CHROMIUM

Ambient Water Quality Criteria

Criteria and Standards Division
Office of Water Planning and Standards
U.S. Environmental Protection Agency
Washington, D.C.

CRITERION DOCUMENT

CHROMIUM

CRITERIA

Aquatic Life

For trivalent chromium the criterion to protect freshwater aquatic life as derived using the Guidelines is "$e^{(0.83 \cdot \ln(\text{hardness})+2.94)}$" as a 24-hour average (see the figure "24-hour average trivalent chromium concentration vs. hardness") and the concentration should not exceed "$e^{(0.83 \cdot \ln(\text{hardness})+3.72)}$" (see the figure "maximum trivalent chromium concentration vs. hardness") at any time.

For hexavalent chromium the criterion to protect freshwater aquatic life as derived using the Guidelines is 10 µg/l as a 24-hour average concentration and the concentration should not exceed 110 µg/l at any time.

For saltwater aquatic life, no criterion for trivalent chromium can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

For hexavalent chromium the criterion to protect saltwater aquatic life as derived using the Guidelines is 25 µg/l as a 24-hour average and the concentration should not exceed 230 µg/l at any time.

Human Health

For the protection of human health from the toxic properties of chromium (except hexavalent chromium) ingested through water and contaminated aquatic organisms, the recommended water quality criterion is 50 µg/l.

For the maximum protection of human health from the potential carcinogenic effects of exposure to hexavalent chromium through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of hexavalent chromium estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 8 ng/l, 0.8 ng/l, and .08 ng/l, respectively.

CHROMIUM

Introduction

Chromium is a metallic element which can exist in several valence states. However, in the aquatic environment it virtually is always found in valence states +3 or +6. Hexavalent chromium is a strong oxidizing agent which reacts readily with reducing agents such as sulfur dioxide to give trivalent chromium. Cr III oxidizes slowly to Cr VI, the rate increasing with temperature. Oxidation progresses rapidly when Cr III absorbs to MnO, but is interfered with by Ca II and Mg II ions. Thus, accumulation would probably occur in sediments where chemical equilibria favor the formation of Cr III, while Cr VI, if favored, would presumably dissipate in soluble forms. Hexavalent chromium exists in solution as a component of an anion, rather than a cation, and therefore, does not precipitate from alkaline solution. The three important anions are: hydrochromate, chromate, and dichromate. The proportion of hexavalent chromium present in each of these forms depends on pH. In strongly basic and neutral solutions the chromate form predominates. As pH is lowered, the hydrochromate concentration increases. At very low pH the dichromate species predominates. In the pH ranges encountered in natural waters the proportion of dichromate ions is relatively low. In the acid portion of the environmental range, the predominant form is hydrochromate ion (63.6 percent at pH 6.0 to 6.2) (Trama and Benoit, 1960). In the alkaline portion of the range, the predominant form is chromate ion (95.7 percent at pH 8.5 to 7.8) (Trama

and Benoit, 1960). The anionic form of chromium can affect its toxicity.

Trivalent chromium in solution forms numerous types of hexacoordinate complexes (Cotton and Wilkinson, 1962). The best known and one of the most stable of these is the amine class (complexes include aquo ions, acido complexes (which are anionic), and polynuclear complexes. Complex formation can prevent precipitation of the hydrous oxide or other insoluble forms at pH values at which it would otherwise occur.

Chromium salts are used extensively in the metal finishing industry as electroplating, cleaning, and passivating agents, and as mordants in the textile industry. They also are used in cooling waters, in the leather tanning industry, in catalytic manufacture, in pigments and primer paints, and in fungicides and wood preservatives. Kopp reported a mean surface water concentration in the United States of 9.7 µg/l, based on 1,577 samples. Trivalent chromium is recognized as a essential trace element for humans. Hexavalent chromium in the workplace is suspected of being carcinogenic.

In the freshwater environment, hexavalent chromium has been shown acutely toxic to invertebrates at concentrations as low as 22 µg/l (Baudouin and Scoppa, 1974) and 17,600 µg/l for vertebrates (Pickering and Henderson, 1966). For marine waters the figures are 2,000 µg/l for invertebrates (Eisler and Hennekey, 1977) and 30,000 µg/l for vertevrates (Mearns, et al. 1976).

For trivalent chromium the figure is 2,000 µg/l in freshwater (Biesinger and Christensen, 1972) and no data on marine organisms are available. Hexavalent chromium has been shown chronically toxic to freshwater organisms at 105 µg/l (Sauter, et al. 1976) and to marine organisms at 38 µg/l (Oshida, 1978). For trivalent chromium in freshwater the figure is 445 µg/l (Biesinger and Christensen, 1972) and no data on the chronic toxicity of trivalent chromium in marine waters are available.

Since chromium is an element, it will not be destroyed and may be expected to persist indefinitely in the environment in some form.

Both Cr VI and Cr III have shown mutagenic activity (Rafetto, et al. 1977). Occupational exposure to chromate fumes is suspected of causing cancer in humans (Natl. Acad. Sci. 1974).

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AQUATIC LIFE TOXICOLOGY*

FRESHWATER ORGANISMS

Introduction

Chromium is a chemically complex metal which occurs in valence states ranging from -2 to +6. The hexavalent and trivalent chromium compounds are the biologically and environmentally significant forms of the element, but they have very different chemical characteristics. Hexavalent chromium is very soluble in natural water. As with many other metal cations, the solubility of trivalent chromium in natural water is low and varies with water quality, being less soluble at high pH, alkalinity, and hardness.

Trivalent chromium is substantially more toxic to aquatic life in soft than in hard water. The effect of water hardness on the toxicity of hexavalent chromium is insignificant. As a result of these relationships the criterion for trivalent chromium is hardness related while that for hexavalent chromium is a single concentration for the 24-hour average.

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*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life [43 FR 21506 (May 18, 1978) and 43 FR 29028 (July 5, 1978)] in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of each table are the calculations for deriving various measures of toxicity as described in the Guidelines.

Acute Toxicity

As shown in Table 1, the data base for freshwater fish and chromium has 73 LC50 values, but about half of the values are for goldfish and fathead minnows from one report. Values include data for 14 species from seven families. Fifty-three percent of the values did not need adjustment for standardization. For the LC50 values that required adjustment for test methods or duration of the test, only four of the tests were less than 96 hours. Adjustment was required for 34 static tests and for 26 tests in which the concentrations were not measured.

No side-by-side static and flow-through tests or measured and unmeasured test concentrations are available for either hexavalent or trivalent chromium for direct comparison of these two conditions with regard to the appropriateness of the adjustment factors.

The adjusted 96-hour LC50 values for hexavalent chromium for nine species ranged from 9,620 µg/l for the fathead minnow tested in soft water to a high of 138,500 µg/l for the largemouth bass in hard water. Wallen, et al. (1957) studied the toxicity of hexavalent chromium to mosquitofish using potassium and sodium salts of both dichromate and chromate. Based on chromium, both dichromate salts were about half as toxic as either chromate salt. Trama and Benoit (1960) also studied the toxicity of hexavalent chromium using potassium dichromate and potassium chromate. The unadjusted 96-hour LC50 values are 110,000 µg/l for the dichromate salt and 170,000 µg/l for the chromate salt. They attributed the lower LC50 value of the dichromate salt as due to its acidity

being greater than that of the chromate salt because chromium is slightly more toxic at lower pH values.

The variation in toxicity of hexavalent chromium due to water hardness was less than the variation between the dichromate and chromate salts of hexavalent chromium in soft water (Pickering and Henderson, 1966). The unadjusted fathead minnow 96-hour LC50 values for dichromate and chromate salts in soft water were 17,600 µg/l and 45,600 µg/l, respectively. The unadjusted 96-hour LC50 values for dichromate in soft and hard water were 17,600 µg/l and 27,300 µg/l, respectively. The unadjusted 96-hour LC50 value of hexavalent chromium, using the dichromate salt, to the bluegill in soft water was 118,000 µg/l and in hard water was 133,000 µg/l. For both of the species, the difference in LC50 values due to hardness is less than a factor of 2.

The data from Adelman and Smith (1976) as shown in Tables 1 and 7 indicate that the threshold lethal concentration for hexavalent chromium does not occur within 96 hours. For the mean of 16 LC50 values, the ratio of 11-day to 96-hour values is 0.37 for the fathead minnow and 0.27 for the goldfish.

The geometric mean of the adjusted values for hexavalent chromium is 51,000 µg/l. When divided by the species sensitivity factor (3.9), the Final Fish Acute Value obtained for hexavalent chromium is 13,000 µg/l.

The adjusted 96-hour LC50 values for trivalent chromium for 11 species of fish ranged from 1,820 µg/l for the guppy in soft water to 39,300 µg/l for the bluegill tested in hard water.

Following the Guidelines, an exponential equation describing the relationship of toxicity of trivalent chromium to hardness for each species was fit by least squares regression of the natural logarithms of the toxicity values and hardness.

For trivalent chromium, sufficient acute toxicity data and hardness ranges were available for only two fish species to fit regression equations. The slopes of these equations were 0.89 for fathead minnows and 0.78 for bluegills, with a mean of 0.83. Although these regressions were for only two LC50 values each, and therefore not statistically significant, they were the only values available and were in reasonable agreement.

As a measure of relative species sensitivity to trivalent chromium, logarithmic intercepts were calculated for each species by fitting the mean slope (0.83) through the geometric mean toxicity value and hardness for each species. These intercepts varied from 5.02 for guppies to 6.22 for rainbow trout, with a mean intercept of 5.81 for all 11 fish species. This variation in logarithmic intercepts indicates a narrow range of species sensitivity to trivalent chromium of 3.5 times when adjusted for hardness effects.

When the mean intercept of 5.81 is adjusted by the species sensitivity factor (3.9), an adjusted mean intercept of 4.45 is obtained. Thus, the Final Fish Acute Value is given by $e^{(0.83 \cdot \ln(\text{hardness})+4.45)}$.

As shown in Table 2, the data base for freshwater invertebrate species has 20 LC50 values for 14 invertebrate forms of

which eight are identified to species. All LC50 values were from static tests. The adjusted LC50 values varied from 19 µg/l as hexavalent chromium for Daphnia hyalina to a high of 55,000 µg/l as trivalent chromium for a caddisfly. The data in Table 2 indicate that cladocerans are more sensitive to the lethal effects of chromium than the aquatic insects.

Debelak (1975) studied the acute toxicity of hexavalent chromium to Daphnia magna (Table 7) in both a reconstituted water with a hardness of 163 mg/l (as $CaCO_3$) and pH value of 8.3 and pond water with a hardness of 86 mg/l (as $CaCO_3$) and pH value of 8.4. The mean of five 72-hour LC50 values was 39 µg/l in the pond water and 73 µg/l in the reconstituted water. Thus, hexavalent chromium was slightly more toxic in the softer dilution water.

No data were available to indicate hardness effects on acute toxicity of trivalent chromium to invertebrate species since no species has been tested over a range of water hardness. Assuming that a similar relationship to hardness probably exists for acute toxicity to invertebrate species as with fish, the slope from the fish acute equation (0.83) was used to determine the logarithmic intercepts (relative species sensitivity) for invertebrate species.

Variation observed for invertebrate acute values for trivalent chromium is seen to be only slightly greater than the acute data on fish; the calculated intercepts for invertebrate LC50 values ranged from 4.30 for mayfly larvae to 7.77 for caddisfly.

However, there also was a relatively narrower range of hardness in the toxicity test waters (44 to 50 mg/l) as compared to the fish acute tests. Since eight invertebrate species are represented in the data base for trivalent chromium and the range of species sensitivities is narrower than indicated by the species sensitivity factor (21) from the Guidelines, a sensitivity factor was calculated from the variance of the logarithmic intercepts. This factor is 1.645 times the standard deviation (1.44), which is 2.37. The mean intercept (6.09) when adjusted by 2.37 is 3.72. Thus, the Final Invertebrate Acute Value is given by $e^{(0.83 \cdot \ln(\text{hardness})+3.72)}$. Since the invertebrate species are slightly more sensitive to trivalent chromium than fish, the Final Invertebrate Acute Value becomes the Final Acute Value.

The data in Table 2 indicate that the freshwater invertebrate species are also more sensitive to the lethal effects of hexavalent chromium than are freshwater fish. Thus the Final Invertebrate Acute Value (110 µg/l) becomes the Final Acute Value for hexavalent chromium.

Chronic Toxicity

The data base for fish chronic values for chromium (Table 3) is for seven species. Benoit (1976) reported on the long-term effects of hexavalent chromium to brook trout and rainbow trout. The maximum acceptable toxicant concentration (MATC) of 200 to 350 µg/l was established on the basis of survival. Growth in weight was retarded at all test concentrations during the first eight months of the exposure. However, this was a temporary effect on growth and was not used by the author to establish the MATC.

Sauter, et al. (1976) studied the toxicity of hexavalent chromium (sodium dichromate) to eggs and fry of six fish species: rainbow and lake trout, northern pike, white sucker, channel catfish, and bluegill. The eggs and fry were continuously exposed in soft water for a maximum of 60 days after hatching. Observations were made of the hatchability of eggs, and the survival, length, and weight of the fry after 30 and 60 days. The majority of the data generated from these chromium exposures indicates a very significant cumulative effect on fry. This was especially true for the rainbow and lake trout since significant mortality occurred between 30 and 60 days. This cumulative effect is consistent with the observed low geometric mean application factor of 0.004 (Table 3) based on life cycle tests with the rainbow and brook trout (Benoit, 1976). The chronic value for rainbow trout (Table 3) is 37 µg/l from the embryo-larval test and 265 µg/l from the life cycle test. This variation is due in part to the effect on growth that was considered to be temporary and was not used to establish the MATC in the chronic test while in the embryo-larval test the effect was on growth. In addition, the geometric mean of the limits is divided by the adjustment factor of 2 for the embryo-larval data. The chronic value for brook trout was the same as that for the rainbow trout derived from the life-cycle tests (Benoit, 1976).

All of the life cycle and embryo-larval tests were conducted with hexavalent chromium in soft water with a hardness range of 34 to 45 mg/l (as $CaCO_3$). Since the effect of hardness on acute toxicity of hexavalent chromium was insignificant, the same

relationship will be assumed for chronic toxicity to fish. Therefore, a geometric mean of the chronic values was calculated and is 177 µg/l. After division by the sensitivity factor (6.7), a Final Fish Chronic Value of 26 µg/l is obtained for hexavalent chromium.

