

## Chromium (Cr) and its compounds

### Forms of chromium

For the purpose of evaluating health impact, it is important to distinguish between three forms of chromium.

**Metal chromium** (chromium (0)) is used mainly for making steel and other alloys. Little is known about the health effects of this form of chromium. However there is no reason to believe that chromium (0) is a major cause for concern.

**Chromium (III)** is the form of chromium naturally found in the environment. It is used for brick lining for high-temperature industrial furnaces and for making alloys, chrome plating, dye manufacture, leather tanning and wood preserving. In air, most of the chromium is from man-made sources in the form of chromium (III). This form is also an essential nutrient. An intake of 50 to 200 µg of chromium (III) per day is recommended for adults. Chromium (III) is required for the body to utilize sugars, proteins and fat properly. Insufficient levels of chromium (III) may cause weight loss, impact growth, cause diabetes-like conditions and affect the nervous system. Chromium (III) appears to enhance sensitivity to insulin by facilitating the interaction of insulin with its receptor site. The main concern with the exposure to chromium (III) appears to be allergic reactions causing skin rashes as well as redness and swelling of the skin in sensitive people.

**Chromium (VI)** is released into the environment primarily as a result of industrial activity. Chromium (VI) is not an essential nutrient. High air levels ( $2 \mu\text{g}/\text{m}^3$ ) may cause irritation of nasal mucosa, nose bleeds, ulcers and holes in the nasal septum. High exposure levels may also cause skin ulcers. Sensitive people may develop skin allergies similar to those caused by chromium (III). Very high ingested doses may cause stomach upset, ulcers, convulsion, liver or kidney damage, or death. Such effects are observed only at high doses, which are not normally encountered in food or drinking water. The main cause for concern with chromium (VI) is induction of lung cancer after long-term exposure to this toxicant. Because chromium (VI) is the most toxic of the three forms of chromium, the focus of the assessment is on this compound.

### 1. Physico-chemical properties (based on ATSDR, 1993)

Chromium is a metal, a naturally occurring element found in rock and soil as well as in the tissues of animals and plants. The physico-chemical properties of this metal and its compounds are listed in table 1.

Table 1. Physico-chemical properties of chromium and chromium-containing compounds.

Characteristic	Chromium (0)	Chromium (III) acetate, monohydrate	Chromium (III) nitrate, nonahydrate	Chromium (III) chloride
synonyms	chrome	acetic acid, chromium salt	Nitric acid, chromium (III) salt, nonahydrate; chromium nitrate, nonahydrate	chromium trichloride
chemical formula	Cr	$\text{Cr}(\text{CH}_3\text{COO})_3 \cdot \text{H}_2\text{O}$	$\text{Cr}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$	$\text{CrCl}_3$
CAS No.	7440-47-3	25013-82-5	7789-02-8	10025-73-7
Molecular Weight	52	247.15	400.15	158.36
Colour	steel-grey	gray-green or bluish green	Purple or violet	Purple or violet
Physical state	solid	solid	solid	solid
Melting point °C	1857	no data	60	1150
Boiling point °C	2672	no data	decomposes @ 100	sublimes @ 1300
Density, g/cm <sup>3</sup>	7.2 @ 28°C	no data	no data	2.76 @ 15 °C
Odour	no data	no data	no data	no data
Odour threshold				
water	no data	no data	no data	no data
air	no data	no data	no data	no data
Solubility				
water	insoluble	soluble	soluble	slightly soluble in hot water
organic solvents	insoluble in common organic solvents	insoluble in ethanol	soluble in ethanol and acetone	Insoluble in common organic solvents

