF_{75-85} (14.4%). The current smokers were more abnormal even though compared specifically to the Michigan smokers. These large reductions in FVC effectively confounded the slow (effort independent) portion of the expiratory flow and brought the mid and terminal flow FEF_{25-75} and FEF_{75-85} to normal.

In order to make the cross shift comparisons of function, any welder who worked for an hour or more on stainless steel belonged to that group and an

hour or more on aluminum to be an aluminum welder. Very few of the cohort worked entire shifts on either stainless steel or aluminum. A very small number worked on both. The aluminum welding had little effect on FEF_1 or FVC. The welding of mild or black steel caused a small decrease in nonsmokers but an increase of 50 ml in FVC and 80 ml in FEV_1 in smokers. When nonsmokers welded stainless steel they had slightly greater decreases in FEV_1 and FVC than when nonsmokers welded mild steel. However, when the smokers welded stainless steel, they had decreases of 130 ml in FEV_1 and 110 ml in FVC. These contrasted with net <u>increases</u> for when the smokers welded mild steel and, in effect, doubled the cross shift difference.

To Kilburn, it appeared that smokers were more susceptible to fumes of stainless steel welding containing hexavalent chromium than were nonsmokers and that the smokers cross-shift decreases were greater than those of smokers welding mild steel, who improve cross shift. These sizeable differences, as group means, suggest a specific adverse effect from stainless steel fumes which would be attributed to hexavalent chromium.

TABLE 5-2

SUMMARY OF STUDIES ON HUMAN EXPOSURES TO CHROMIUM COMPOUNDS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Occupation	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Inhalation	Cr Cr(VI)	Atomic Absorption Spectrometry and Colorimetric Spectrophotomety for Cr(VI)	Catalyst Plant worker at 2 plants	Cr = 37 - 1ig/m^3 Cr(VI) = 0.8 - 4.2 u/m^3		69% + 72% of employers reported 1 or more symtoms (cough, nasal sores, skin rashes.)	Zey and Lucas 1985
Inhalation	Cr Cr(VI) (lead chromate)	NIOSH method #319 for Cr(VI) NIOSH method #173 to determine total chromium or chronium metal.	Farm machinery painters/ coaters	Cr = LO.004 - 0.429 mg/m^3 Cr(VI) = 0.001 - 0.742 mg/m^3		For the painter job, 85% of the measurements exceeded the NIOSH recommended exposure limit of 0.001 mg/m^3 or Cr(VI). An measurements of the 8-TWA's for total Cr were below the OSHA PEL of 1mg/m^3 for metal and insoluble Cr salts.	Bloom and Pequese 1985
Inhalation	Cr Cr(VI)	Atomic Absorption or conductivity Coupled Plasma-Atomic Emission Spectroscopy for Cr. For Cr(VI)-Colormetric	97 Silicon steel rollers	Cr = ND-0.2mg/m^3 Cr(VI)=0 8-1.8 1ig/m_3	Up to 10 hrs/day 40 hrs/week	Only 1 area sample of Cr(VI) exceeds NIOSH standards. for term of employment (machine grinding operation in the slapboard). Total Cr levels were within the ACGIH and OSHA standards. 41-43% had mucosal symtoms. 43% recurrent cough and 23% chronic bronchitis. Eye and nasal irritation were statistically associated with work in a dustier job. P<0.05)	Stephenson and Cherniak 1984
Direct contact vs Inhalation	Chromic acid	Abell and Carlberg	Electroplaters	Cr(VI) <0.001 mg/m^3 - 0.020 mg/m^3 (0.004 mg/m^3 mean value)	Average duration of employment 9 years, 4 months	Cr(VI) was within acceptable limits yet widespread author believes that direct contact with the Cr(VI) chromate 1ig (vs. inhalation) is the cause of nasal and cutaneous pathology.	Lucas et al 1975

TABLE 5-2 (Cont.)