No chronic data for fish and trivalent chromium are available.

The data base for the invertebrate chronic values for trivalent chromium is limited to Daphnia magna (Table 3). The geometric mean of the limits of the chronic values is 445 µg/l which is about one-fifth of the acute value (Table 2) in the same dilution water.

Daphnia magna is among the most sensitive species tested (Table 2). Therefore, it would appear to be inappropriate to use the Guidelines species sensitivity factor of 5.1 with the chronic data for Daphnia magna. Consequently, that sensitivity factor is not used in the calculations to derive the Final Invertebrate Chronic Value. Since appropriate invertebrate data were not available to establish a relationship between chronic toxicity values and hardness, a relationship was established by using the slope (0.83) from the Final Fish Acute Value and the trivalent chromium value and water hardness from the Daphnia magna chronic test. The calculated intercept for invertebrate species is 2.94. The derived equation for invertebrate species ($e^{(0.83 \cdot \ln(\text{hardness}) + 2.94)}$) becomes the Final Chronic Value since there are no chronic exposure data for fish and trivalent chromium.

Trabalka and Gehrs (1977) studied the chronic toxicity of hexavalent chromium to Daphnia magna. They found a significant

effect on both life span and fecundity at all test concentrations including the lowest of 10 µg/l. Because there was no concentration for the lower limit of the MATC, this datum is included in Table 7 instead of Table 4. On the basis of these data, the Final Invertebrate Chronic Value for hexavalent chromium would be less than 10 µg/l, which is lower than the Final Fish Chronic Value.

Plant Effects

The data on seven species of algae and Eurasian watermilfoil (Table 5) indicate that some algae are sensitive to the effects of chromium. All tests were conducted with hexavalent chromium, and reduction in growth and photosynthesis was the effect used to measure toxicity. The concentration of chromium ranged from 10 µg/l for a green alga to 9,900 µg/l for Eurasian watermilfoil. Growth of the green alga, Chlamydomonas reinhardi, was reduced at a concentration of 10 µg/l in Bold's basal medium. The Final Plant Value for hexavalent chromium is 10 µg/l.

Residues

Data are available for the rainbow trout and the bioconcentration factor is about one (Table 6). No maximum permissible tissue concentration is available; therefore, no Residue Limited Toxicant Concentration can be calculated.

Miscellaneous

The data in Table 7 indicate that low concentrations of hexavalent chromium have a deleterious effect on the growth of fishes. Olson and Foster (1956) reported a statistically significant effect on growth of chinook salmon at 16 µg/l and on rainbow trout at 21 µg/l. At these concentrations, growth was reduced about ten percent.

Olson (1958) studied the comparative toxicity of hexavalent and trivalent chromium to chinook salmon. As shown in Table 7, hexavalent chromium at a concentration of 200 µg/l was more toxic in Columbia River water (hardness, 70 mg/l as $CaCO_3$) than a similar concentration of trivalent chromium. Survival and growth in the trivalent chromium exposure was similar to controls; however, survival and growth in the hexavalent chromium exposure was only about 50 percent of the control.

The lowest concentration to produce an adverse effect was reported by Dowden and Bennett (1965). They reported a 48-hour LC50 for Daphnia magna of 30 µg/l of chromic sulfate. It is not possible to determine the formula weight of the salt. If it were anhydrous, the 48-hour LC50 value would be 8 µg/l. This value for trivalent chromium is so much lower than the value of 2,000 µg/l reported by Biesinger and Christensen (1972) that 8 µg/l is considered to be an outlier, and the value is in doubt.

Using the data of Trabalka and Gehrs (1977) and comparing the results with other chronic tests with hexavalent chromium, it is estimated that a concentration of 5 µg/l would not produce any deleterious effects.

CRITERION FORMULATION

Freshwater-Aquatic Life

Summary of Available Data

The concentrations below have been rounded to two significant figures. All concentrations herein are expressed in terms of chromium.

Hexavalent chromium

Final Fish Acute Value = 13,079 µg/l

Final Invertebrate Acute Value = 110 µg/l

Final Acute Value = 110 µg/l

Final Fish Chronic Value = 26 µg/l

Final Invertebrate Chronic Value = less than 10 µg/l

Final Plant Value = 10 µg/l

Residue Limited Toxicant Concentration = not available

Final Chronic Value = less than 10 µg/l

0.44 x Final Acute Value = 48 µg/l

Trivalent chromium

Final Fish Acute Value = $e^{(0.83 \cdot \ln(\text{hardness})+4.45)}$

Final Invertebrate Acute Value = $e^{(0.83 \cdot \ln(\text{hardness})+3.72)}$

Final Acute Value = $e^{(0.83 \cdot \ln(\text{hardness})+3.72)}$

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = $e^{(0.83 \cdot \ln(\text{hardness})+2.94)}$

Final Chronic Value = $e^{(0.83 \cdot \ln(\text{hardness})+2.94)}$

Final Plant Value = not available

Residue Limited Toxicant Concentration = not available

Hexavalent chromium

The maximum concentration of hexavalent chromium is the Final Acute Value of 110 µg/l and the 24-hour average concentration is

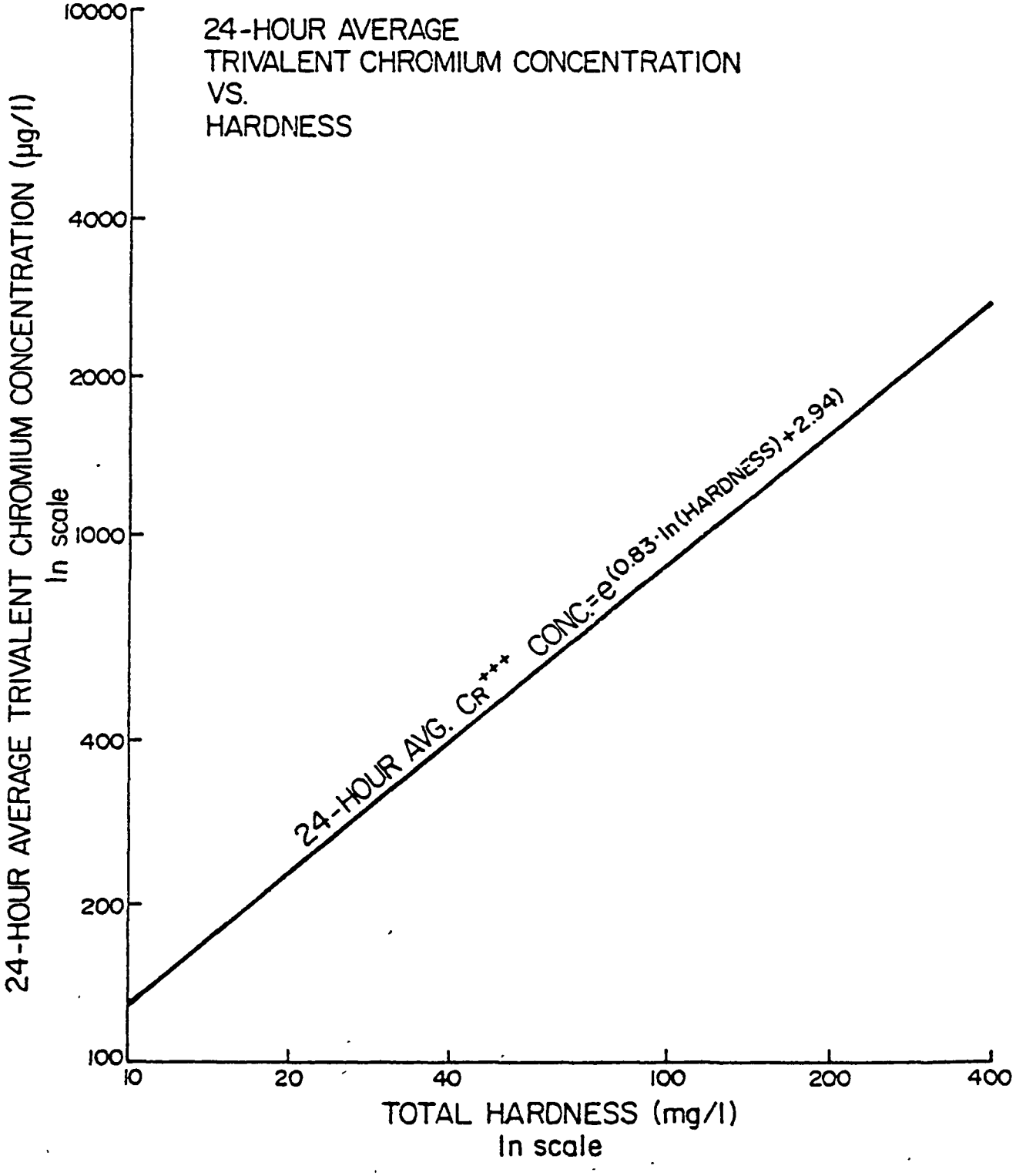
the Final Chronic Value of less than 10 µg/l. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For hexavalent chromium the criterion to protect freshwater aquatic life as derived using the Guidelines is 10 µg/l as a 24-hour average and the concentration should not exceed 110 µg/l at any time.

Trivalent chromium

The maximum concentration of trivalent chromium is the Final Acute Value of $e^{(0.83 \cdot \ln(\text{hardness}) + 3.72)}$ and the 24-hour average concentration is the Final Chronic Value of $e^{(0.83 \cdot \ln(\text{hardness}) + 2.94)}$. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentraion.

CRITERION: For trivalent chromium the criterion to protect freshwater aquatic life as derived using the Guidelines is "$e^{(0.83 \cdot \ln(\text{hardness}) + 2.94)}$" as a 24-hour average (see the figure "24-hour average trivalent chromium concentration vs. hardness") and the concentration should not exceed "$e^{(0.83 \cdot \ln(\text{hardness}) + 3.72)}$" (see the figure "maximum trivalent chromium concentration vs. hardness") at any time.


24-HOUR AVERAGE
TRIVALENT CHROMIUM CONCENTRATION
VS.
HARDNESS
24-HOUR AVERAGE TRIVALENT CHROMIUM CONCENTRATION (µg/l)
ln scale
10000
4000
2000
1000
400
200
100
24-HOUR AVG. CR^{+++} CONC.=e(0.83·ln(HARDNESS)+2.94)
10
20
40
100
200
400
TOTAL HARDNESS (mg/l)
ln scale

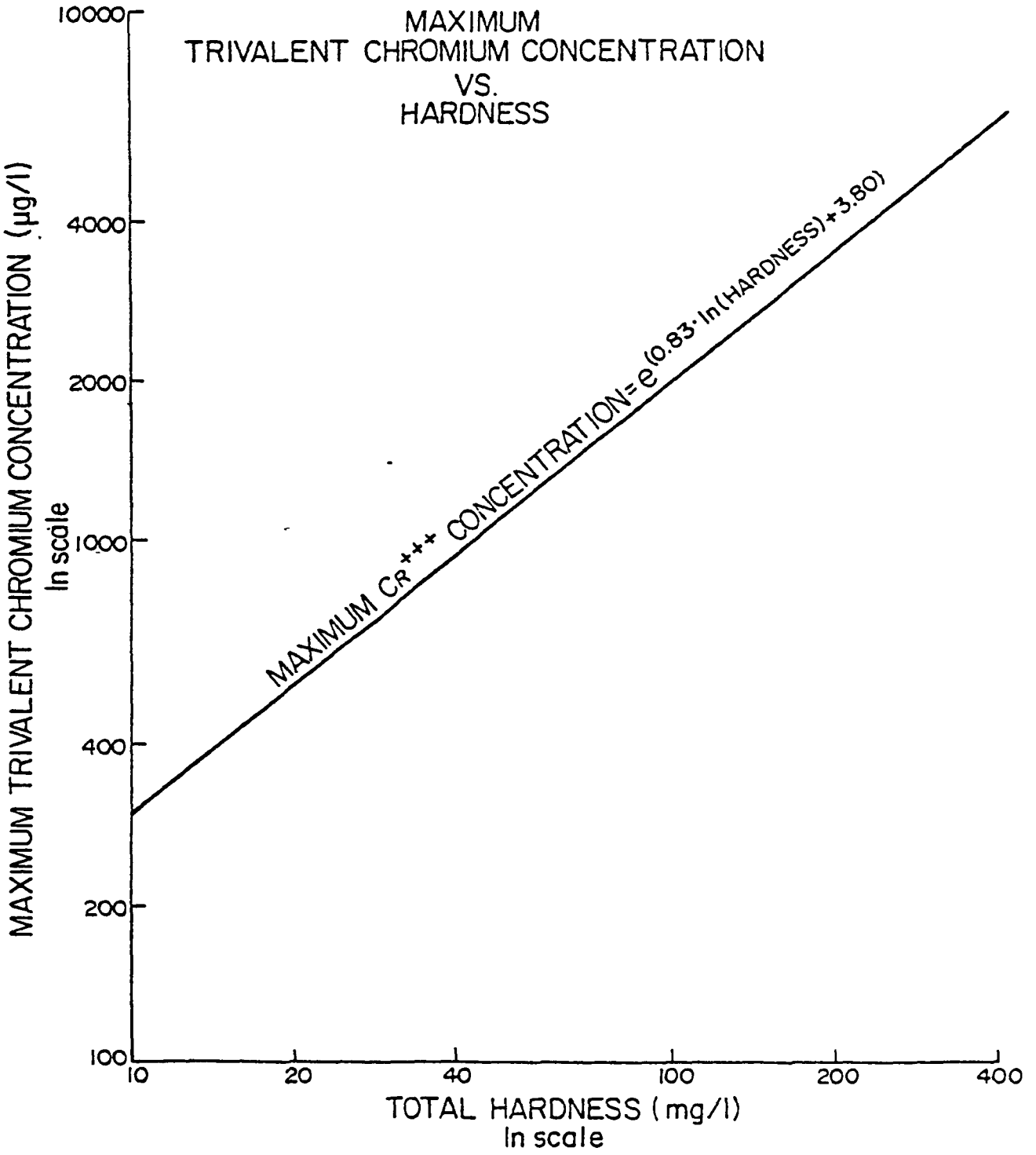

MAXIMUM
TRIVALENT CHROMIUM CONCENTRATION
VS.
HARDNESS
MAXIMUM TRIVALENT CHROMIUM CONCENTRATION (µg/l)
ln scale
10000
4000
2000
1000
400
200
100
MAXIMUM Cr^{+++} CONCENTRATION = $e^{(0.83 \cdot \ln(\text{HARDNESS}) + 3.80)}$
10
20
40
100
200
400
TOTAL HARDNESS (mg/l)
ln scale