Characteristic	Chromium (III) chloride hexahydrate	Ferrochromite [chromium (III)]	Chromium (III) oxide	chromium (III) phosphate
synonyms	Hexaaquachromium (III) chloride	chromite	chromium sesquioxide; dichromium trioxide	chromium orthophosphate; phosphoric acid, chromium (III) salt
chemical formula	$\text{Cr}(\text{Cl})_3 \cdot 6\text{H}_2\text{O}$	$\text{FeCr}_2\text{O}_4$	$\text{Cr}_2\text{O}_3$	$\text{CrPO}_4$
CAS No.	10060-12-5	1306-31-2	1306-38-9	7789-04-0
Molecular Weight	266.45	223.84	151.99	146.97
Colour	violet	brown-black	green	gray-brown to black
Physical state	solid	solid	solid	solid
Melting point °C	83	no data	2266	>1800
Boiling point °C	no data	no data	4000	no data
Density, g/cm <sup>3</sup>	1.76	4.97 @ 20°C	5.21	2.94 @ 32.5 °C
Odour	no data	no data	no data	no data
Odour threshold				
water	no data	no data	no data	no data
air	no data	no data	no data	no data
Solubility				
water	585 g/L @ 25 °C	insoluble	insoluble	insoluble
organic solvents	soluble in ethanol	no data	insoluble in ethanol	no data

Characteristic	Chromium (III) sulphate	sodium chromite [chromium (III)]	Chromium (IV) oxide	Amonium dichromate [chromium (VI)]
synonyms	sulphuric acid, chromium (III) salt	no data	chromium dioxide	chromic acid, diamonium salt
chemical formula	$\text{Cr}_2(\text{SO}_4)_3$	$\text{NaCrO}_2$	$\text{CrO}_2$	$(\text{NH}_4)_2\text{Cr}_2\text{O}_7$
CAS No.	10101-53-8	12314-42-0	12018-01-8	7789-09-5
Molecular Weight	392.16	106.98	83.99	252.06
Colour	violet or red	no data	brown – black	orange
Physical state	solid	no data	solid	solid
Melting point °C	no data	no data	decomposes @ 300°C	decomposes @ 170°C
Boiling point °C	no data	no data	not applicable	not applicable
Density, g/cm <sup>3</sup>	3.01	no data	no data	2.15 @ 25°C
Odour	no data	no data	no data	no data
Odour threshold				
water	no data	no data	no data	no data
air	no data	no data	no data	no data
Solubility				
water	insoluble	no data	insoluble	308 g/L @ 15°C
organic solvents	slightly soluble in ethanol	no data	no data	soluble in ethanol

Characteristic	Calcium chromate [chromium (VI)]	Chromium (VI) oxide	Lead chromate [chromium (VI)]	Potassium chromate [chromium (VI)]
synonyms	chromic acid, calcium salt	chromic acid, chromic anhydride	chromic acid, lead salt	chromic acid, dipotassium salt
chemical formula	CaCrO <sub>4</sub>	CrO <sub>3</sub>	PbCrO <sub>4</sub>	K <sub>2</sub> CrO <sub>4</sub>
CAS No.	13765-19-0	1333-82-0	7758-97-6	7789-00-6
Molecular Weight	156.07	99.99	323.18	194.20
Colour	yellow	red	yellow	yellow
Physical state	solid	solid	solid	solid
Melting point °C	no data	196	844	968.3
Boiling point °C	no data	decomposes	decomposes	no data
Density, g/cm <sup>3</sup>	2.89	2.7 @ 25 °C	6.12 @ 15 °C	2.73 @ 18°C
Odour	no data	odourless	no data	no data
Odour threshold				
water	no data	no data	no data	no data
air	no data	no data	no data	no data
Solubility				
water	22.3g/L	617g/L @ 0 °C	58 µg/L	629 g/L @ 20 °C
organic solvents	no data	soluble in ethanol and ether	insoluble in acetic acid	insoluble in ethanol