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Route of Exposure	Compound/ Oxidation State	Analytical Method	Occupation	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Inhalation	Water soluable Cr(VI)	Sodium Carbonate Solution Scanning electron microscopy.	welders	MMA/ss 0.2mg/m^3 MIG/ss 0 1mg/m^3 (average)		Cr(VI) exhibits fibrogenic potential	Stern et al 1983
Inhalation	chromic acid	Atomic Absorption spectrophotometry	Chrome plating plant workers	0.05 µg/m^3 46 µg/m^3		Investigation of work places showed that 3 of 16 chrome plating balhs exceeded the sanitary limit of 20 µg/m^3.	Lindberg et al 1985
Inhalation	Cr in high nickel alloy welding	Electrothermal Atomic Absorption	welders	0 10 mg/m^3 average	5.8 hr/day 17 years = median total welding time	Welding of high nickel alloy causes more symtoms in the respiratory tract than ordinary stainless steel welding. ($p<0.006$)	Akesson and Skerfving 1985
Inhalation	Chromic acid	N/A	Chrome plating plant workers	0 18-1.4 mg/m^3	Employment ranged from 2 weeks to 1 year	Chromic acid is the agent responsible for the ulcerated nasal septa among 7 workers affected (and perforation in 4 of these)- out of 9 workers examined.	Klienfield and Rosso 1965
Inhalation	Cr	Neution Activation Analysis	Copper smelter workers		27-31 years	($p = 0.001$) A four-fold increase of chromium in lung tissue was found for smelter workers' compared to controls. The concentration of Cr did not decline with time after exposure had ended; indicating a long biological half-time.	Gerhardsson et al 1984

TABLE 5-2 (Cont.)

SUMMARY OF STUDIES ON HUMAN EXPOSURES TO CHROMIUM COMPOUNDS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Analytical	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Inhalation	Chromium oxide		Spray-painters	0.005-0 008 mg/m^3 (TLV=0 05 mg/m^3	Employed 1-26 years	Histological changes in the exposed group are significantlly higher than that of the non-industrial control group ($p<0.01$). Although exposure values were well below TLV, histopathological changes and clinical symptoms had developed.	Hellquist et al 1983
Inhalation	Cr	Atomic Absorption Speatrometry and Neutron Activation analysis	Lungs of 6 individuals		lifetime	Accumulated dust in the lungs of ordinary persons contain significant levels of Cr. Approximately 0.329 µg/g	Vanoeteren et al 1982
Inhalation	Cr(VI)	Air samples collected by high volume samples and midget impirgers	Cr chemical production workers. From 1945 1949	413 $\mu g/m^3$ averages during 1945-49	13 years or more at 52 $\mu g/m^3$ 4Cr(VI) or 100 $\mu g/m^3$ of	estimates of exposure levels at which increased cancer risk occured suggest potential excess lung cancer risk from exposure to 52 $\mu g/m^3$, the current OSHA standard for Cr(VI).	Braver et al 1985
Inhalation	FeO-Cr_2O_3 $NaCrO_4$ CrO_3 $K_2Cr_2O_4$	Atomic Absorption Spectrophoto-metry	Chromate factory workers (10 of the 11 were heavy smokers)	Cr(III) content in lungs ranged from 13.9 to 2,368.43 µg/g dry tissue (489.79 µg/g average)	23.9 years average term of employment	7 had perforation of the nasal septom. 8 had squamous cell carcinomas. 3 had small cell carcen-omas. Chromate carcinogenesis cannot be explained simply by lung Cr content or duration of exposure.	Nishiyama 1985

TABLE 5-2 (Cont.)

SUMMARY OF STUDIES ON HUMAN EXPOSURES TO CHROMIUM COMPOUNDS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Occupation	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Inhalation	Chrome mist	Statistical sign determined by chi-square and Fisher exact test	Die-casting and electroplating plant workers	Little data available in 1978 airborne Cr acid levels were less than PEL of OSHA (100 $\mu g/m^3$) 1959 breathing zone sample was 5X the current PEL	At least 10 years of credited pension service	The proportional mortality analysis demonstrated a statistically significant excess of total cancer deaths. (PMR = 1.27, $p<0.001$)	Silverstein et al 1981
	CrO_3		Chromeplating workers: (116 "hard" 62 "bright")	CrO_3 our concentration average = $7 \mu g/m^3$ (range=1-12 $\mu g/m^3$) near middle of room	1 year +	Most deaths from cancer occurred among hard Cr platers, the excess against the expected rate being statistically significant (7 observed, 2.7 expected, $p=0.02$) All deaths from lung cancer occurred in this subcohort (3 observed, 0.7 expected, $p=0.03$). Increased mortality from cancer among Cr platers seems to be related to exposure intensity.	Franchini et al 1983
Inhalation		X-ray microanalyser and scanning electron microscope for Cr particles in lungs Atomic absorption measured Cr content in other organs.	Chronate worker (cigarette smoker)	Cr content in lungs was 90x that in normal lungs (2 60-36 67 $\mu g/g$) (normal = 1 17 $\mu g/g$) Autopsy performed 7 hours after death Cr concentration in tumor tissue of lung was also high at 23 30 $\mu g/g$	35 years	Cr induced pulmonary cancer Nasal septum perforation Differentialed squamous cell carcinoma	Kim et al 1985

TABLE 5-2 (Cont.)