Table 1. Freshwater fish acute values for chromium

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Hardness (mg/l as $CaCO_3$)	Reference
American eel, Anguilla rostrata	S	M	Trivalent	96	16,900	12,000	55	Rehwoldt, et al. 1972
Rainbow trout, Salmo gairdneri	FT	M	Hexavalent	96	69,000	69,000	45	Benoit, 1976
Rainbow trout, Salmo gairdneri	S	U	Trivalent	96	11,200	6,100	-	Bills, et al. 1977
Rainbow trout, Salmo gairdneri	FT	M	Trivalent	96	24,100	24,100	105***	Hale, 1977
Rainbow trout, Salmo gairdneri	S	M	Hexavalent	24	110,000	46,900	334	Schiffman & Fromm, 1959
Brook trout, Salvelinus fontinalis	FT	M	Hexavalent	96	59,000	59,000	45	Benoit, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	123,000	123,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	123,000	123,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	90,000	90,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	125,000	125,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	109,000	109,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	135,000	135,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	110,000	110,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	129,000	129,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	98,000	98,000	220	Adelman & Smith, 1976

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Hardness (mg/l as $CaCO_3$)	Reference
Goldfish, Carassuis auratus	FT	M	Hexavalent	96	133,000	133,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	102,000	102,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	133,000	133,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	126,000	126,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	126,000	126,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	133,000	133,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	126,000	126,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT	M	Hexavalent	96	124,000	124,000	220	Adelman & Smith, 1976
Goldfish, Carassius auratus	S	U	Hexavalent	24	249,000	89,800	100	Dowden & Bennett, 1965
Goldfish, Carassius auratus	S	U	Hexavalent	96	37,500	20,500	20	Pickering & Henderson, 1966
Goldfish, Carassius auratus	S	U	Trivalent	96	4,100	2,240	20	Pickering & Henderson, 1966
Carp, Cyprinus carpio	S	M	Trivalent	96	14,300	10,200	55	Rehwoldt, et al. 1972
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	56,000	56,000	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	51,000	51,000	220	Adelman & Smith
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	53,000	53,000	220	Adelman & Smith, 1976

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Hardness (mg/l as $CaCO_3$)	Reference
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	49,000	49,000	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	48,000	48,000	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	60,000	60,000	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	50,000	50,000	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	53,000	53,000	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	49,000	49,000	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	37,000	37,000	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	66,000	66,000	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	55,000	55,000	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	38,000	38,000	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	34,000	34,000	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	29,000	29,000	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	34,000	34,000	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	26,000	26,000	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	S	U	Hexavalent	96	17,600	9,620	20	Pickering & Henderson, 1966
Fathead minnow, Pimephales promelas	S	U	Hexavalent	96	27,300	14,900	360	Pickering & Henderson, 1966

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Hardness (mg/l as $CaCO_3$)	Reference
Fathead minnow, Pimephales promelas	S	U	Hexavalent	96	45,600	24,900	20	Pickering & Henderson, 1966
Fathead minnow, Pimephales promelas	S	U	Trivalent	96	5,070	2,770	20	Pickering & Henderson, 1966
Fathead minnow, Pimephales promelas	S	U	Trivalent	96	67,400	36,800	360	Pickering & Henderson, 1966
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	52,000	52,000	231***	Ruesink & Smith, 1975
Fathead minnow, Pimephales promelas	FT	M	Hexavalent	96	37,000	37,000	231***	Ruesink & Smith, 1975
Banded killifish, Fundulus diaphanus	S	M	Trivalent	96	16,900	12,000	55	Rehwoldt, et al. 1972
Mosquitofish, Gambusia affinis	S	U	Hexavalent	96	107,000	58,500	≥ 100***	Wallen, et al. 1957
Mosquitofish, Gambusia affinis	S	U	Hexavalent	96	99,000	54,100	≥ 100***	Wallen, et al. 1957
Mosquitofish, Gambusia affinis	S	U	Hexavalent	96	135,000	73,600	≥ 100***	Wallen, et al. 1957
Mosquitofish, Gambusia affinis	S	U	Hexavalent	96	92,000	50,400	≥ 100***	Wallen, et al. 1957
Guppy, Poecilia reticulata	S	U	Hexavalent	96	30,000	16,400	20	Pickering & Henderson, 1966
Guppy, Poecilia reticulata	S	U	Trivalent	96	3,330	1,820	20	Pickering & Henderson, 1966
White perch, Morone americana	S	M	Trivalent	96	14,400	10,200	55	Rehwoldt, et al. 1972
Striped bass, Morone saxatilis	S	U	Hexavalent	96	35,000	19,100	35	Hughes, 1971
Striped bass, Morone saxatilis	S	U	Hexavalent	96	26,500	14,500	35	Hughes, 1970
Striped bass, Morone saxatilis	S	M	Trivalent	96	17,700	12,600	55	Rehwoldt, et al. 1972

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Hardness (mg/l as $CaCO_3$)	Reference
Pumpkinseed, Lepomis gibbosus	S	M	Trivalent	96	17,000	12,100	55	Rehwoldt, et al. 1972
Bluegill, Lepomis macrochirus	S	U	Hexavalent	96	113,000	61,800	44	Cairns & Scheier, 1969
Bluegill, Lepomis macrochirus	S	U	Hexavalent	24	261,000	94,200	100	Dowden & Bennett, 1965
Bluegill, Lepomis macrochirus	S	U	Hexavalent	96	118,000	64,500	20	Pickering & Henderson, 1966
Bluegill, Lepomis macrochirus	S	U	Hexavalent	96	133,000	72,700	360	Pickering & Henderson, 1966
Bluegill, Lepomis macrochirus	S	U	Trivalent	96	7,460	4,100	20	Pickering & Henderson, 1966
Bluegill, Lepomis macrochirus	S	U	Trivalent	96	71,900	39,300	360	Pickering & Henderson, 1966
Bluegill, Lepomis macrochirus	S	U	Hexavalent	96	110,000	60,100	45	Trama & Benoit, 1960
Bluegill, Lepomis macrochirus	S	U	Hexavalent	96	170,000	92,900	45	Trama & Benoit, 1960
Bluegill, Lepomis macrochirus	S	U	Hexavalent	48	213,000	94,300	120	Turnbull, et al. 1954
Largemouth bass, Micropterus salmoides	S	M	Hexavalent	96	195,000	138,500	334	Fromm & Schiffman, 1958

* S = static, FT = flow-through

** U = unmeasured, M = measured

*** Alkalinity

Table 1. (Continued)

Organism	Bioassay Method	Test Conc.	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Hardness (mg/l as $CaCO_3$)	Reference

Hexavalent chromium:

Geometric mean of adjusted values = 51,007 µg/l $\quad \frac{51,007}{3.9} = 13,079$ µg/l

Lowest value from a flow-through test with measured concentrations = 26,000 µg/l

Trivalent chromium:

Adjusted LC50 vs. hardness:

Fathead minnow: slope = 0.89, intercept = 5.25, r = 1.0, not significant, N = 2

Bluegill: slope = 0.78, intercept = 5.98, r = 1.0, not significant, N = 2

Geometric mean slope = 0.83

Mean intercept for 11 species = 5.81

Adjusted mean intercept = 5.81 - ln(3.9) = 4.45

Final Fish Acute Value = $e^{(0.83 \cdot \ln(\text{hardness})+4.45)}$.

Table 2. Freshwater invertebrate acute values for chromium

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Hardness (mg/l as $CaCO_3$)	Reference
Rotifer, *Philodina acuticornis*	S	U	Hexavalent	96	3,100	2,600	25	Buikema, et al. 1974
Rotifer, *Philodina roseola*	S	M	Hexavalent	96	12,000	13,200	-	Schaefer & Pipes, 1973
Rotifer, *Philodina roseola*	S	M	Hexavalent	96	8,900	9,800	-	Schaefer & Pipes, 1973
Rotifer, *Philodina roseola*	S	M	Hexavalent	96	7,400	8,100	-	Schaefer & Pipes, 1973
Rotifer, *Philodina roseola*	S	M	Hexavalent	96	5,500	6,100	-	Schaefer & Pipes, 1973
Rotifer, *Philodina roseola*	S	M	Hexavalent	96	4,400	4,800	-	Schaefer & Pipes, 1973
Annelid, *Nais* sp	S	M	Trivalent	96	9,300	10,200	50	Rehwoldt, et al. 1973
Snail, *Amnicola* sp.	S	M	Trivalent	96	12,400	13,600	50	Rehwoldt, et al. 1973
Snail, *Amnicola* sp.	S	M	Trivalent	96	8,400	9,200	50	Rehwoldt, et al. 1973
Cladoceran, *Daphnia hyalina*	S	U	Hexavalent	48	22	19	66	Baudouin & Scoppa, 1974
Cladoceran, *Daphnia magna*	S	M	Trivalent	48	2,000	2,200	45	Biesinger & Christensen, 1972
Cladoceran, *Daphnia magna*	S	U	Hexavalent	48	6,400	5,400	-	Dowden & Bennett, 1965
Copepod, *Cyclops abyssorum*	S	U	Hexavalent	48	10,000	8,500	66	Baudouin & Scoppa, 1974
Copepod, *Cyclops padanus*	S	U	Hexavalent	48	10,100	8,600	66	Baudouin & Scoppa, 1974
Scud, *Gammarus* sp	S	M	Trivalent	96	3,200	3,500	50	Rehwoldt, et al. 1973

Table 2. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Hardness (mg/l as $CaCO_3$)	Reference
Mayfly, Ephemerella subvaris	S	U	Trivalent	96	2,000	1,700	44	Warnick & Bell, 1969
Damselfly, Unidentified	S	M	Trivalent	96	43,100	47,400	50	Rehwoldt, et al. 1973
Caddisfly, Hydropsyche betteni	S	U	Trivalent	96	64,000	54,500	44	Warnick & Bell, 1969
Caddisfly, Unidentified	S	M	Trivalent	96	50,000	55,000	50	Rehwoldt, et al. 1973

* S = static

** U = unmeasured, M = measured

Hexavalent chromium:

Geometric mean of adjusted values = 2,315 µg/l $\quad \frac{2,315}{21} = 110$ µg/l

Trivalent chromium:

Adjusted LC50 vs. hardness:

No hardness relationship could be derived for any invertebrate species.

Using the geometric mean slope (0.83) from the fish acute values, the mean intercept for 8 vertebrate species = 6.09, with a standard deviation of 1.44.

Adjusted mean intercept = $6.17-(1.645 \cdot 1.44)=3.72$

Final Invertebrate Acute Value = $e^{(0.83 \cdot \ln(\text{hardness})+3.72}$

Table 3. Freshwater fish chronic values for chromium

Organism	Test*	Limits (ug/l)	Chronic Value (ug/l)	Hardness (mg/l as $CaCO_3$)	Reference
Rainbow trout, Salmo gairdneri	E-L	51 - 105	37	34	Sauter, et al. 1976
Rainbow trout, Salmo gairdneri	LC	200 - 350	265	45	Benoit, 1976
Brook trout, Salvelinus fontinalis	LC	200 - 350	265	45	Benoit, 1976
Lake trout, Salvelinus namaycush	E-L	105 - 194	72	34	Sauter, et al. 1976
Northern pike, Esox lucius	E-L	538 - 963	360	38	Sauter, et al. 1976
White sucker, Catostomus commersoni	E-L	290 - 538	198	39	Sauter, et al. 1976
Channel catfish, Ictalurus punctatus	E-L	150 - 305	107	36	Sauter, et al. 1976
Bluegill, Lepomis macrochirus	E-L	522 - 1122	368	38	Sauter, et al. 1976

* LC = life cycle or partial life cycle, E-L = embryo-larval

** All data are for hexavalent chromium.

No chronic data are available for trivalent chromium.

Geometric mean of chronic values = 177 µg/l $\quad \frac{177}{6.7}$ = 26 µg/l

Lowest chronic value = 37 µg/l

Application Factor Values (Benoit, 1976)

Species	96-hr LC50 (µg/l)	MATC (µg/l)	AF
Rainbow trout, Salmo gairdneri	69,000	265	0.004
Brook trout, Salvelinus fontinalis	59,000	265	0.004

Organism	Test*	Limits (ug/l)	Chronic Value (ug/l)**	Hardness (mg/l as $CaCO_3$)
Cladoceran, Daphnia magna	LC	330-600	445	45

* LC = life-cycle or partial life-cycle

** Trivalent chromium

Geometric mean of chronic values = 445 µg/l $\quad \frac{445}{5.1} = 87$ µg/l

Lowest chronic value = 445 µg/l

Trivalent chromium:

Invertebrate chronic value vs. hardness:

No hardness relationship could be derived for any invertebrate species.

Using the geometric mean slope (0.83) from the fish acute values, the intercept for Daphnia magna (only species tested) = 2.94

Final Invertebrate Chronic Value = $e^{(0.83 \cdot \ln(\text{hardness})+2.94)}$

Table 5. Freshwater plant effects for chromium*

Organism	Effect	Concentration (ug/l)	Reference
Green alga, Chlamydomonas reinhardi	Reduction in growth	10	Zarafonetis & Hampton, 1974
Green alga, Chlorella pyrenoidosa	50% inhibition in photosynthesis	5,000	Wium-Andersen, 1974
Green alga, Chlorella sorokiniana	44% inhibition in growth	1,000	Moshe, et al., 1972
Green alga, Selenastrum capricornutum	Inhibition in growth	45	Garton, 1972
Green alga, Scenedesmus sp.	Inhibition in growth	500	Staub, et al. 1973
Diatom, Nitzschia palea	50% inhibition in photosynthesis	800	Wium-Andersen, 1974
Diatom, Nitzschia palea	Growth	150	Wium-Andersen, 1974
Alga, Natural algae population	32% inhibition in photosynthesis	20	Zarafonetis & Hampton, 1974
Eurasian watermilfoil, Myriophyllum spicatum	50% root weight inhibition	1,900	Stanley, 1974
Eurasian watermilfoil, Myriophyllum spicatum	50% root weight inhibition	9,900	Stanley, 1974

* All data are for hexavalent chromium.