Characteristic	Potassium dichromate [chromium (VI)]	Sodium chromate [chromium (VI)]	sodium dichromate, dihydrate [chromium (VI)]	strontium chromate [chromium (VI)]	Zinc chromate [chromium (VI)]
synonyms	chromic acid, dipotassium salt	chromic acid, disodium salt	chromic acid, disodium salt, dihydrate	chromic acid, strontium salt	chromic acid, zinc salt
chemical formula	$K_2Cr_2O_7$	$Na_2CrO_4$	$Na_2Cr_2O_7 \cdot 2H_2O$	$SrCrO_4$	$ZnCrO_4$
CAS No.	7778-50-9	7775-11-3	7789-12-0	7789-06-2	13530-65-9
Molecular Weight	294.18	161.97	298.00	203.61	181.37
Colour	red	yellow	red	yellow	lemon-yellow
Physical state	solid	solid	solid	solid	solid
Melting point °C	398	792	356.7	no data	no data
Boiling point °C	decomposes @ 500	no data	decomposes @ 400	no data	no data
Density, g/cm <sup>3</sup>	2.676 @ 25 °C	2.710-2.736	2.52 @ 13 °C	3.895 @ 15 °C	3.4
Odour	odourless	no data	no data	no data	odourless
Odour threshold water	no data	no data	no data	no data	no data
air	no data	no data	no data	no data	no data
Solubility water	49 g/L @ 0 °C	873 g/L @ 30 °C	2300 g/L @ 0 °C	1.2 g/L @ 15 °C	insoluble
Organic solvents	insoluble in ethanol	soluble in methanol	insoluble in ethanol	soluble in acetyl acetone, acetone	insoluble in acetone

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**Sources (Based on ATSDR, 1993)**

The largest source of chromium in air is the combustion of fossil fuels (oil-based and coal-based). However, most of the chromium from this source is chromium (III). The largest sources of chromium (VI) are chemical manufacturing processes. Chrome plating, steel welding and chromium (VI) manufacturers and industrial users (textile industry, manufacturers of dyes and pigments etc.) can discharge chromium (VI) waste into the waterways. The soil levels of chromium (VI) are increased primarily by disposal of commercial products containing chromium, industrial waste containing chromium and by coal ash from electric utilities.

**2. Environmental Fate (Based on ATSDR, 1993)**

In air, chromium is present mostly in the form of dust particulate (median diameter of about 1  $\mu\text{m}$ ). Rain or snow may help settle chromium to the ground or waterways. Airborne chromium (VI) may be reduced to chromium (III) by ( $\text{V}^{2+}$ ,  $\text{V}^{3+}$ ,  $\text{VO}^{2+}$ ,  $\text{Fe}^{2+}$ ,  $\text{HSO}_3^-$  and  $\text{AS}^{3+}$ ). The particles of chromium remain in air for only a short time (days) before settling.

In the water, most chromium is insoluble and is found mostly as part of the sediment. Chromium (VI) tends to get reduced to chromium (III) in the sediment, but relatively slowly. Some chromium is in a water-soluble form and may persist in the water column. Under anaerobic conditions, chromium (VI) is reduced quickly (hours to days) to chromium (III). Under aerobic conditions, slow oxidation (years) from chromium (III) to chromium (VI) may take place. Chromium does not bioaccumulate in fish, but the bottom-feeding invertebrates do accumulate this substance. Terrestrial plants may have elevated levels of chromium in the roots but minimal increases were observed in the above ground component of the edible plants. There is no indication of biomagnification of chromium along the terrestrial food chain.

In soils, chromium exists primarily in the water-insoluble form. In this form, it will be firmly attached to soil and display little mobility within the soil strata. A small proportion of chromium in soils is water-soluble. This form may be mobile and contaminate ground water. Most soil conditions favour chromium (III) over chromium (VI).

The population is normally exposed to chromium primarily from food (about 96%) and to a lesser degree from drinking water (about 3%) and air (about 1%). Dermal exposure is possible from chrome-treated consumer goods, such as wood treated with copper dichromate or leather tanned with chromic sulphate.

The subpopulations that may be exposed to higher than normal levels of chromium are those living near the following locations.