SUMMARY OF STUDIES ON HUMAN EXPOSURES TO CHROMIUM COMPOUNDS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Occupation	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Inhalation			Welders	2-10 mg/m^3	17 year average occupational experience	Of 22 epidemiological studies of cancer incidence among welding populations, 17 report more than 3 cases of lung cancer, 16 of the 22 cases based on 600,000 man-years of observation. Welders are at excess risk due to their occupation.	Stern 1983
Inhalation	Cr Cr(VI)	NIOSH method P & CAM 173. for Cr. NIOSH method P & CAM 169 for Cr(VI)	Welders	total Cr 0.02 mg/m^3 Cr(VI): 0 0006 mg/m^3	16.8 average years, working as welder	Significant excess prevalence of cardio-vascular disease and a significant increased prevalance of some respiratory symtoms (productive cough) among workers.	Johnson and Milius 1980
Inhalation and Direct Contact	Chromic acid	Atomic Absorption for Cr Abell and Carlson for Cr(VI)	Electroplaters	mean total chrome 0 0071 mg/m^3		Association between length of employment and development of increasingly severe nasal pathology is significantly positive ($p = .01$)	Cohen and Kramkowski 1974
Inhalation and Direct Contact	Chromic acid		Chrome Plating worker		2 days rash development 3-5 months	Specified allergic asthma due to chrome sensitization	Joules 1932
Inhalation	Chromic acid		104 workers exposed to chrome plating	0.2 - 20+μg/m^3	Exposure time correlated with age of the subject (r:0.65)	Nasal septal ulceration and perforation seen in 2/3 of subjects exposed to 20 of μg/m^3 or more for a short term. An 8 hour mean exposure above 2μg/m^3 may cause a transient decrease in lung function.	Lindberg and Hedenstierna 1983

TABLE 5-2 (Cont.)

SUMMARY OF STUDIES ON HUMAN EXPOSURES TO CHROMIUM COMPOUNDS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Occupation	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Direct Contact	Cr(VI)					Applications of sodium dithionite applied to skin ($Na_2S_2O_4$) to areas of the skin exposed to Cr(VI) offers an acceptable alternative to the ferrous sulfate approach. Sodium dithionite converts Cr(VI) to Cr(III).	Wall 1982
Uniary Excretion (as a trace element) of Chromium in Men		Multi-element argon-plasma emissions systems	11 healthy male adults		3 hour urine specimens over 27 hours	Group mean on 24 hour time scale ranged from 2.3±1.1 µg/3 hours. ($p<0.02$) 151% increase statistically significant circadian rhythm.	Kanabrocki et al 1983
Inhalation	Cr(VI) as chromic acid		Plating workers			Significantly increased SCE frequencies ($p<0.001$)	Stella et al 1982
Inhalation	Cr(VI)	Atomic Absorption Spectrometry	Stainless steel welders	Average Cr level: 81 µg/m^3 Urine: 47 µmol/mol creatinine	mean: 19 years	No statistically significant differences were observed as to frequency of cells with: breaks and fragments; gaps and isogaps; interchanges, dicentrics, lungs, and makers total number of cells with structural abberations; hypordiploidy; no differences in the frequencies of micronuclear or SCE'S in lymphocytes of peripheral blood.	Littorin et al 1983

TABLE 5-2 (Cont)