Lowest plant value = 10 µg/l

Table 6. Freshwater residues for chromium

Organism	Bioconcentration Factor	Time (days)	Reference
Rainbow trout, Salmo gairdneri	<1	22	Buhler, et al. 1977
Rainbow trout, Salmo gairdneri	1	36	Fromm & Stokes, 1962
Rainbow trout, Salmo gairdneri	1	30	Fromm & Stokes, 1962

Table 7. Other freshwater data for chromium

Organism	Test Duration	Effect	Hardness (mg/l as $CaCO_3$)	Result (ug/l)	Reference
Algal community	1 mo	Diatoms reduced blue green algae dominant	-	400*	Patrick, et al. 1975
Algal community	1 mo	Diversity of diatoms reduced	-	100*	Patrick, et al. 1975
Algal community	1 mo	Bioconcentration of chromium: 8,500	-	400*	Patrick, et al. 1975
Protozoa, Colpidium campylum	48 hrs	50% inhibition of growth	-	12,900*	Subo & Aiba, 1973
Protozoa, Blepharisma sp.	3 hrs	Some living	-	32,000*	Ruthven & Cairns, 1973
Protozoa, Opercularia sp.	48 hrs	50% inhibition of growth	-	21,200*	Sudo & Aiba, 1973
Protozoa, Vorticella microstoma	48 hrs	50% inhibition of growth	-	530*	Sudo & Aiba, 1973
Cladoceran, Daphnia magna	64 hrs	LC50	160	1,200**	Anderson, 1948
Cladoceran, Daphnia magna,	72 hrs	LC50	163	64*	Debelak, 1975
Cladoceran, Daphnia magna	72 hrs	LC50	163	72*	Debelak, 1975
Cladoceran, Daphnia magna	72 hrs	LC50	163	73*	Debelak, 1975
Cladoceran, Daphnia magna	72 hrs	LC50	163	74*	Debelak, 1975
Cladoceran, Daphnia magna	72 hrs	LC50	163	81*	Debelak, 1975
Cladoceran,	72 hrs	LC50	86	31*	Debelak, 1975

Organism	Test Duration	Effect	Hardness (mg/l as $CaCO_3$)	Result (ug/l)	Reference
Cladoceran, Daphnia magna	72 hrs	LC50	-	38*	Debelak, 1975
Cladoceran, Daphnia magna	72 hrs	LC50	86	39*	Debelak, 1975
Cladoceran, Daphnia magna	72 hrs	LC50	86	42*	Debelak, 1975
Cladoceran, Daphnia magna	72 hrs	LC50	86	44*	Debelak, 1975
Cladoceran, Daphnia magna	48 hrs	LC50	-	4-8*	Dowden & Bennett, 1965
Cladoceran, Daphnia magna	100 hrs	LC50	100	140*	Dowden & Bennett, 1965
Cladoceran, Daphnia magna	100 hrs	LC50	100	130*	Freeman & Fowler, 1953
Cladoceran, Daphnia magna	96 hrs	LC50	-	50*	Trabalka & Gehrs, 1977
Cladoceran, Daphnia magna	Life span > 32 days	Life span reduced fecundity reduced	-	10*	Trabalka & Gehrs, 1977
Midge, Chironomus sp.	96 hrs	LC50	50	11,000	Rehwoldt, et al. 1973
Stonefly, Acroneuria lycorias	7 days	LC50	44	32,000**	Warnick & Bell, 1969
Coho salmon, Oncorhynchus kisutch	13 days	LC50***	-	25,000*	Holland, et al. 1960
Chinook salmon, Oncorhynchus tshawytscha	4 mos	Growth	70	16*	Olson & Foster, 1956
Chinook salmon, Oncorhynchus tshawytscha	12 wks	Mortality and growth	70	200*	Olson, 1958
Chinook salmon, Oncorhynchus tshawytscha	12 wks	No effect on mortality or growth	70	200**	Olson, 1958
Rainbow trout, Salmo gairdneri	14 wks	Growth	70	21*	Olson & Foster, 1956

Table 7. (Continued)

Organism	Test Duration	Effect	Hardness (mg/l as $CaCO_3$)	Result (ug/l)	Reference
Rainbow trout, *Salmo gairdneri*	7 days	Plasma "cortisol"	70	20*	Hill & Fromm, 1958
Rainbow trout, *Salmo gairdneri*	2 days	Inhibition Na/K- ATPase	-	2,500*	Kuhnert, et al. 1976
Rainbow trout, *Salmo gairdneri*	24 hrs	Hematocrits	334	2,000*	Schiffman & Fromm, 1959
Goldfish, *Carassius auratus*	11 days	LC50****	220	30,400*	Adelman & Smith, 1976
Fathead minnow, *Pimephales promelas*	11 days	LC50****	220	17,300*	Adelman & Smith, 1976
Largemouth bass, *Micropterus salmoides*	36 hrs	Pathology of intestine	334	94,000*	Fromm & Schiffman, 1958

* Hexavalent chromium.

** Trivalent chromium.

*** Calculated from data

**** Geometric mean of 16 tests

SALTWATER ORGANISMS

Introduction

All available toxicity data are for hexavalent chromium, and all bioconcentration data are for trivalent chromium. Studies which reported toxicity data for trivalent chromium used static test conditions and stated that a precipitate formed. This has been interpreted as meaning that actual exposure levels were not known. The only bioconcentration data reported here were derived from two flow-through studies using trivalent chromium where no precipitation was reported. The kinetics of the precipitation of trivalent chromium in saltwater systems is complex, but regardless of its form, it may still be ingested and bioconcentrated.

Acute Toxicity

Acute toxicity data for hexavalent chromium and saltwater fishes are limited to two species (Table 8) and all studies were conducted with adult fish. The experiments on Fundulus heteroclitus performed at 20° and 20 °/oo salinity (Eisler and Hennekey, 1977) resulted in a higher acute toxicity value than in those with Citharichthys stigmaeus in full strength saltwater at 11.7 to 12.7°C (Sherwood, 1975). Adjustment of the fish acute toxicity data gives a Final Fish Acute Value of 7,800 µg/l.

Saltwater invertebrate species are more sensitive to hexavalent chromium than saltwater fishes. Adjusted acute toxicity values ranged from 1,694 µg/l for the polychaete worm, Nereis virens to 88,935 µg/l for the mud snail Nassarius obsoletus, (Eisler and Hennekey, 1977). Larvae of Capitella capitata were found to be slightly less sensitive than adults, with adjusted

acute toxicity values of 6,776 µg/l and 4,234 µg/l, respectively (Table 9). The sensitivity of the brackish water clam, Rangea cuneata, to acute hexavalent chromium poisoning was dependent on salinity, with acute toxicity values of 35,000 and 14,000 µg/l, in water of salinities of 22 and 5.5 °/oo, respectively. Acute toxicity values for the bivalve molluscs were between those for the relatively insensitive gastropods (mud snails) and the annelids (polychaete worms). Within the invertebrate species, the arthropods demonstrated the widest range of adjusted LC50 values from 4,338 µg/l for sea urchin larvae, Strongylocentrotus pupuratus, (Oshida and Wright, 1978), to 44,044 µg/l for zoea of the crab, Sesarma haemotocheir (Okubo and Okubo, 1962). The Final Invertebrate Acute Value of 230 µg/l, derived by using the Guidelines, is lower than any value in Table 9 and thus protects 95 percent of the species represented. Since this value is lower than the Final Fish Acute Value of 7,800 µg/l, the Final Acute Value for chromium is 230 µg/l.

Chronic Toxicity

There are no life cycle or embryo-larval chronic toxicity data with chromium and saltwater fishes. There are chronic toxicity data for hexavalent chromium and three species of saltwater polychaete worms (Table 10). All these studies use reproductive success as a measure of chronic toxicity, and all were tests with renewed solutions and unmeasured (except Oshida, 1978) toxicant concentrations. The chronic values for Neanthes arenaceodentata ranged from 25 µg/l to 71 µg/l with a geometric mean of 40 µg/l. The chronic toxicity of chromium to Capitella capitata of 71 µg/l while similar to Neanthes is an order of magnitude less than that

reported for Ophryotrocha diadema (707 µg/l). The chronic toxicity of hexavalent chromium to these species ranges from 9 to 89 times greater than the reported acute toxicity. The geometric mean of the chronic values is 126 which, divided by the species sensitivity factor (5.1), results in a chronic value of 25 µg/l. This value is identical to the lowest chronic value reported and the Final Invertebrate Chronic Value is 25 µg/l. Since there is no Fish Chronic Value or suitable Residue Limited Toxicant Concentration, the Final Invertebrate Chronic Value becomes the Final Chronic Value of 25 µg/l.

Plant Effects

The data available on sensitivity of plants to chromium poisoning is limited to the algal species Macrocystis pyrifera. Hexavalent chromium has been shown to inhibit photosynthesis in this alga at 1,000 µg/l (10 to 20 percent inhibition in 5 days) and 5,000 µg/l (50 percent inhibition in 96-hours). Therefore the Final Plant Value is 1,000 µg/l.

Bioconcentration

The only bioconcentration data available are for trivalent chromium from studies with three different species of bivalve molluscs. A bioconcentration factor of 84 was reported for Mytilus edulis, 116 for Crassostrea virginica, and 152 for Mya arenaria. No data are available to calculate the Residue Limited Toxicant Concentration (RLTC) for chromium.

Miscellaneous

Hexavalent chromium seems to be a cumulative toxicant (Table 13). For example, the 96-hour LC50 for the polychaete worm, Capitella capitata, is 4,235 µg/l, whereas the 28-day LC50 value

is 280 µg/l. The 96-hour LC50 is 48,279 µg/l and the 7-day LC50 is 8,000 µg/l for the soft shell clam. For the starfish, Asteria forbesi, the 96-hour LC50 is 27,104 µg/l, whereas the 7-day LC50 is 10,000 µg/l. The 96-hour LC50 for the speckled sanddab is 16,948 µg/l but the 21-day LC50 is 5,400 µg/l.

In addition to the chronic mortality data reported in Table 13, there are two sublethal measures of chromium toxicity. Oshida, et al. (1976) reported a reduction in brood size of Neanthes arenaceodentata exposed to 12.5 µg/l. Although this value is slightly lower than the Final Chronic Value of 25 µg/l it does not warrant lowering the latter. Oshida and Reish (1975) reported inhibition of tube building in the same species after a 14-day exposure to 79 µg/l. This concentration is 43 times lower than the 96-hour acute toxicity value and is similar to a chronic value of 71 µg/l (Table 10). Thus tube building may be a potential predictor of chronic reproductive effects.

RITERION FORMULATION

Saltwater-Aquatic Life

ummary of Available Data

The concentrations below have been rounded to two significant igures. All concentrations herein are expressed in terms of :hromium.

Iexavalent chromium

Final Fish Acute Value = 7,800 µg/l

Final Invertebrate Acute Value = 230 µg/l

Final Acute Value = 230 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = 25 µg/l

Final Plant Value = 1,000 µg/l

Residue Limited Toxicant Concentration = not available

Final Chronic Value = 25 µg/l

0.44 x Final Acute Value = 100 µg/l

The maximum concentration of hexavalent chromium is the Final Acute Value of 260 µg/l and the 24-hour average concentration is the Final Chronic Value of 25 µg/l. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For hexavalent chromium the criterion to protect saltwater aquatic life as derived using the Guidelines is 25 µg/l as a 24-hour average and the concentration should not exceed 230 µg/l at any time.

For saltwater aquatic life, no criterion for trivalent chromium can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Table 8 Marine fish acute values for chromium

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Speckled sanddab, Citharichthys stigmaeus	S	U	96	31,000	16,948	Sherwood, 1975
Speckled sanddab, Citharichthys stigmaeus	S	U	96	30,000	16,401	Mearns, et al. 1976
Mummichog, Fundulus heteroclitus	S	U	96	91,000	49,750	Eisler & Hennekey, 1977

* S = static

** U = unmeasured

Geometric mean of adjusted values = 28,800 µg/l $\frac{28,800}{3.7}$ = 7,800 µg/l

Table 9. Marine invertebrate acute values for chromium

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Polychaete worm (larvae), Capitella capitata	S	U	96	8,000	6,776	Reish, et al. 1976
Polychaete worm (adult), Capitella capitata	S	U	96	5,000	4,235	Reish, et al. 1976
Polychaete worm, Ctenodrilus serratus	S	U	96	4,300	3,642	Reish & Carr, 1978
Polychaete worm, Neanthes arenaceodentata	S	M	96	3,100	3,410	Mearns, et al. 1976
Polychaete worm, Neanthes arenaceodentata	S	M	96	2,220-4,300	3,399***	Oshida & Reish, 1975
Polychaete worm, Nereis virens	S	U	96	2,000	1,694	Eisler & Hennekey, 1977
Polychaete worm, Ophryotrocha diadema	S	U	96	7,500	6,352	Reish & Carr, 1978
Soft shell clam, Mya arenaria	S	U	96	57,000	48,279	Eisler & Hennekey, 1977
Brackish water clam, Rangea cuneata	S	U	96	14,000	11,858	Olson & Harrel, 1975
Brackish water clam, Rangea cuneata	S	U	96	35,000	29,645	Olson & Harrel, 1975
Mud snail, Nassarius obsoleutus	S	U	96	105,000	88,935	Eisler & Hennekey, 1977
Hermit crab, Pagurus longicarpus	S	U	96	10,000	8,470	Eisler & Hennekey, 1977
Crab (zoea), Sesarma haemotocheir	S	U	24	200,000	44,044	Okubo & Okubo, 1962
Starfish, Asterias forbesi	S	U	96	32,000	27,104	Eisler & Hennekey, 1977

Table 9. (Continued)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Sea urchin (larvae), *Strongylocentrotus purpuratus*	S	M	48	2,900 - 29,000	4,338***	Oshida & Wright, 1978

* S = static

** U = unmeasured, M = measured

*** Corrected geometric mean of LC50 range

Geometric mean of adjusted values = 11,101 µg/l $\frac{11,101}{49}$ = 230 µg/l

Table 10. Marine invertebrate chronic values for chromium

Organism	Test *	Limits (ug/l)	Chronic Value (ug/l)	Reference
Polychaete worm, Capitella capitata	LC	50-100	71	Reish, 1977
Polychaete worm, Ophryotrocha diadema	LC	500-1000	707	Reish & Carr, 1978
Polychaete worm, Neanthes arenaceodentata	LC	25-50	35	Oshida & Reish, 1975
Polychaete worm, Neanthes arenaceodentata	LC	50-100	71	Oshida, et al. 1976
Polychaete worm, Neanthes arenaceodentata	LC	17-38	25.2	Oshida, 1978

* LC = life cycle or partial life cycle
Geometric mean of chronic values = 126 µg/l $\frac{126}{5.1}$ = 25 µg/l

Lowest chronic value = 25 µg/l

Table 11. Marine plant effects for chromium

Organism	Effect	Concentration (ug/l)	Reference
Alga, Macrocystis pyrifera	96-hr EC50 50% inhibition of photosynthesis	5,000	Clendenning & North, 1959
Alga, Macrocystis pyrifera	10-20% inhibition of photosynthesis in 5 days	1,000	Bernhard & Zattera, 1975

Lowest plant value = 1,000 ug/l

Organism	Bioconcentration Factor	(days)	Reference
American oyster, *Crassostrea virginica*	116	140	Shuster & Pringle, 1969
Soft shell clam, *Mya arenaria*	152*	168	Capuzzo & Sasner, 1977
Blue mussel, *Mytilus edulis*	84*	168	Capuzzo & Sasner, 1977

* Dry to wet weight conversion
** All bioconcentration data is based on trivalent chromium.