- landfill sites with chromium-containing waste
- industrial sites which manufacture or use chromium
- cement-producing plants, because cement contains chromium
- industrial cooling towers, which use chromium as rust inhibitors
- waterways that receive discharges from electroplating, leather tanning and textile industries
- major roadways, because of the emissions from brake linings and from the catalytic converters

In addition, subpopulations exposed to tobacco products may also be exposed to higher levels of chromium, since these products contain chromium.

### **3. Toxicokinetics (Based on ATSDR, 1993)**

The differences in absorption of chromium in different valence states may be the most important factor in the toxicity of this metal from different sources. Chromium (VI) is more readily absorbed across the body barriers (lung tissue, gastrointestinal tract and skin) than trivalent chromium. However in the stomach, hexavalent chromium (chromium VI) is largely reduced to chromium (III). As a result, chromium (VI) is less readily absorbed by oral route than by the other routes. In order to exert its toxicity, chromium (VI) needs to cross the cellular membranes and it enters the cells much more readily than chromium (III). Inside the cells, chromium (VI) is reduced, mostly to chromium (V). During the reduction process, highly reactive molecules (radicals) are formed, which may react with surrounding cellular material and thus cause tissue damage. For example, after exposure to chromium (VI) in an animal model, chromium (V) has been shown to react with DNA, forming chromium (V)-glutathione DNA adducts. This transformation may be the cause of the tumour-initiating capability of chromium (VI) and some of its other toxic effects (see below).

Chromium is distributed to most tissues to some degree, but the highest levels tend to be found consistently (in no order) in the lung, liver, spleen and kidneys. The lung levels are particularly high when exposure takes place via the respiratory tract. The chromium levels found in the lungs are considerably lower when exposure is via routes other than inhalation

Inorganic chromium (III) can be incorporated into a dinicotinato chromium (III) glutathione-like complex (GTF). This complex has not as yet been fully characterized but believed to be the biologically active form of chromium, which facilitates the action of insulin. Chromium (VI) can be reduced to chromium (III) before it enters the tissues in the stomach, by gastric acid and ascorbate and also in the lungs by the epithelial lining fluid (ELF). Once it crosses into the cells, chromium (VI) can be reduced to chromium (III) through a process requiring the enzymes, cytochrome P450 and an endogenous reducing agent NADPH. Alternatively, chromium (VI) can be reduced by glutathione to a chromium (V)-glutathione complex. Chromium (VI) is ultimately reduced to chromium (III) in the cell and eliminated from the cell in the form of chromium (III)-glutathione complex and excreted in the urine.

### **4. Human Health effects**

Chromium can induce, at high enough doses, a range of systemic effects. However, at much lower environmental levels, humans are unlikely to experience the same effects (ATSDR, 1993). For instance, inhaled chromium (VI) at air levels above 20 ng/m<sup>3</sup> may cause irritation to nasal mucosa, nosebleeds, ulcers and holes in the nasal septum. While the typical level of chromium in ambient air is about 10 to 30 ng/m<sup>3</sup>, most of the chromium in the ambient air is chromium (III) and not the more toxic chromium (VI) (ATSDR, 1993).

Exposure to low doses of chromium (any form) induces allergic reactions causing skin rashes as well as redness and swelling of the skin in sensitive people. Exposure to chromium (VI) and perhaps chromium (III) may also cause reproductive effects (ATSDR, 1993). However, there are no human data, which allow one to estimate the potency of chromium in humans directly. Furthermore, to estimate the potency of chromium in humans based on animal data is difficult. Therefore what the health impact may be at environmentally relevant levels is unclear. Chromium (III) is an essential element in human nutrition and the recommended daily intake for adults is between 50 and 200 µg (NRC, 1989). For other age groups, the recommended daily intake is lower.