SUMMARY OF STUDIES ON HUMAN EXPOSURES TO CHROMIUM COMPOUNDS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Occupation	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Inhalation		Electrothermal Atomic Absorption	53 Stainless Steel Welders (24 smokers)	Air Mean 124 $\mu g/m^3$ median 103 $\mu g/m^3$ Urine. Mean 124 $\mu g/ml$ median 32 $\mu g/l$	Mean: 43 years	Air concentration of total Cr showed a linear relationship to post-shift urine concentration ($r = 0.72$, $p<0.001$) Tendency for smokers to have higher urine con-concentrations. No relationship between welding years and Cr urine concentrations. But, results show that current and previous exposure contribute to urinary Cr. A single urinary Cr measurement is not exact. But urine measurements can be used to estimate airborne exposure.	Tamino et al 1981
Inhalation	Cr	Flameless Atomic Absorption Spectrometry	Tannery workers			Urinary Cr, Cr/Creatinine ratio, daily Cr excretion, and hair Cr concentrations were significally higher and urinary B_2- microglobulin/Crevatics significantlly lower in both tannery workers and control. A significant negaline correlation was found between urinary B_2- microglobulin/ Cre and Cr/Cre ratios of tannery workers and controls. ($p<0.02$) No correlations between duration of exposure to Cr, and hair and urinary Cr.	Saner et al 1984

TABLE 5-2 (Cont)

SUMMARY OF STUDIES ON HUMAN EXPOSURES TO CHROMIUM COMPOUNDS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Occupation	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Inhalation and Dermal Uptake	Cr(VI)	Electrothermal Atomic Absorption spectrometry	8 Chromeplaters	< 2 $\mu g/m^3$	urine samples collected during a period of 5d.	Urine Cr increased from Monday morning to Tuesday after noon and then remained constant for the rest of the work week. ($p = 0.71$)	Lindberg and Vesterberg 1983
Inhalation	Cr	Direct Flameless Atomic absorption	Manual metal arc stainless steel welders		mean exposure time· 20 years	Welders had far higher levels of Cr in urine than individually matched controls, both in morning and afternoon. However, there were no signs of kidney damage in tests. ($p<0.001$)	Littorin et al. 1984
Inhalation	Cr in urine	Spectrophotometric	Stainless Steel Welders		mean exposure time· 20 years range. 7-41 years	Results show a slow and fast compartment for Cr. Slow = 14d to infinity Fast = 4-35 h. Significant correlation ($p<0.001$) between Gr in air and urinary Cr. However, the variation of urinary Cr on Cr in air was considerable, especially at Cr air levels at or below the hygenic standards.	Welinder et al 1983
Inhalation	Cr(III) as chromic acid Cr(VI) as potassium dichromate	Direct flameless Atomic Absorption	dichromate production workers	Cr(III). 048-1.710 mg/m^3 Cr(VI) 0.018-0.312 mg/m^3		Level of Cr(III) in the air failed to show any significant correlation to the urinary concentration of total Cr. Levels of Cr in urine of workers exposed to Cr(VI) are higher than those exposed to Cr(III) in spite of very large concentrations of Cr(III) in the air.	Minoia et al 1983

TABLE 5-2 (Cont.)

SUMMARY OF STUDIES ON HUMAN EXPOSURES TO CHROMIUM COMPOUNDS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Occupation	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
						Cr is excreted only in the trivalent state. Once observed and bound in biological tissue, Cr compounds are all in the trivalent term.	
Inhalation	Chromium Sulfate	Electrothermal Atomic Absorption Spectrometry (graphite furnace)	leather tannery workers	air concentration < 30 µg/m³ Hides treated with with 7 g/l Cr sulfate		Cr urine concentrations showed a workshift related diurnal fluctuation, but it was very high even after vacation, indicating accumulation of Cr in the body. Cr in blood stream was taransported exclusively by the plasma.	Aitio et al 1984
Inhalation	Cr(III) as Chomium lignosulfonate dust	Atomic Absorption spectrophotometer (air-acetylene) Flame Electrothermal atomization	Wokers exposed to Chromium lignosulfonate dust	Air 5-230 µg/m³ Urine 0 01 0 59 µmol/l		Cr(III) lignosulfonate dust was rapidly absorbed, and a peak of urinary excretion was seen immediately after exposure. Concluded that Cr(III) lignosulfonate dust yeilds Cr(III) which acts pharmacokinetically like water-soluble Cr(VI) compounds	Kiilunen et al 1983
Inhalation	Cr (Primarily Cr(VI))	NIOSH method #P&CAM 351	Electric arc gouging workers	Welder's exposure 5 1 mg/m³ 12.9 mg/m³ 0 32 mg/m³ follow up survey: 0.23 mg/m³ 0 14 mg/m³	30 minutes sample. area sample. 8 hour TWA. plasma & carbon are use exposures	Likely that the respiratory irritation symptoms are caused by the arc welding fume constituents and ozone if adequate ventilation is not provided.	Crandall 1984 (NIOSH)