Geometric mean bioconcentration factor for all species = 114

Table 13. Other marine data for chromium

Organism	Test Duration	Effect	Result (ug/l)	Reference
Polychaete worm, *Ctenodrilus serratus*	21 days	100% mortality	50,000	Reish & Carr, 1978
Polychaete worm, *Ophryotrocha diadema*	21 days	100% mortality	50,000	Reish & Carr, 1978
Polychaete worm (juvenile) *Neanthes arenaceodentata*	28 days	50% mortality	700	Reish, et al. 1976
Polychaete worm (adult), *Neanthes arenaceodentata*	28 days	50% mortality	550	Reish, et al. 1976
Polychaete worm, *Neanthes arenaceodentata*	7 days	50% mortality	1,440-1,890	Oshida, et al. 1976
Polychaete worm, *Neanthes arenaceodentata*	440 days	Brood size decreased	12.5	Oshida, et al. 1976
Polychaete worm, *Neanthes arenaceodentata*	56 days	50% mortality	200	Oshida & Reish, 1975
Polychaete worm, *Neanthes arenaceodentata*	14 days	Inhibition-tube building	79	Oshida & Reish, 1975
Polychaete worm, *Neanthes arenaceodentata*	59 days	50% mortality	200	Mearns, et al. 1976
Polychaete worm, *Neanthes arenaceodentata*	7 days	50% mortality	1,630	Mearns, et al. 1976
Polycahete worm, *Neanthes arenaceodentata*	350 days	Brood size decrease	12.5	Mearns, et al. 1976
Polychaete worm (adult) *Capitella capitata*	28 days	50% mortality	280	Reish, et al. 1976
Polychaete worm, *Nereis virens*	21 days	50% mortality	1,000	Raymont & Shields, 1963
Polychaete worm, *Nereis virens*	7 days	50% mortality	700	Eisler & Hennekey, 1977

Table 13 (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Soft shell clam, *Mya arenaria*	7 days	50% mortality	8,000	Eisler & Hennekey, 1977
Mudsnail, *Nassarius obsoletus*	7 days	50% mortality	10,000	Eisler & Hennekey, 1977
Hermit crab, *Pagurus longicarpus*	7 days	50% mortality	2,700	Eisler & Hennekey, 1977
Shore crab, *Carcinus maenas*	12 days	50% mortality	60,000	Raymont & Shields, 1963
Prawn (juvenile), *Leander squilla*	7 days	Toxic threshold	5,000	Raymont & Shields, 1963
Prawn (adult), *Leander squilla*	7 days	Toxic threshold	10,000	Raymont & Shields, 1963
Brittle star, *Ophiothrix spiculata*	7 days	50% mortality	1,700	Oshida & Wright, 1978
Starfish, *Asterias forbesi*	7 days	50% mortality	10,000	Eisler & Hennekey, 1977
Mummichog, *Fundulus heteroclitus*	7 days	50% mortality	44,000	Eisler & Hennekey, 1977
Speckled sanddab, *Citharichthys stigmaeus*	21 days	50% mortality	5,400	Sherwood, 1975
Speckled sanddab, *Citharichthys stigmaeus*	21 days	EC50-feeding response	2,200	Sherwood, 1975
Speckled sanddab, *Citharichthys stigmaeus*	21 days	50% mortality	5,000	Mearns, et al. 1976
Silver salmon, *Oncorhynchus kisutch*	5 days	33% mortality	31.8	Holland, et al. 1960
Silver salmon, *Oncorhynchus kistuch*	11 days	100% mortality	31.8	Holland, et al. 1960

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CHROMIUM

Mammalian Toxicology and Human Health Effects

Introduction

Chromium is a common element, present in low concentrations throughout nature. Its toxicity has long been recognized, but detailed analysis of toxic effects is complicated by the occurrence of many different compounds of the metal; these may contain Cr in different valence states and are distinguished by their chemical, physical and toxicological properties.

This document briefly considers some relevant chemical and physical properties of Cr compounds to which man may be exposed, and attempts to evaluate possible health hazards associated with such exposures. The general area of environmental effects of chromium compounds was recently reviewed by the U.S. Environmental Protection Agency (1978); a valuable discussion of the medical and biological effects of Cr in the environment is found also in a volume published by the National Academy of Sciences (1974). Occupational hazards of chromium were assessed in a Criteria Document prepared in 1975 (Natl. Inst. Occup. Safety Health, 1975). Mertz (1969) provided a valuable survey of the biochemical properties of Cr compounds.

To avoid unnecessary duplication, previously reviewed material will not be considered at great length except when it impinges directly on present critical considerations. Detailed documentation for most of the available information can be found in the earlier reviews.

There is little need to discuss here the detailed chemstry of chromium, as this subject has been adequately reviewed n the recent past (U.S. EPA, 1978). However, an evaluation f the significance of various routes of exposure to Crontaining compounds, and of the factors determining rates f uptake and toxicity of such compounds, requires an understanding of their physical properties and of their chemical nd biochemical reactions.

The metallic element Cr belongs to the first series f transition elements, and occurs in nature primarily as ompounds of its trivalent (Cr III) or hexavalent (Cr VI) orms. Generally speaking, the hexavalent compounds are elatively water-soluble and readily reduced to the more nsoluble and stable forms of Cr III by reaction with organic educing matter. Because large amounts of Cr VI are produced and utilized in industry (primarily as chromates and lichromates), and because of their ready solubility, traces of such compounds are frequently found in natural waters.

As pointed out, Cr VI is rapidly reduced when in contact with biological material. The reverse reaction is not known to occur in the human body. Trivalent Cr forms stable hexacoordinate complexes with many molecules of biochemical interest. Interaction of Cr III with such compounds may involve binding to carboxy groups of proteins or smaller metabolites, coordination with certain amino acids, and binding to nucleic acids and nucleoproteins. This last reaction is of special significance in the consideration of the carcinogenic potential of Cr compounds. The field

was reviewed by Mertz (1969) and it suffices here to emphasize the stability of these Cr complexes, and the fact that the element is found combined with both RNA and DNA; an effect of Cr on the tertiary structure of nucleic acids is clearly indicated. In general, it may be concluded that reduction of Cr VI to Cr III and its subsequent coordination to organic molecules of biochemical interest explain in large measure the biological reactivity of Cr compounds. Thus, the well-known reaction of Cr with skin proteins (i.e., the tanning process) involves coordination sites of Cr III. For reasons of solubility, however, uptake of compounds of Cr VI by the living organism generally exceeds that of Cr III compounds (see section on "Acute, Sub-acute, and Chronic Toxicity").

A good illustration of the behavior of Cr compounds in biological systems is furnished by the reaction of Cr with erythrocytes (Gray and Sterling, 1950). These cells do not react to any significant extent with Cr III; in contrast, they rapidly take up anions of hexavalent Cr compounds, utilizing presumably the broadly specific anion transport facilitation in erythrocytes reviewed by Fortes (1977). Thus we may invoke as a likely explanation for the greater toxicity of Cr VI than of Cr III compounds their more rapid uptake by tissues due to their solubility and to the facilitation of their translocation across biological membranes. Once within cells, the Cr VI is likely to be reduced to the trivalent state before reacting with cell constituents such as proteins and nucleic acids. In the case of red cells, it is such an intracellular reaction of Cr III with

hemoglobin which explains the essentially irreversible uptake of the metal and permits use of chromium-51 as red cell marker.

Stable and soluble compounds of Cr III are found in many biological systems. Among these is the so-called glucose tolerance factor (GTF) (Mertz, 1969), a compound of unknown structure whose absence is believed responsible for symptoms of chromium deficiency. In the form of GTF and perhaps of other similar complexes Cr III can also cross biological membranes with relative ease; thus it is readily absorbed from the intestine in this form (Doisy, et al. 1971). One may recall in this connection the general importance of metal ligands in determining movement of heavy metals within the body (Collins, et al. 1961; Foulkes, 1974). It is not surprising therefore that distribution of Cr in the body also critically depends on the presence of specific ligands (Mertz, 1969).

Chromium plays a role in human nutrition. Because of this fact, lowering of ambient Cr levels to a value where total uptake might lead to overt Cr deficiency must be avoided. Indeed, effects of Cr-deficiency in man and experimental animals have been described (Mertz, 1969). Levels of Cr compounds required for optimal nutrition fall greatly below those which have been reported to cause toxic effects (see "Acute, Sub-acute, and Chronic Toxicity" section); therefore normal nutritional levels need not be considered further here. It must be pointed out, however, that the American diet may be potentially deficient in Cr so that some increased

Cr uptake might be beneficial.

Sources of chromium in the environment have been recently reviewed (U.S. EPA, 1978). Although Cr is widely distributed, with an average concentration in the continental crust of 125 mg/kg, it is rarely found in significant concentrations in natural waters. Air levels in non-urban areas usually fall below detection limits and may be as low as 5 pg/m^3. Much of the detectable Cr in air and water is presumably derived from industrial processes, which in 1972 consumed 320,000 metric tons of the metal in the United States alone. A significant fraction of this amount entered the environment; additional amounts are contributed by combustion of coal and other industrial processes (U.S. EPA, 1974). As a result, levels of Cr in air exceeding 0.010 $\mu g/m^3$ have been reported from 59 of 186 urban areas examined (U.S. EPA, 1973). Mean concentration of Cr in 1577 samples of surface water were reported as 9.7 $\mu g/l$ (Kopp, 1969). The significance of 9.7 $\mu g/l$ as a mean value is questionable because only 25 percent of the samples tested contained any detectable Cr. Occasional values of total Cr (Cr III and Cr VI) exceeded 50 $\mu g/l$, a fact which must be noted in relation to the recommended standard for domestic water supplies (see section on "Existing Guidelines and Standards").

It is important to reemphasize at this time the analytical difficulties attending estimation of low concentrations of Cr, especially in biological materials. Additionally, the different chemical species of Cr which may be

present often cannot be clearly separated. Considerable uncertainty attaches to the significance of some results, particularly those obtained with some of the older techniques. This topic was considered in detail recently (U.S. EPA, 1978).

Ingestion from Food and Water

At an average concentration of approximately 10 µl Cr/l drinking water (Kopp, 1969), and a daily water consumption of 2 L, about 20 µg Cr would be ingested in water per day compared to about 50 to 100 µg per day in the American diet (Tipton, 1960). On the basis of the levels of Cr reported for food and water in the general environment of the United States, average oral intake will seldom exceed 100 µg/day (Tipton, 1960). Fractional absorption of such an oral load from the intestine depends on the chemical form in which the element is presented (see "Introduction"). In addition, even though mechanisms involved in the movement of Cr compounds across intestinal epithelial barriers are not understood, it is likely that the extent of this absorption will be greatly influenced by the presence of other dietary constituents in the intestinal lumen (MacKenzie, et al. 1958), as has frequently been observed in the case of other dietary metals.

For a variety of reasons, therefore, net fractional absorption of Cr from the intestine is low and may amount to only a few percent or even less (Mertz, 1969), depending especially on the chemical form in which the element is ingested. Intake of Cr from the air normally amounts to less than 1 µg/day (see "Inhalation"), and thus does not contribute significantly to normal Cr balance. Average urinary excretion of Cr has been reported as 5 to 10 ug per day (Volkl, 1971); recent work suggests that because

of analytical difficulties, actual values may be somewhat lower (Guthrie, et al. 1979). In any case it follows that the American diet may become marginally deficient in this element, unable to provide the optimum level required for normal function (see "Introduction" section). This conclusion is supported by the finding that Cr levels in tissues generally decrease with age (Mertz, 1969). The situation is not greatly altered by application of Cr-containing fertilizers or sewage sludges to agricultural land. Indeed, uptake of Cr by plants from soil is generally low. However, biomagnification factors for Cr have been reported in rainbow trout of 1 and below and are quoted in "Freshwater Residues for Chromium" of the ecological effects chapters.

A bioconcentration factor (BCF) relates the concentration of a chemical in water to the concentration in aquatic organisms. Since BCF's are not available for the edible portion of all four major groups of aquatic organisms consumed in the United States, some have to be estimated. A recent survey on fish and shellfish consumption in the United States (Cordle, et al. 1978) found that the per capita consumption is 18.7 g/day. From the data on the nineteen major species identified in the survey, the relative consumption of the four major groups can be calculated.