Chromium (VI) is genotoxic in humans and in a number of experimental tests (ATSDR, 1993). But probably the most important effect of chromium is its cancer-inducing potential. Based on the weight of evidence, International Agency of Research on Cancer (IARC, 1990) classified chromium (VI) into Group 1 (*The agent is carcinogenic to humans*). USEPA (1998b) classified Cr (VI) into Group A (*known human carcinogen*) by the inhalation route of exposure, but into Group D (*not classified as to its human carcinogenicity*) by oral exposure, reflecting its low potency by this route.

On the other hand, Chromium (III) was classified by IARC (1990) into Group 3 (*agent is unclassifiable as to carcinogenicity in humans*) and USEPA (1998a) placed it into Group D (*not classified as to its human carcinogenicity*). However, the classification of hexavalent chromium as a known human carcinogen raises some concern for the carcinogenic potential of trivalent chromium (USEPA, 1998a). Canadian Environmental Protection Act (CEPA, 1994) classified chromium (III) into Group VI (*unclassifiable with respect to carcinogenicity in humans*).

## **5. Potency**

### **CHROMIUM (III)**

USEPA (1998a) developed an (oral) Reference Dose (RfD) of 1.5 mg/kg/day for chromium (III). The assessment is based on the study of Ivankovic and Preussmann (1975). In this study, rats were fed chromium (III) oxide, Cr<sub>2</sub>O<sub>3</sub>, in the diet, 5 days a week for 600 days. Chromium was administered as 0, 1%, 2%, or 5% Cr<sub>2</sub>O<sub>3</sub>. On completion of the treatment, the animals were maintained until they became moribund or died. All tissues were then examined histologically. No effect was observed at any treatment level. USEPA (1998c) selected the treatment group receiving 5% Cr<sub>2</sub>O<sub>3</sub> in the diet to establish the *No Adverse Effect Level* (NOAEL). The dose of Cr (III) corresponding to the NOAEL was estimated at 1468 mg/kg/day.

In a separate set of experiments, Ivankovic and Preussmann (1975) fed rats 0, 2%, or 5% Cr<sub>2</sub>O<sub>3</sub> in bread, 5 days/week for 90 days. No changes were observed in serum protein, bilirubin, haematology, urinalysis, and histopathology, but the livers and spleens weighed less in the high-dose group. The high dose is equivalent to 1,400 mg/kg/day of Cr<sub>2</sub>O<sub>3</sub>.

In order to derive the RfD, USEPA (1998c) divided the NOAEL value of 1468 mg/kg/day by an *uncertainty factor* (UF) of 100 and again by a *modifying factor* (MF) of 10. The UF accounts for species difference in sensitivity and for the variation of sensitivity within human population to the effects of chromium (III). The MF is designed to compensate for database deficiencies. No data are available for mammals other than rodents and there is a concern about possible reproductive effects. In addition, some limitations of the Ivankovic and Preussmann (1975) study have also been raised.

## **CHROMIUM (VI)**

### Oral-Non-Cancer

USEPA (1998b) developed a (oral) *Reference Dose* (RfD) for chromium (VI) of 3 E-3 mg/kg/day based on the *No Adverse Effect Level* (NOAEL) of 25 mg/L. The NOAEL was derived from the study of MacKenzie *et al.* (1958). In this study, rats received drinking water containing 0.45-11.2 mg/L chromium (VI) (potassium chromate, K<sub>2</sub>CrO<sub>4</sub>) for 1 year. The control animals received distilled water. In a second experiment rats received 25 mg/L chromium (VI) in the form of K<sub>2</sub>CrO<sub>4</sub> or chromium (III) in the form of chromic chloride or distilled water. No significant adverse effects were seen in terms of appearance, weight gain, or food consumption, and there were no pathologic changes in the blood or other tissues in any treatment group. The rats receiving chromium (VI) showed an approximate 20% reduction in water consumption. The drinking water concentration of 25 mg/L was converted to daily consumption of 2.5 mg of chromium (VI) per kg body weight based on a body weight of 0.35 kg and an average daily drinking water consumption of 0.035 L/day for the rat. This dose (2.5 mg of chromium (VI) /kg/day) was considered the NOAEL. The RfD was derived by dividing the NOAEL by an uncertainty factor of 300 and a modifying factor of 3. The uncertainty factor accounts for differences in sensitivity within the human population, for species differences and for a less than lifetime exposure regiment of the rats in the study of MacKenzie *et al.* (1958). A modifying factor of 3 was introduced as a conservative measure to account for concerns raised by the study of Zhang and Li (1987). This study showed adverse human health effects after drinking water containing approximately 20mg/L of chromium. Detailed information about exposure, magnitude and duration were not available in the study and the study was not considered sufficient to be used to develop a NOAEL or LOAEL.