TABLE 5-2 (Cont)

SUMMARY OF STUDIES ON HUMAN EXPOSURES TO CHROMIUM COMPOUNDS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Occupation	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Dermal (Patch Test)	potassium dichromate		healthy adult volunteers	0 5%	2 days	Most of the positive reactions occurred in the group with present occupational exposure to Cr. Among the remaining test population, sensitivity to dichromate was rare.	Peltonen and Fraki 1983
Inhalation	Cr/Cr(VI)	atomic absorption spectrophotometer	MMA Stainless Steel Welders	Personal air samples 5 4 mg/m³ total partical (3 6% Cr) (35% Cr(VI)/Cr)	mean time as welders 13 years (50±6)	Use of Cr and Ni urinary analysis as indices of short-term exposure is <u>not</u> as dependable as previously assumed. The Cr and Ni concentrations in whole blood and plasma did not correlate with the measured exposure but the daily mean increase in the Cr concentration reflected exposure to Cr and Cr(VI) very well. Retention rate of magnetic dust in lungs correlated well ($p<0.01$) with the daily mean increase of Cr in blood. Good correlations ($p<0.000$) found between the retention rate of magnetic dust and the personel air samples of Cr and Cr(VI).	Rahkonen et al 1983

TABLE 5-2 (Cont)

SUMMARY OF STUDIES ON HUMAN EXPOSURES TO CHROMIUM COMPOUNDS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Occupation	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Inhalation		atomic absorption spectroscopy electrothermal method NIOSH method P&CAM 319 for Cr(VI)	workers exposed to Chromium	7-122 $\mu g/m^3$		End-of-shift urinary chromium and its increase above pre-exposure levels were closely related to the concentration of water soluble Cr(VI) in workers exposed to water insoluble chromates or to water soluble chromic[3] sulfate was, definately higher than that observed in subjects not occupationally exposed to Cr compounds; but it cannot be recommended as short-term exposure test for evaluation of the job-related hazard.	Mutti et at 1984
Inhalation (Direct Contact)	Chromic acid	Abell and Carlberg	Hard chrome platers	1 μg-20 $\mu g/m^3$	2 day evaluation 8 hour workday 40 hour week Ave. duration and employment 7 1/2 years	Much nasal and cutaneous pathology from direct contact with Cr(VI). Questions the protectiveness of NIOSH standards. Difficult to related nasal pathology to inhalation of Cr.	Lucas and Kramkoski 1975
Inahalation	Cr(III)		shipyard welders	0 003-0 05 mgm/m^3		Total fumes in welder's breathing zone exceeded threshold limit value (13 mg/m^3) when local until after system was shut down.	Bell 1976
Inhalation	Chromium containing dust (Cr_2O_3FeO)		Chromite miners		8 1/2 - 18 years mining service	Pneumonocis in chromite chromite miners is due to the deposition of radio-opaque chromite dust in the tissues. The condition is benign and does not cause fibrosis.	Sluis-Cremer and DoToit 1968

TABLE 5-2 (Cont)

SUMMARY OF STUDIES ON HUMAN EXPOSURES TO CHROMIUM COMPOUNDS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Occupation	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Inhalation	Chromium (electro-plating)		chrome plating workers	µg Cr/g Creatinine (urinary) <6 to >15		$p<0.05$ Dynamic values of spirometry (FeV_1 and FeF_{25-75}) ARE LOWER AMONG the workers with higher urinary chromium. No observed effect of chromium on VC. Electroplate workers (esp. hard) are at risk in developing obstructive respiratory syndrome.	Bovet et al 1977
Inhalation	CrO_3		Chrome and ferrochrome workers	0 001 - 0 583 mg/m^3		Pulmonary disease of occupational origin found in 4 medical cases. It is characterized by: acute pheumonitis, cough, wheezing, anerexia, loss of weight, increased sedimentation rate, linear and modular fibrosis in the chest. Roentgenograns, ventilatory impairment, and is associated with exposure to high concentrations of metallic silicide.	Princi et al 1962
Inhalation	Chromic acid solution		workers using Chromic acid anodizing operations	5% Chromic Acid solution	2 weeks	Anterior nasal ulceration in 50-60% of the cases and found in workers not initially associated with the tanks, in an atmosphere higher than safe concentrations of Cr acid fumes. Larger ulcerations (deeper and reaches the cartilage) were found in workers who work on the tanks or are in intimate contact with the fumes (35%). 5-10% have something similar to atrophic rhinitis.	Zvaifler 1944