Several bioconcentration tests have been conducted with chromium:

Organisms	Bioconcentration factor	Valence	Reference
American oyster, Crassostrea virginica	116	+3	Shuster & Pringle, 1969
Soft shell calm, Mya arenaria	152	+3	Capuzzo & Sasner, 1977
Blue mussel, Mytilus edulis	84	+3	Capuzzo & Sasner, 1977
Rainbow trout, Salmo gairdneri	1	+6	Buhler, et al. 1977
Rainbow trout, Salmo gairdneri	1	+6	Fromm & Stokes, 1962

These data result in geometric means of 114 for saltwater molluscs and 1 for freshwater fish. Because these data are not inconsistent with those for other metals, it seems reasonable to use the values for the two valence states of chromium interchangeably, and to assume that saltwater fishes and decapods would have values comparable to that for freshwater fishes.

Group	Consumption (Percent)	Bioconcentration factor
Freshwater fishes	12	1
Saltwater fishes	61	1
Saltwater molluscs	9	114
Saltwater decapods	18	1

Using the data for consumption and BCF for each of these groups, the weighted average BCF is 11 for consumed fish and shellfish.

Inhalation

Levels of Cr in air have been carefully monitored. In the United States in 1964 an average value of 0.015 $\mu g/m^3$

was reported, with a maximum of 0.35 $\mu g/m^3$. More recent values show levels below detection limits in most non-urban and some urban areas (U.S. EPA, 1973); yearly averages exceeded 0.01 $\mu g/m^3$ in only 59 of 186 urban areas.

The chemical form of Cr in air will vary, depending primarily on its source. There is little information on the size distribution of the particles, but it is safe to assume that a significant portion will be in the respirable range. Uptake, of course, depends on the aerodynamic diameter of the particles. Assuming an average alveolar ventilation of 10 m^3/day, with an alveolar retention of 50 percent of Cr present at a level of 0.015 $\mu g/m^3$, alveolar uptake would only amount to approximately 0.1 μg/day. Additional Cr could also be deposited in the upper respiratory passages and contribute ultimately to the intestinal load of Cr. In any case, however, inhalation under normal conditions does not contribute significantly to total Cr uptake.

Even in the non-occupational environment the concentration of Cr in air may rise significantly above normal background levels. Thus, increased ambient concentrations of Cr have been reported in the vicinity of industrial sites (U.S. EPA, 1978). In the proximity of water cooling towers, for instance, where Cr was employed as a corrosion inhibitor, air levels of Cr as high as 0.05 $\mu g/m^3$ have been reported. However, even such a relatively high level is not likely, to alter greatly total Cr uptake. The possibility that smoking might contribute to the pulmonary load of Cr has not been fully evaluated.

Of course, to the extent that the lungs represent a target organ for Cr, additional pulmonary loads may assume significance even though total body Cr may not have been materially increased by the inhalation exposure. Although such exposure can lead to significantly increased urinary excretion of Cr, it is not clear to what extent the Cr added to systemic pools originated in the lungs or was alternatively absorbed from the intestines following pulmonary clearance of the Cr-containing particles. In any case, pulmonary Cr does not appear to be in full equilibrium with other Cr pools in the body. This conclusion is based on the fact that the Cr content of the lungs, unlike that of the rest of the body, may actually increase with age (Mertz, 1969). Prolonged pulmonary retention of inhaled Cr is also reflected by the fact that the pulmonary concentration of the element usually exceeds that of other organs. The relatively slow clearance of Cr from the lungs was also noted by Baetjer, et al. (1959), who found that 60 days after intratracheal instillation into guinea pigs, 20 percent of a dose of $CrCl_3$ remained in the tissue.

Dermal

Compounds of Cr permeate the skin fairly readily when applied in the hexavalent form; trivalent Cr compounds react directly with epithelial and dermal tissue. Cutaneous exposure is primarily a problem of the workplace: many lesions have been described under these conditions, including ulceration and sensitization reactions. There is little evidence, however, to suggest that cutaneous absorption significantly

contributes to the total body load of Cr in the normal environment.

The three previous sections review briefly the uptake of Cr by ingestion, inhalation, and cutaneous absorption. None of the three routes of entry will lead to harmful levels of Cr in the body when exposure involves only the low levels of the element normally found in food, water and air. Indeed, it may be recalled ("Ingestion" section) that the average American may actually suffer from mild Cr deficiency. The major fraction of body Cr originating in the general environment is contributed by ingestion. In industrial surroundings, by contrast, other routes of exposure may become more significant. Uptake of Cr by inhalation may pose special risks here. This conclusion follows from the fact that the lungs tend to retain Cr more than do other tissues (see "Inhalation" section). The "Carcinogenicity" section deals further with pulmonary effects of exposure to Cr in air.

Under normal conditions of exposure, considerable variability has been observed in the Cr concentrations of different tissues. It is difficult to assess to what extent the wide range of values reported reflects analytical problems rather than true individual variations. As a first approximation, an average level of around 2 μg Cr/g ash may be derived from the work of Tipton and Cook (1963) and of Imbus, et al. (1963) for most soft tissues and for whole blood of non-exposed humans. Levels of Cr in the lungs may be ten times higher; there is no evidence to suggest that Cr is a bone-seeking element. If we further assume that the aver-

age ash content of soft tissues approximates 1 percent of fresh weight, a total body burden in the adult of the order of 2 mg may be calculated. Results of Schroeder, et al. (1962) showed values of Cr in human tissues of the order of 0.05 µg/g fresh weight, which would correspond to a total adult body burden of around 3 to 4 mg; Schroeder (1965) suggested an upper limit of 6 mg Cr in a 70 kg man. These values are presented here to indicate the net result of Cr uptake by ingestion, inhalation and cutaneous absorption under normal conditions. As pointed out, this body burden may actually represent a marginally deficient state.

PHARMACOKINETICS

Absorption, Distribution, Metabolism, and Excretion

Analysis of the movement of Cr through various body pools, and determination of the size and turnover rates of these pools, are complicated by several facts. In the first place it is likely that different Cr compounds will exhibit different kinetic characteristics in the body; this is well illustrated by the wider body distribution of Cr injected in the form of the glucose tolerance factor than when administered as $CrCl_3$ (Mertz, 1969). Second, the chemical methods employed for the estimation of biological Cr concentrations do not adequately distinguish between different forms of Cr present in the original sample. The results of Schroeder, et al. (1962) do suggest, however, that both hexavalent and trivalent Cr may occur in the ash of biological materials. Precise conclusions on this point are difficult because the chemical forms of Cr may be changed during the

ashing. Third, difficulties of interpretation arise from the fact that one chemical species of Cr may be transformed into another in the body, for instance as by reduction of Cr VI to Cr III.

The complexity of the pharmacokinetics of Cr to be predicted from such considerations is observed both in man and in experimental animals. This situation may be illustrated by reference to the urinary excretion of Cr under normal conditions. In man the kidneys account for 80 percent or more of Cr excretion by non-exposed individuals (Natl. Acad. Sci., 1974); urinary excretion amounts on the average to 5 to 10 μg/day or less (see "Ingestion from Water and Foods" section). Such a value corresponds to less than 1 percent of the total body burden as estimated in the section on "Evaluation of Relative Contribution of Different Exposure Routes to Body Burden"; it also approximately equals the average daily retention of Cr (see section on "Ingestion from Water and Foods"). The body thus appears roughly to be in steady state with regard to Cr. It would not be correct to infer, however, that the turnover rates of the various Cr pools in the body all fall below 1 percent/day; this would be true only if Cr taken in by one of the routes of entry discussed in the section on "Exposure" always equilibrated evenly with different body pools.

Although unfortunately little information is available on changes in specific radioactivities of Cr in different body compartments following administration of ^{51}Cr, there is strong evidence to show that different compartments exhi-

bit distinctly different turnover kinetics. Lim (1978) reports the kinetics of radiochromium III distribution in humans. Three major accumulation and clearance components were found for liver, spleen, and thigh; liver and spleen contained the higher concentrations. Normally in man, the highest concentration of Cr is found in the lungs, and pulmonary levels tend to rise with age while the Cr content of other tissues falls. Apparently the lung obtains most of its Cr from the air, not from oral loads, and pulmonary Cr does not come into equilibrium with other body pools of Cr (see "Inhalation" section).

Similar conclusions on non-equilibration of body pools can be drawn from measurements on the excretion kinetics of ^{51}Cr III injected into rats. At least three kinetic compartments were observed in this case (Mertz, et al. 1965), with half-lives respectively of 0.5, 5.9 and 83.4 days. A slowly equilibrating Cr compartment in man was estimated to possess a half-life of 616 days (U.S. EPA, 1978). Injection of 1 mg of unlabeled Cr into rats, a very large dose compared to the presumptive body burden as calculated in the section on "Evaluation of Relative Contributions of Different Exposure Routes to Body Burdens" exerted little effect on the rate of tracer excretion from the slow compartment. The finding that even a very large excess of Cr does not affect this compartment further indicates that ingested or injected Cr does not necessarily pass through every body compartment on its way to excretion. Finally, this conclusion is supported by the observation that the pool from which

Cr (at least in some systems) enters plasma following administration of glucose is not readily labeled by injected ^{51}Cr (administered as $CrCl_3$) (Mertz, 1969).

As is the case with other metals, chromium normally circulates in plasma primarily in a bound, non-diffusible form (Mertz, 1969). At low levels of Cr III the iron-binding protein siderophilin complexes most of the Cr present, but at higher levels of Cr other plasma proteins also become involved. The high affinity of Cr III for siderophilin presumably reflects the fact that this protein provides the normal mechanism of transport for Cr to the tissues. A small fraction of plasma Cr is also present in a more diffusible form, complexed to various small organic molecules which are filtered at the glomerulus and partially reabsorbed in the renal tubule. The suggestion that this reabsorption may involve an active transport process (Davidson, et al. 1974) is not supported by the evidence presented. Chromium very tightly bound in low-molecular weight complexes such as Cr-EDTA may serve as a glomerular indicator, being freely filtered but not at all reabsorbed (Stacy and Thorburn, 1966).

The half-life of plasma Cr is relatively short, and cells tend to accumulate the element to levels higher than those present in plasma. Presumably this accumulation results from intracellular trapping of Cr compounds which penetrate cells in the hexavalent form and then react with cell constituents, such as hemoglobin in the case of the erythrocyte. Within the cells, Cr VI will be reduced to Cr III and remain

trapped in this form. In any case, the lack of equilibration of Cr between plasma and cells renders invalid the use of plasma levels as indicators of total exposure.

Another reason for the limited usefulness of plasma Cr levels as measure of body burden is the likelihood that plasma Cr can be identified with one of the rapidly excreted Cr compartments discussed above. This is suggested by the finding that even though the rise in plasma Cr reported by some authors to occur after administration of a glucose load is not derived from a rapidly labeled pool, it is followed by increased urinary excretion of Cr (Mertz, 1969). In summary, little can be concluded definitely at this time about nature, size or location of the various body pools of Cr whose existence was inferred from tracer equilibration and excretion studies.

The importance of the chemical form of Cr in determining distribution of various compounds between pools is further illustrated by the observation that while inorganic Cr III does not appreciably cross the placental barrier, Cr III injected into pregnant rats in the form of natural complexes obtained from yeast can readily be recovered from the fetuses (see section on "Mutagenicity").

As further considered in the Effects sections, compounds of Cr VI may act as acute irritants whereas those of Cr III exert little acute toxic action. Presumably, this fact reflects primarily the poor intestinal absorption of the trivalent compounds, and the strong oxidizing power of Cr VI. The lungs, however, may accumulate and retain relatively

insoluble Cr III from respired air although even in this case Cr VI appears to be much more toxic than Cr III. Here again toxicity is determined as much by the chemical form of Cr as by its concentration. The additional factor of length of exposure to Cr is apparent in the need to implant the test compound or to inject it intramuscularly before sarcomas are produced at those sites (see "Carcinogenicity" section). In terms of human exposure such routes of administration possess little relevance except to emphasize the importance of long-term Cr concentrations in specific body compartments as major determinants of toxicity.

EFFECTS

Acute, Sub-acute, and Chronic Toxicity

Because Cr is generally accepted to be an essential element, the effects of exposure to low levels may be beneficial in deficiency states; such an action of Cr would of course have to be separated from the harmful consequences of exposure to higher concentrations. This can be readily achieved because the amounts of Cr required to produce toxic effects are very much higher than those involved in the correction of possible deficiencies. Thus, the LD_{50} for Cr III following its intravenous administration (10 mg/kg weight) exceeds by at least four orders of magnitude the dose needed to relieve impairment of glucose tolerance in Cr-deficient rats (U.S. EPA, 1978). Still higher levels of Cr III must be fed by mouth before toxic symptoms appear, a fact related to the relative insolubility and poor intestinal absorption of most compounds of trivalent chromium.

Unlike compounds of Cr III, those of Cr VI tend to cross biological membranes fairly easily and are somewhat more readily absorbed from the gut or through the skin. The strong oxidizing power of hexavalent Cr explains much of its irritating and toxic properties.

That the concentrations of chromium normally encountered in nature barely meet the requirements for this element in the American diet underlines the fact that natural levels do not constitute a human health hazard. However, acute and chronic toxicity problems associated with exposure to Cr are of concern in the industrial environment or in areas potentially polluted by industrial sources. Such toxic effects are reviewed in detail by the National Institute for Occupational Safety and Health (1975); they include systemic actions of Cr compounds, in addition to primary lesions at the level of the skin, the respiratory passages and the lungs. It must be emphasized again that the findings of lesions following exposure to high concentrations of Cr compounds under experimental conditions, or as a result of accidental or deliberate human exposure, may bear little relevance to the probability of Cr exerting similar actions at more normally encountered levels.

Exposure to relatively high levels of Cr has been studied in some detail. Thus, when Cr in the form of K_2CrO_4 was administered to dogs over a period of 4 years at a level of 0.45 mg/l in drinking water, increases in the Cr concentration of liver and spleen were reported; at exposure levels 25 times higher, accumulation in the kidneys also became

apparent (Anwar, et al. 1961). However, there were no significant pathological changes associated with such exposures. Similarly, a concentration of 0.45 mg Cr/l did not lead to any overt effects in four cases of prolonged human exposure (Davids, et al. 1951). Rats tolerated 25 mg of Cr III or of Cr VI per liter drinking water for one year (MacKenzie, et al. 1958); exposure to Cr VI, however, led to a nine times higher concentration of Cr in tissues, than Cr III, a fact reflecting the more ready intestinal absorption of the hexavalent form. These findings support the conclusion that few systemic changes would be expected to result from even moderately elevated oral exposure to Cr. On that basis the standard of Cr established for drinking water (see section "Existing Guidelines and Standards") should provide adequate protection against general systemic effects. The question of the safety of such a level in terms of possible carcinogenic effects is considered in the section on "Carcinogenicity".