### Inhalation- Non-Cancer

USEPA (1998d) developed 2 *Reference Concentrations* (RfCs) for chromium (VI). The first one was developed for chromic acid mists and aerosols. The second was developed for chromium (VI) in a particulate form.

### **Aerosols**

A RfC for aerosols was developed based an occupational study (Lindberg and Hedenstierna, 1983). Subjects exposed almost exclusively to chromic acid were divided into a low-exposure group, exposed to 8-hr, 5 days a week time-weighted average (TWA) below 0.002 mg/m<sup>3</sup> and a high-exposure group exposed above this level. Office employees were used as controls for nose and throat symptoms and auto mechanics were the controls for lung function measurements. Smoking habits of workers were evaluated

as part of the study. The authors concluded that 8-hour mean exposures to chromic acid above 0.002 mg/m<sup>3</sup> may cause a transient decrease in lung function, and that short-term exposures to greater than 0.02 mg/m<sup>3</sup> may cause septal ulceration and perforation.

Based on the results of this study, USEPA (1998d) determined the LOAEL to be 0.002 mg/m<sup>3</sup>, for an 8-hr TWA exposure to chromium (VI) mists. After conversion to continuous exposure, the LOAEL became 7.14 E-4 mg/m<sup>3</sup>. This continuous exposure LOAEL was divided by an uncertainty factor of 90 for the following reasons.

- to extrapolate from a subchronic to a chronic exposure (factor of 3)
- to account for extrapolation from a LOAEL to a NOAEL (factor of 3)
- to account for inter-human variation (factor of 10)

The result is an RfC of 8 E-6 mg/m<sup>3</sup> for upper respiratory effects caused by chromic acid mists and dissolved chromium (VI) aerosols (USEPA, 1998d).

### Particulates

Glaser *et al.* (1985, 1990) studied the effects of particulate chromium (VI) on the lower respiratory tract. In the 1990 study, rats were exposed to sodium dichromate at 0.05 - 0.4 mg Cr(VI)/m<sup>3</sup> 22 hr/day, 7 days/wk for 30-90 days. Chromium-induced effects occurred in a strong dose-dependent manner and involved respiratory tract structure and function, white blood cell count, and body weight.

Glaser *et al.* (1985) exposed 5-week-old male Wistar rats to aerosols of sodium dichromate at concentrations ranging from 0.025 to 0.2 mg Cr(VI)/m<sup>3</sup>, 22 hr/day for 28 days or 90 days. Again the chromium-induced effects occurred in a dose-dependent manner. Effects on the lung and spleen and immune system were observed.

Together, these studies present dose-dependent results on sensitive indicators of lower respiratory toxicity. Potential upper respiratory impacts resulting from the exposures were not addressed.

The USEPA (1998d) assessment made use of the benchmark concentration (BMC) derived by Malsch *et al.* (1994) for chromium (VI). The BMC range was developed for lung and spleen weights and for indicators of lung structure and function based on the two studies by Glaser *et al.* (1985, 1990). The data with exposures of less than 90 days were excluded from the assessment. Malsch *et al.* (1994) defined the benchmark concentration as the 95% lower confidence limit on the dose corresponding to a 10% relative change in the endpoint when compared to the control. Dose-effect data were adjusted to account for discontinuous exposure (22 hr/day) and the maximum likelihood model was used to fit continuous data to a polynomial mean response regression, yielding maximum likelihood estimates of 0.036 - 0.078 mg/m<sup>3</sup> and BMCs of 0.016 - 0.067 mg/m<sup>3</sup>. Next, Malsch *et al.* (1994) applied dosimetric adjustments and uncertainty factors to determine a RfC based on the following equation.