TABLE 5-2 (Cont)

SUMMARY OF STUDIES ON HUMAN EXPOSURES TO CHROMIUM COMPOUNDS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Species/ Strain	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Inhalation	Chromic acid	iodometric method	Chromium platers	0- 55 7 mg/10 m^3	1 week to 3 years	16% had perforated nasal septa. 21% ulcerated septa 47% mucosa inflamation 58% nosebleeds 43% chrom holes on hands Proper ventilation and sanitary measures needed.	Bloomfield and Blum 1928
Inhalation	Chromic acid		Chromium workers	original exhaust system 0 09 - 1 2 mg/m^3 revised exhaust system neg		New ventilation system was needed to prevent chromic acid injuries	Gresh et al 1944
						Case reports on Chromate lung cancer	Letterer et al 1944
Inhalation	Various Chromium compounds		Chromium producing plant	(available data) 0 01 - 21 0 mg/m^3	4-47 years of employment	42 deaths from cancer of the respiratory system. 21% of all deaths 63% of all deaths from cancer.	Machle and Gregorius 1948

TABLE 5-3

ANIMAL STUDIES ON CHROMIUM DISPOSITION, PHARMACOKINETICS, AND EFFECTS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Species/ Strain	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Inhalation	Cr in MMA/SS and MIG/SS welding 3-10% (water soluble hexavalent, alkaline chromates)	Neutron activation analysis and AA	rats/Wistar maximum inhaled	164 mg/m^3	1 hour/day for 1, 2, 3, and 4 weeks	p<0.001 Linear retention of Cr in lungs. Slow clearance mechanism. Lungs are the main target organ of inhaled chromium. The water soluable hexavalent alkaline chromates are chemically transferred into insoluble Cr compounds in the respiratory tract.	Kalliomaki et al. 1983
Inhalation exposure to aerosols	Cr(VI) + Cr(III) Suzuki et al	absorption spectrophotometer.	atomic Dawley	rats/Sprague- mg/m^3	7 4~15.9 6 hours	2 hours Cr(VI) (severe asthmatic symptoms). No deaths after Cr(III) exposure. Cr(VI) exposure caused weight loss. Cr(VI) is transported from lungs to blood (more rapidly than Cr(III)) and taken up by erythrocytes and viscerol organs.	8 died after 1984
Inhalation	Cr	X-ray fluorescence spectroscopy and scanning electron microscopy	bovine lungs (buffalo)			Animals inhabiting mining and industrial complexes can accomulate large amounts of particulate matter with absorbed heavy metals in their lungs.	Dogra et al 1984
Inhalation	Chromium in MIG/SS MMA/SS welding fumes	Neutron activation analysis	rats/Wistar	MMA. 2 4-7% of welding fumes MMG. 4-15% of fumes	1 hour/day for 1, 2, 3 and 4 weeks	Cr accumulation on lungs was very high. It cleared with the half-time of 240d. for MIG/SS (insoluable form of Cr) 40d for MMA/SS.	Kalliomaki et al 1983

TABLE 5-3 (Cont)

ANIMAL STUDIES ON CHROMIUM DISPOSITION, PHARMACOKINETICS, AND EFFECTS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Species/ Strain	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Intratracheal Administration	Cr(VI) (sodium chromate) Cr(III) (chromium chloride)		rats/sprague Dawley	0 1 - 10 µg	24 hours	Cr(III) taken up as such by organs may be distributed inside the cells differently from that generated by reduction of Cr(VI). Study suggests that the low-molecular-weight components should be involved in the passage of this element from the lung to the other tissues.	Edel and Sabbioni 1985
Inhalation	Cr in MMA/SS welding fumes (95% of which is water-soluble hexavalent alakaline chromates: $CaCrO_4$ and $K_2C_2O_7$	atomic absorption spectrometry and neutron activation analysis	rats/Wister	3 6% of 43 mg/m^3 (total welding time)	10 hour maximum	Lung Cr rentention rate = 1 9 µg/hour. The retention in lungs was linear ($p<0.001$) Kidney Cr retention = 0.10 µg/h Liver Cr retention = 0 19 µg/h Blood Cr retention = 0.47 µg/h Blood Cr concentration correlated well ($p<0.001$) with the cumulative exposure time. water-soluble hexavalent alkaline chromates seem to undergo chemical transactions into insoluble Cr compounds in the respiratory tract.	Kalliomaki et al 1982
Intratracheally Administered	$^{51}CrCl_3$ $Na^{51}CrO_4$	atomic absorption spectrometry	rabbits/ New Zealand White	0 5 - 0 5 mg	0-240 minutes	Cr(VI) may enter the blood unreduced via the lung and is partly deposited in cells over a prolonged period of time.	Weigand et al 1984