On the other hand, evidence for systemic lesions following more massive exposure, is well documented (U.S. EPA, 1978; Natl. Acad. Sci. 1974).

Renal damage is caused by high concentrations of Cr. Thus intraarterial injection of dichromate has been used for the experimental production of lesions restricted to the first portion of the proximal tubule (Nicholson and Shepherd, 1959). Similarly, tubular necrosis has repeatedly been observed following massive accidental or deliberate exposure (suicide attempts) to Cr (Natl. Acad. Sci. 1974). These cases, however, represent acute effects of very high

doses and their significance to environmental considerations is small.

In only one instance was an association between occupational chromium exposure and hepatic lesions reported. A small number of workers were excreting large amounts of Cr in their urine. Hepatic changes were observed in biopsies although no overt clinical symptoms were seen. Among other systems shown to respond to high doses of Cr is the dog intestine (quoted in U.S. EPA, 1976). Although the possibility of more subtle and long range systemic effects of high Cr exposure cannot be excluded, there is no evidence to support its likelihood.

Dermal effects have been reviewed in considerable detail (Natl. Acad. Sci. 1974). The effects of Cr compounds on the skin were recognized over 150 years ago. Since that time they have been studied in depth by many investigators. The earlier cases were ulcerative changes developing from contact with various compounds of Cr VI. Later studies emphasized that workers exposed to Cr VI can develop allergic contact dermatitis; sensitivity also appears to develop to higher levels of Cr III. No evidence could be found for an association between chromium exposure and skin cancers.

In general, these reports concern relatively massive exposures, unlikely to occur outside the occupational environment, and made even less likely at the present time because of generally improved industrial hygiene practices, (Natl. Inst. Occup. Safety Health, 1975). It is worth noting that the standard set for permissible levels of Cr in drinking

water (see section on "Existing Guidelines and Standards") is much lower than those reported to affect the skin. No evidence was found to suggest that presently permissible concentrations of Cr in domestic water supplies possess much significance in terms of skin disease.

Subtle changes in pulmonary dynamics have been observed among workers employed in the chromium electroplating industry (Bovett, et al. 1977). The major effect of Cr on respiratory passages consists of ulceration of the nasal septum, with subsequent perforation, and of chronic rhinitis and pharingitis. The incidence of such effects may become remarkably high at elevated Cr levels in air. Thus, Mancuso (1951) observed nasal septal perforations in 43 to 85 percent of workers exposed in a chromate plant to both tri- and hexavalent Cr in concentrations as high as 1 mg/m^3. The reported incidence of rhinitis and pharingitis was even higher. In another survey (U.S. Pub. Health Serv. 1953), 509 out of 897 chromate workers were found with nasal septal perforations. Bloomfield and Blum (1928) had concluded that daily exposure to chromic acid concentrations exceeding 0.1 mg/m^3 causes injury to nasal tissue. Effects of lower concentrations have not been carefully studied, so no accurate conclusions on dose-effect relationships can be drawn.

An additional difficulty in interpreting these results arises from the fact that the exposure of the workers discussed here may not have been associated primarily with air-borne Cr: poor work practices leading to local contact almost certainly caused a high proportion of the nasal lesions

(Natl. Inst. Occup. Safety Health, 1975). All nasal effects, however, presumably reflect, the irritating action of soluble compounds of Cr VI. There is no evidence to suggest that the ulcerative lesions can give rise to cancerous reactions.

In an average concentration of 68 $\mu g/m^3$, Cr VI caused some irritation to eyes and throat in a chromate-producing plant (U.S. Pub. Health Serv. 1953). Information available does not permit derivation of meaningful dose-effect relationships. Nevertheless, current evidence indicates that the presently permissible standard for the concentration of non-carcinogenic compounds of Cr VI in air will protect most workers against irritation of the respiratory passages. This standard permits a time-weighted average exposure to 25 μg Cr/m^3 of ambient air for a 40-hour week, with a maximum exposure to 50 $\mu g/m^3$ of breathing zone air for any 15-minute period.

Teratogenicity

Although the mutagenic properties of certain compounds of Cr are well established, little evidence could be found for fetal damage directly attributable to such compounds. This is somewhat unexpected in light of placental permeability to at least some forms of Cr (Mertz, 1969). Embryonic abnormalities were produced in the chick when $Na_2Cr_2O_7$ or $Cr(NO_3)_3$ were injected into the yolk sac or onto the chorioallantoic membrane (Ridgway and Karnofsky, 1952). The significance of these data in relation to ingestion of chromium compounds is questionable.

Mutagenicity

Because of the close correlation emerging between carcinogenicity of chemicals and their mutagenic properties in suitable test systems, it is of interest to refer to the work of Venitt and Levy (1974), who reported that soluble chromates of Na, K and Ca stimulated mutagenesis in E. coli. Negative results were obtained with soluble salts of the two metals closest to Cr in the periodic table (tungsten and molybdenum), as well as with a soluble compound of Cr III. Earlier reports (Hueper, 1971) classifying Cr salts under the heading of carcinogenic chemicals without mutagenic properties appear to have been in error.

In recent years much evidence has accumulated to show that compounds of Cr possess the definite ability to cause transformation and mutation. Both Cr III (as $CrCl_3$) and Cr VI (as $K_2Cr_2O_7$) in concentrations equitoxic to mice produced similar morphologic changes in tertiary cultures of mouse fetal cells (Rafetto, et al. 1977); it is interesting to note that Cr VI caused more extensive chromosomal aberrations than did Cr III. Wild (1978) reported that potassium chromate produces a dose-dependent cytogenetic effect on bone marrow in mice. Hexavalent Cr has also been suspected of being responsible for the mutagenic effects of welding fumes (Hedenstedt, et al. 1977). Bigalief, et al. (1976) observed a significant increase in the frequency of bone marrow cells with chromosome aberrations in rats acutely or chronically poisoned with potassium dichromate. Further, aerosols of Cr VI have been held responsible for mutagenic effects found in a group

of workers engaged in the production of chromium (Bigalief, et al. 1977). The full significance of these results could not be evaluated in the absence of the detailed publications.

In bacterial test systems, compounds of Cr VI caused mutations in Salmonella typhimurium (Petrilli and De Flora, 1977). Two compounds of Cr III tested were neither toxic nor mutagenic for this organism. The conclusion may be recalled that the major risk of carcinogenicity for humans arises from Cr VI compounds (see "Carcinogenicity" section). In concentrations as low as 10^{-5}M, potassium dichromate significantly increased gene conversion in a strain of yeast (Bonatti, et al. 1976). The transformation frequency of simian adenovirus in Syrian hamster cells was raised by calcium chromate (Casto, et al. 1977).

Carcinogenicity

In addition to the many acute and chronic effects discussed in preceeding sections, carcinogenicity of various Cr compounds has been well documented, at least in man. A series of Cr compounds was listed by the National Institute of Occupational Safety and Health (1977) under the heading of suspected or identified carcinogens in humans. Inclusion in this list was largely based on results of animal experimentation. If, however, one excludes sarcoma production at the site of implantation or injection of the suspected carcinogen, the evidence for cancer production in experimental animals is not convincing.

In spite of the demonstration that Cr compounds can cause tumors at various sites in experimental animals, the only well-documented evidence for cancers associated with Cr exposure of humans involves the lungs. The relatively high incidence of lung cancer in the chromate industry has been well documented (Natl. Acad. Sci. 1974). Industrial exposure, as discussed below, greatly exceeds that attributable to food, water, and air under normal conditions. In considering the risks of pulmonary carcinogenesis in man, the low systemic levels of Cr originating from the diet or from drinking water can be ignored; unlike the pulmonary load of Cr, which does not appear to be in equilibrium with other body stores of the element (see "Pharmacokinetic" section), ingested Cr is poorly absorbed and presents no risks at normal ambient levels.

The primary emphasis in this field must be placed on the problems associated with pulmonary exposure; no evidence has been adduced for an association in humans between Cr and initiation of cancer at sites other than the lungs. The literature on respiratory cancer in humans up to 1950 has been reviewed by Baetjer (1950): 109 cases had been reported up to that date in the chromate-producing industry, and an additional 11 cases were reported from chromate pigment plants. It seems likely that in all instances Cr VI was involved in the effect. In any case, the incidence of respiratory cancer among these work populations significantly exceeded expected values.

Further work on this subject after 1950 is considered in the review prepared by the National Academy of Sciences (1974). Of particular interest is the study of Taylor (1966) on a large group of chromate workers who were followed over a period of 24 years on the basis of records from the U.S. Social Security Administration. Death rate from lung cancer in this group exceeded expected values by a factor of 8.5. Excess incidence of all other cancers amounted only to a factor of 1.3, in agreement with the conclusion stated above that respiratory cancers constitute the major cancer risk associated with Cr exposure in humans. Taylor further reported that the age-adjusted death rate from respiratory cancer increased with the period of exposure, a finding suggesting the existence of a definite dose-response relationship. Little predictive use can be made of this fact as no information on the concentration of potential carcinogens in these studies was available.

An additional difficulty arises in attempts to interpret this information because the specific carcinogen (or carcinogens) responsible for the increased incidence of cancer found in the chromate industry has not been fully identified. Several compounds of Cr are likely to be present in industrial surroundings. Further, a significant portion of workers investigated must have been exposed to other potential or actual carcinogens used in the chemical industry. Finally, the lung cancers observed in industry generally resulted from prolonged exposure. Initial exposure levels are often not known and the only information available refers

to Cr levels in air at the time of the final survey. All these factors make it difficult to extract from data on human subjects conclusions concerning any significant relationship between degree of Cr exposure and the incidence of lung cancer.

This problem may be illustrated by Table 1, based on the work of Mancuso and Hueper (1951). In this study an incidence of cancer of the respiratory system of 66.7 percent of all cancers was observed, compared with a figure of 11.4 percent in a control group. Details of the six Cr workers concerned, with the addition of one worker who died of respiratory cancer outside of the county and who was not included in the above calculation, are shown in the table. As clearly emerges from these data, lung cancer arises only after a prolonged exposure and latency period (Bidstrup and Case, 1956). A second point apparent from the table is that the reported levels of Cr in air (average 0.74 mg CrO_3/m^3) were very high. These exposure levels were calculated for each individual with adjustments for the occupational history, and show that in each case the major exposure involved water-insoluble Cr. It is not certain to what extent compounds of Cr VI were included under the heading of water-insoluble Cr. The suggestion that carcinogenicity in these cases could be attributed to Cr III is probably not justified (U.S. Pub. Health Serv. 1953); this is further borne out by more recent work with Cr VI.

TABLE 1

Deaths Due to Lung Cancer in Chromate Workers
(adapted from Mancuso & Hueper, 1951)

SUBJECT	YEARS OF EXPOSURE	LATENT PERIOD (years)	EXPOSURE LEVELS ($mg\ CrO_3/m^3$)		
			WATER INSOLUBLE	WATER SOLUBLE	TOTAL
CB	9.0	10.0	0.37	0.17	0.54
TG	14.5	14.3	0.37	0.08	0.45
FJ	12.5	12.5	0.19	0.02	0.21
JK	7.5	9.0	0.92	0.29	1.21
EL	9.2	14.0	1.12	0.15	1.27
ESM	2.0	7.2	0.19	0.02	0.21
WDS	7.2	7.2	1.12	0.15	1.27
Mean	8.8	10.6	0.61	0.13	0.74

The exposure levels were calculated for each individual on the basis of his occupational history, and are expressed in terms of CrO_3.

Thus, Davies (1978) reported that among workers exposed to Zn chromate in three British factories, an increased mortality due to lung cancer was seen after an induction time as short as one year. Concentrations of Cr were not given. Similarly, Langard and Norseth (1975) observed an increased cancer rate among workers in a Zn chromate plant where no trivalent Cr was utilized. Pulmonary cancer was identified in three workers who had been exposed to levels of 0.5 to 0.9 mg Cr/m^3 for 6 to 9 years. In addition, a single case of adenocystic carcinoma of the nasal cavity was also reported. Attention must again be drawn to the fact that such exposures involve Cr concentrations which are relatively massive when compared to recommended standards (see "Existing Guidelines and Standards" section). The standard for occupational exposure in air mandates levels of poorly soluble mono- or dichromates not exceeding 1 ug/m^3.

Attempts to produce lung cancers in experimental animals by inhalation exposure or by feeding Cr compounds have not been successful. Inhalation did cause, however, a variety of pulmonary symptoms (Steffee and Baetjer, 1965). Permitting animals to breathe air from a chromate factory, 1 to 3 mg Cr/m^3, produced no bronchogenic carcinomas (Baetjer, et al. 1959). Nettesheim, et al. (1970) exposed mice to Cr_2O_3 dust (25 mg/m^3) for 5½ hours per day, five times each week, for as long as 18 months with similarly negative results. Distribution and elimination of Cr from the lungs were affected by simultaneous infection of the animals with influenza virus. This underscores the importance of factors other

than Cr itself in determining possible effects. In any case, not even the relatively prolonged retention of inhaled Cr in the lungs (see "Inhalation" section) suffices to assure an inhalation exposure adequate for the production of lung cancer under experimental conditions. Experimental lung tumors could only be observed following implantation of pellets prepared from Cr VI compounds dispersed in an equal quantity of cholesterol carrier (Laskin, et al. 1970). As was already stated above in reference to the data gathered in epidemiological surveys of lung cancer in humans, such results do not lend themselves to the derivation of dose-effect relationships, nor to extrapolation down to acceptable levels by a linear or any other model.