$$\text{RfC} = \frac{\text{BMC} \times \text{RDDR}}{\text{UF}_A \times \text{UF}_F \times \text{UF}_H}$$

where:

RfC	is the inhalation reference concentration
BMC	is the benchmark concentration (lower 95% confidence limit on the dose corresponding to a 10% relative change in the endpoint when compared to the control)
RDDR	is the regional deposited dose ratio to account for pharmacokinetic differences between species
UF <sub>A</sub>	uncertainty factor of 3.16 (midpoint between 1 and 10 on a log scale) to account for pharmacodynamic differences not addressed by the RDDR
UF <sub>F</sub>	uncertainty factor 3.16 to account for extrapolating from subchronic to chronic exposures; and
UF <sub>H</sub>	is a 10-fold uncertainty factor to account for variation in sensitivity among members of the human population

The RDDR factor of 2.1576 is incorporated to account for differences in the deposition pattern of inhaled hexavalent chromium dusts in the respiratory tract of humans and the Wistar rat test animals. A total uncertainty factor of 100 (UF<sub>A</sub> x UF<sub>F</sub> x UF<sub>H</sub>) was applied to the BMC in addition to the RDDR. The resulting RfC was 1 E-4 mg/m<sup>3</sup>.

#### Inhalation-Cancer

##### USEPA

USEPA (1998d) conducted the assessment based on the work of Mancuso (1975). This study is an update of an earlier study (Mancuso and Hueper, 1951). Mancuso (1975) followed 332 of the workers employed in an Ohio chromate plant from 1931-1951 until 1974. Lung cancer death rates increased by gradient of exposure to total chromium, and significant deposition of chromium was found in the lungs of workers long after the exposure ceased. Mancuso's (1975) study was insufficient to identify the specific form of chromium responsible for the lung cancer.

The cancer mortality in the Mancuso (1975) study was assumed to be due to Cr(VI), which was further assumed to be no less than one-seventh of total chromium, which was reported in the study. The quantitative dose-response estimation process is described in USEPA (1998d). First, the occupational exposures were converted into continuous exposures (8 hrs to 24 hrs, 240 days to 365 days). The estimated lifetime extra risk is 1.2 E-2 (µg/m<sup>3</sup>)<sup>-1</sup>. The unit risk should not be used if the air concentration exceeds 8E-1 µg/m<sup>3</sup>, as the unit risk may not be appropriate above this concentration.

##### World Health Organization (WHO)

WHO (1995) examined a number of epidemiological studies (unnamed, but apparently not the same as those used by USEPA) and derived cancer risks ranging between 1.3E-1 to 1.1E-2 (µg chromium (VI)/m<sup>3</sup>)<sup>-1</sup>. WHO (1995) recommends a unit risk of 4 E-2 (µg chromium (VI)/m<sup>3</sup>)<sup>-1</sup>, which corresponds to the geometric mean of the range of unit risk estimates.

CEPA (1994)

CEPA (1994) estimated the TD<sub>0.05</sub> for total chromium to be 4.6 µg/m<sup>3</sup> and for chromium (VI) to be 0.66 µg/m<sup>3</sup>, which is equivalent to a slope factor of about 7.6E-2 (µg chromium (VI)/m<sup>3</sup>)<sup>-1</sup>. Similar to the USEPA assessment, CEPA's assessment utilizes the Manusco data (1975) and CEPA's approach to quantitative assessment is also similar.