TABLE 5-3 (Cont)

ANIMAL STUDIES ON CHROMIUM DISPOSITION, PHARMACOKINETICS, AND EFFECTS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Species/ Strain	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Inhalation	$CrCl_3$	atomic absorption spectrometry	rats/SD	13 3 mg/m^3 particle size $<2_1m$	5 hours	Total Cr contents in lungs were 8-25% higher than those in liver. Statistically significant correlation btween LMCR in the lungs and each of Cr-HMW (high-molecular-weight) LMCR and total Cr contents in the liver. LMCR in lungs is in equilibrium with Cr in the rest of the body.	Wada et al 1983

TABLE 5-3 (Cont)

ANIMAL STUDIES ON CHROMIUM DISPOSITION, PHARMACOKINETICS, AND EFFECTS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Species/ Strain	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Subcutaneous Injection	Cr(III) extracted From 5g of leather		various tests performed	0 08 - 0 78 mg/ml		All leather glove extracts caused a reaction in the skin irritation test by the subcutaneous injection method. The causes of the irritation were the low pH and chromium sulfate of the leather glove extract. Contact dermatitis was the result.	Naruse et al 1982
Injection	potassium dichromate		mice	1, 5, or 10 mg/ kg body weight	single i p injection	Lowest effective dose of hexavalent chromate for micronuclei induction in mouse bone marrow is 1/50 of that reported previously [Fabry (1980)] Chromosmal damage resulting by induction of micronucle in bone marrow cells.	Paschin and Toropzev 1982
Injection	$K_2Cr_2O_7$	atomic absorption spectrometry	mice	15 mg/kg	single i.p.	Highest concentrations of Cr are found in the soluble fraction of liver. Binding substances for Cr are mainly a low-molecular-weight compound, which decrease more rapidly in the liver soluble fraction than the H-M-W.	Suzuki and Wada 1982

TABLE 5-3 (Cont)

ANIMAL STUDIES ON CHROMIUM DISPOSITION, PHARMACOKINETICS, AND EFFECTS

Route of Exposure	Compound/ Oxidation State	Analytical Method	Species/ Strain	Concentration of Chromium	Duration of Exposure	Author's findings/ Statistical Significance	Reference
Injection	sodium dichromate Cr(III) chloride	electrothermal atomic absorption spectroscopy [Noted that the natural levels of iron did not alter the AA readings.]	rats/male Spraque-Dawley	20 mg/kg 80 mg/kg		Chromium entered liver and kidney tissues at a slower rate after injection of Cr(III) chloride than after sodium dichromate. However, Cr(III) did not penetration liver and kidney cells and was slowly bound to both RNP and chromatin.	Cupo and Wetteshahn 1985
I P. Injection	sodium dichromate chromic chloride		rat/male Spraque-Dawley	20 or 40 mg/kg 80 mg/kg		Cr(VI) rapidly induced significant levels of cross-linking in rat kidney, liver, and lung. DNA-protein cross-links persisted 36 to 40 hours after injection in rat kidney and lung yet had been repaired in liver by 36h. Data suggests lung and kidney are more sensitive than lines to Cr-induced DNA damage.	Tsapakos et al 1983
I.V. Injection	Cr(VI) as ($Na_2^{51}Cr_2O_7$) Cr(III) as ($CrCl_3$)	autoradiographic Spectrophotometric	mice/C57BL	5 µg/kg body weight	1, 4, 24 hours	Embryonic and fetal uptake of Cr(VI) was about 10x higher than that of Cr(III). The ratioactivity after administration of Cr(VI) may represent Cr(III) after reduction in the tissues.	Danielsson et al 1982