In the very high concentrations employed for the experimental production of cancer, compounds of Cr may also possess some cocarcinogenic properties. As illustrated by the observation of Lane and Mass (1977), 2.5 mg of chromium carbonyl acted mildly synergistically with 2.5 mg benzo(a)pyrene in producing carcinomas in tracheal grafts in rats. No further reports on the possible cocarcinogenicity of Cr compounds were found. It is conceivable, however, that in the very high concentrations employed experimentally, other Cr compounds might also possess cocarcinogenic properties. Especially likely in view of the recognized risks associated with smoking is the probability that smoking increases the incidence of lung cancer following pulmonary exposure to Cr.

CRITERION FORMULATION

Existing Guidelines and Standards

A variety of standards have been recommended for permissible Cr VI levels in water and air. Table 2 provides information on standards presently established in the United States, as formulated by various agencies. The high acceptable level of Cr in livestock water is based on the poor absorption of Cr compounds in general from the gut ("Ingestion" section). Because of this low fractional absorption, and in view of the fact that the sensitivity of the lungs to Cr appears to exceed that of other tissues, as discussed in the "Carcinogenesis" section, standards for Cr in air are much lower than those for water.

Current Levels of Exposure

Although lower Cr limits have been prescribed for air than for water, the standard for non-carcinogenic Cr VI in air permits significantly greater uptake of Cr than does that for Cr VI in drinking water designed for human consumption. Thus, if we assume a daily consumption of 2 liters, with a fractional gastrointestinal absorption of 5 percent, total uptake from that source would amount to 10 μg/day. In contrast, the criteria discussed in the section on "Inhalation", i.e., an alveolar ventilation of 10 m^3/24 hours with 50 percent alveolar retention of inhaled Cr, would lead to Cr uptake through the lungs of around 40 μg during an 8 hour exposure to levels of 25 $\mu g/m^3$. The upper limit for carcinogenic Cr VI would similarly cause retention of 1 to 2 μg Cr under these conditions.

TABLE 2

Recommended or Established Standards for Cr in the United States

MEDIUM	CHEMICAL SPECIES	REFERENCE	STANDARD
Drinking Water total	Cr VI	U.S. Pub. Health Serv. (1962)	50 µg/l
Ambient water	Cr VI	U.S. EPA (1976)	50 µg/l
Total Fresh water (aquatic life)	total chromium	U.S. EPA (1976)	100 µg/l
Livestock water	Cr VI	Natl. Acad. Sci. (1972)	1 mg/l
Work place air	carcinogenic[a]	Natl. Inst. Occup. Safety and Health (1975)	1 $\mu g/m^3$
	non-carcinogenic[a]	Natl. Inst. Occup. Safety and Health (1975)	25 $\mu g/m^3$ TWA [b]
	Cr VI	Natl. Inst. Occup. Safety and Health (1975)	50 $\mu g/m^3$ TWA [b]

a) Carcinogenic compounds are here taken to include all forms of Cr VI other than CrO_3 and mono- or dichromates of H, Li, Na, K, Rb, Cs and NH_4.

b) Time-weighted average.

Special Groups at Risk

No such groups have been identified outside the occupational environment.

Basis and Derivation of Criterion

There is evidence which suggests that hexavalent chromium (Cr VI) is a carcinogen. Based on exposure of chromium workers to Cr VI (Mancuso and Hueper, 1951; Taylor, 1966) the U.S. EPA Carcinogens Assessment Group has developed a water quality criterion for Cr VI to keep the lifetime risk level below one in 100,000 (see Appendix I).

Under the Consent Decree in NRDC vs. Train, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Chromium VI is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of Chromium VI in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of Chromium VI corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one

additional case of cancer for every million people exposed, and so forth.

In the Federal Register notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6} or 10^{-7} as shown in the table below.

Exposure Assumptions	Risk Levels and Corresponding Criteria (1)			
	0	10^{-7}	10^{-6}	10^{-5}
2 liters of drinking water and consumption of 18.7 grams of fish and shellfish (2)		0.08 ng/l	0.8 ng/l	8 ng/l
Consumption of fish and shellfish only.		8.63 ng/l	86.3 ng/l	863 ng/l

(1) Calculated by applying a modified "one hit" extrapolation model described in the FR 15926, 1979 to the animal bioassay data presented in Appendix I. Since the extrapolation model is linear to low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

(2) Approximately one percent of the Chromium VI exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 1.0 fold. The remaining 99 percent of Chromium VI exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of Chromium VI (1) occurring from the consumption of both drinking water and aquatic life grown in water containing the corresponding Chromium VI concentrations and, (2) occurring solely from the consumption of aquatic life grown in the waters containing the corresponding Chromium VI concentrations. Although total exposure information for Chromium VI is discussed and an estimate of the contributions from other sources of exposure can be made, this data will not be factored into the ambient water quality criteria. The criteria presented, therefore, assume an incremental risk from ambient water exposure only.

Therefore, the criterion for hexavalent chromium should be at a level of no greater than 8 ng/l to keep the lifetime risk of cancer below 1 in 100,000.

A water quality criterion can be set for other Cr species on the basis of reasonable safety margins applied to the lowest exposure observed to produce effects.

The level of 0.05 mg/l of chromium quoted in Table 2 appears to be an acceptable risk level. This level is 500 times lower than a concentration which remained without overt toxicological effects in rats over a period of one year, and over 200 times lower than a level reported not to affect dogs over four years. With the exception of hexavalent chromium, there is no reason to believe that the level of 0.05 mg/l (50 µg/l) permitted for ambient water poses a significant threat to human health. As a standard, this

level was set in 1962 and has in the meantime been confirmed by several reviewing groups. Therefore, the recommended water quality criterion for chromium, except hexavalent chromium, is 50 µg/l. For practical purposes, it should be noted that it is difficult to analytically distinguish between trivalent and hexavalent chromium.

Because of the low bioconcentration of chromium, consideration of the consumption of fish and shellfish does not change the recommended criterion:

If two liters of drinking water are ingested per day, then a level of 50 µg/l would correspond to an intake of 100 µg from water. To apportion this daily intake to both drinking water and fish and shellfish consumed, the following calculation can be used:

$$2X + (0.0187)(F)(X) = 100\ \mu g$$

where

2 = amount of water ingested in liter/day

X = chromium concentration in water, mg/l

0.0187 = amount of fish consumed per day, kg/day

F = bioconcentration factor, mg chromium/kg fish per mg chromium in water. (F = 11 for chromium)

$$2X + .2X = 100\ \mu g$$

$$2.2X = 100\ \mu g$$

$$X = 45\ \mu g/l\ (\text{or} \sim 50\ \mu g/l)$$

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APPENDIX 1

Summary and Conclusions Regarding the Carcinogenicity of Chromium*

In the aquatic environment chromium is virtually always found in the valence states +3 or +6. Cr III is an essential trace element. The daily requirement for Cr III is provisionally set as a range of 50 to 200 µg Cr III/day (Mertz, 1979). The evidence suggests that Cr VI is a carcinogen. Cr VI is highly soluble in water, whereas the solubility of Cr III is low, depending on pH, alkalinity, and water hardness. Cr VI is a strong oxidizing agent which reacts readily with many reducing agents including organic reducing matter, to yield Cr III. Within the cells, Cr VI will be reduced to Cr III and remain trapped in this form. Cr III forms many hexacoordinate complexes in solution with carboxy groups of proteins, or smaller metabolites, certain amino acids, nucleic acids, and nucleoproteins; very stable bonds to both RNA and DNA are formed by Cr III.

Almost all of the Cr VI found in the environment is produced by industry. Chromium salts (primarily chromates and dichromates which are compounds of Cr VI) are used extensively in the metal finishing, textile, and leather tanning industries. They are also used in cooling waters, (catalytic manufacture, pigments, primer paints, fungicides, and wood preservatives.

*This summary has been prepared and approved by the Carcinogens Assessment Group of U.S. EPA in July, 1979.

The environmental exposure to chromium occurs by inhalation, ingestion from water and food, and by the dermal route. Cr VI compounds are taken up more rapidly by tissues than Cr III due to their greater solubility and facilitated transport across cell membranes by broadly specific anion transport mechanisms. The lung seems to be a target tissue for Cr, as pulmonary Cr content usually exceeds that of other organs, and Cr is cleared relatively slowly from the lungs.

Occupational exposure to CR in the air has lead to gastric and duodinal ulcers, gastritis, ulceration, and subsequent perforation of the nasal septum, chronic rhinitis, and pharyngitis (Mancuso, 1951).

Hexavalent chromium has been shown to be mutagenic. Chromates (Cr VI) and dichromates (Cr VI) have been mutagenic in E. coli (Venitt and Levy, 1974), produced morphologic changes and extensive chromosomal aberrations in tertiary cultures of mouse fetal cells (Raffeto, et al. 1977), and caused cytogenetic effects in mouse (Wild, 1978) and rat (Bigalief, et al. 1976) bone marrow cell. Cr III compounds do not produce these effects. In humans, aerosols of Cr VI are suspected of being responsible for the cytogenetic effects of welding fumes (Hedenstedt, et al. 1977). Cytogenetic effects have also been observed in a group of workers engaged in the production of Cr (Bigalief, et al. 1977). Furthermore, compounds of Cr VI, without metabolic activation, caused mutations in Salmonella typhimurium, Ames strains TA1535, TA100, TA1537, and TA98, while compounds of Cr III were not toxic or mutagenic (Petrilli and DeFlora, 1978).

With metabolic activation, negative results were obtained for Cr VI as well as Cr III. These observations indicate that Cr VI is a direct acting mutagen capable of inducing both frameshift errors and base pair substitutions. As little as 10^{-5}M potassium dichromate significantly increased gene conversion in a strain of yeast.

Six epidemiological studies, five of which were at different locations (Taylor, 1966, Enterine, 1974; Davies, 1978; Langard and Norseth, 1975; Mancuso and Hueper, 1951; Baetjer, 1950), of up to 1200 chromate workers strongly indicate that inhalation of Cr VI produces lung cancer. In addition, Taylor also showed an increase in digestive cancers. Inhalation studies using calcium chromate on rats and hamsters have produced cancers (Laskin, 1973). The carcinogenicity of Cr VI has not been tested by oral administration. Cr VI has been shown to be carcinogenic when implanted in intrabronchial pellets and by subcutaneous as well as intramuscular injection in mice and rats. Oral administration of 5 ppm chromic acetate (a Cr III compound) to mice and rats has had negative results, possibly due to the fact that it is not absorbed in appreciable amounts from the G.I. tract.

There is no animal bioassay data for ingestion of Cr VI on which to base a water quality criterion. A water quality criterion based on a lifetime risk of 10^{-5} was calculated by assuming that the chromium workers studied by Taylor had the same exposure as those in the Mancuso and Hueper study (see Derivation of the Water Quality Criterion for Chromium). The result is that the water concentration of

Cr VI should be less than 8.0 ng/l in order to keep the lifetime risk below 10^{-5}. Cr III, which is required in the diet for good nutrition, does not appear to be a carcinogen based on the available information; consequently, no limit is recommended by the CAG for the water concentration of Cr III. Also, it should be noted that there was no appreciable amount of hexavalent chromium present in the insoluble crude ore (private communication, Dr. Mancuso and Dr. Paul Urone, chemist.)

Summary of Pertinent Data

In order to calculate a water quality criterion for Cr VI, it was necessary to assume that the population's exposure to Cr VI in the Mancuso and Hueper study was the same as the exposure in Taylor's paper. Taylor's is the only study in which the cohort is large enough (1212 people were studied) to see the effects of Cr exposure in areas other than the lungs, which are directly affected by inhaled Cr. The lung cancer risk was very high in this study. The risk of digestive cancer from Cr exposure is statistically significant in Taylor's cohort (as shown in 1974 by Enterline); however, the amount of Cr to which the workers were exposed is not available for Taylor's study. Mancuso and Hueper closely studied 97 chromium workers in which they saw a high incidence of lung cancer (however, less than Taylor's study). The data on exposure in the Mancuso and Hueper study is very detailed, giving information on first exposure date, years of exposure, latent period, amount of Cr exposure in mg Cr/m^3 for Cr III and Cr VI separately, and date of death.

In order to calculate a water quality criterion for Cr, it is necessary to know the exposure levels producing the digestive cancer response in Taylor's study, as the direct lung effects may not be relevant to water exposure.

The following is an account of the calculations used in estimating the water concentration of Cr VI which would result in a lifetime risk of dying from digestive cancer of 10^{-5}.

Assuming that the average exposure in Mancuso and Hueper's study is 0.1 mg Cr/m^3 (this is the mean exposure to water soluble chromium which is Cr VI), then the concentration in Taylor's study is also assumed to be 0.15 mg Cr/m^3. The total exposure in 4.146 years (the mean exposure time in Taylor's study) is 0.15 mg Cr/m^3 x 10 m^3/working day x 240 working days/yr x 4.146 years = 1492.56 mg. If 50 percent of this is swallowed from the respiratory tract, then 2.018 liter/day x 365 days/year x 70 years x C mg/l = 1492.56 x 0.5 (The bioconcentration factor in fish is 1.0)

$$C = 14.40 \ \mu g/l \text{ of Cr VI}$$

C is the estimated concentration in water necessary to produce the observed digestive cancer incidence in the Taylor study. The relative risk in the Taylor study is 1.533 which is statistically significant. The excessive risk corresponding to a concentration of C = 14.40 µg/l is .533 p, where p is the expected population risk of digestive tract cancer. The slope of the excessive risk curve is

$$B = \frac{0.533p}{0.014} = 37.01p \ (mg/l)^{-1}$$

The water quality criterion corresponding to a risk of 10^{-5} is given by

$$X = \frac{10^{-5}}{37.01p} \ mg/l$$

$$= \frac{10^{-2}}{37.01p} \ \mu g/l$$

Based on the HEW Vital Statistics of the United States (1973), the lifetime risk of dying from digestive cancer (p) is estimated by an acturial method to be 3.5 percent.* Therefore, the water concentration of Cr VI should be less than 8.0 ng/l in order to keep the lifetime risk below 10^{-5}.

Using the water concentration of 8 mg/l for Cr VI, the one-hit slope (B_H) may be calculated as follows:

$$B_H = \frac{70 \times 10^{-5}}{C(2 + RxF)}$$

$$R = 1.0$$

$$F = .0187 \text{ kg/day}$$

$$C = 8 \times 10^{-6} \text{ mg/l}$$

$$B_H = 43.345 (\text{mg/kg/day})^{-1}$$

*(Thus, from this data, p = .035).