### **Conclusion**

For oral exposures to chromium (III) or (VI), it is recommended to use the RfDs developed for these two forms of chromium by USEPA (1998c, d) as presented in USEPA's IRIS database (USEPA, 1998a, b). For non-cancer effects of Cr(VI) due to inhalation exposure, the USEPA (1998d) RfCs for aerosols and particulates are recommended where appropriate. To evaluate cancer risk due to inhalation of Cr(VI), there are three options. All potency estimates are within an order of magnitude and should be interpreted as a consensus among the agencies. The assessment by WHO (1995) is based on several epidemiological studies and a range of values has been established. This approach reduces dependence on a single study and its potential idiosyncrasies. It is therefore recommended to use the WHO assessment for cancer effects due to inhalation exposure to chromium (VI).

## **6. References**

ATSDR, 1993. Toxicological profile for chromium. Update April 93. Agency for Toxic Substances and Disease Registry.

Glaser, U., Hochrainer, D., Kloppe, H. *et al.*, 1985. Low level chromium (VI) inhalation effects on alveolar macrophages and immune function in Wistar rats. *Arch. Toxicol.* 57(4): 250-256.

Glaser, U., Hochrainer, D., Steinhoff, D., 1990. Investigation of irritating properties of inhaled Cr (VI) with possible influence on its carcinogenic action. In: *Environmental Hygiene II*. Seemayer, N.O., Hadnagy, W, eds. Springer-Verlag, Berlin/New York.

IARC (International Agency for Research on Cancer), 1990. IARC monographs on the evaluation of carcinogenic risks to humans. Chromium, nickel and welding. Vol. 49. International Agency for Research on Cancer. Lyons, France.

Ivankovic, S., Preussmann, R., 1975. Absence of toxic and carcinogenic effects after administration of high doses of chromic oxide pigment in subacute and long-term feeding experiments in rats. *Food Cosmet. Toxicol.* 13: 347-351.

Lindberg, E., Hedensteirna, G., 1983. Chrome plating: Symptoms, finding in the upper airways and effects on lung function. *Arch. Environ. Health.* 38: 367-374.

MacKenzie, R.D., Byerrum, R.U., Decker, C.F. *et al.*, 1958. Chronic toxicity studies. II.

Hexavalent and trivalent chromium administered in drinking water to rats. *Am. Med. Assoc. Arch. Ind. Health.* 18: 232-234.

Malsch, P.A., Proctor, D.M., Finley, B.L., 1994. Estimation of a chromium inhalation reference concentration using the benchmark dose method: a case study. *Regul. Toxicol. Pharmacol.* 20: 58-82.

Mancuso, T.F., 1975. Consideration of chromium as an industrial carcinogen. International Conference on Heavy Metals in the Environment, Toronto, Ontario, Canada, October 27-31. pp. 343-356.

Mancuso, T.F., Hueper, W.C., 1951. Occupational cancer and other health hazards in a chromate plant: A medical appraisal. In: Lung cancers in chromate workers. *Ind. Med. Surg.* 20(8): 358-363.

NRC. 1989. National Research Council. Recommended dietary allowances. 10th ed. National Academy of Sciences, Washington, DC, pp. 241-243.

USEPA, 1998a, b. Integrated Risk Information System. US Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH.

USEPA, 1998c. Toxicological Review Of Trivalent Chromium (CAS No. 16065-83-1) In Support of Summary Information on the Integrated Risk Information System (IRIS). U.S. Environmental Protection Agency, Washington, DC, August 1998.

USEPA, 1998d. Toxicological Review Of Hexavalent Chromium (CAS No. 18540-29-9) In Support of Summary Information on the Integrated Risk Information System (IRIS). U.S. Environmental Protection Agency, Washington, DC, August 1998.

World Health Organization, 1995. Updating and Revision of the Air Quality Guidelines for Europe. Report on the WHO Working Group on Inorganic Air Pollutants. Düsseldorf, Germany, 24-27 October 1994.

Zhang, J., Li, X., 1987. Chromium pollution of soil and water in Jinzhou. *J. of Chinese Preventive Med.* 21: 262-264.