Hexavalent Chromium-Contaminated Soils: Options for Risk Assessment and Risk Management

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Risk assessment involves establishing scientifically defensible dose–response relationships for end points of concern. For Cr(VI)-contaminated soils, this includes conducting dose–response assessments for blood, liver, and kidney toxicity following oral exposure; lung cancer following inhalation exposure; and allergic contact dermatitis following dermal exposure. This dose–response information is then integrated with a site-specific exposure assessment (or default assumptions) in order to develop a site-specific (or generic) soil criterion within the framework of a comprehensive risk characterization. Risk managers develop cleanup standards designed to protect against all possible adverse effects, taking into account these site-specific (or generic) criteria and other factors such as technical feasibility, cost–benefit analyses, and sociopolitical concerns. Recently a push for cost–benefit analyses of environmental decisions has occurred, further supporting the need for risk assessors to prepare a comprehensive risk characterization, with its attendant uncertainties. These risk assessment and management issues are brought to the forefront by risk assessors and risk managers dealing with Cr(VI)-contaminated soils. This article offers a review and analysis of the risk characterization of Cr(VI)-contaminated soils, showing that the differing toxicities with route of exposures do not necessarily lead to different characterizations of risk. Soil concentrations in the range of 130 to 450 ppm appear to protect against noncancer toxicity from oral exposure, cancer toxicity from inhalation exposure, and allergic contact dermatitis from dermal exposure.

INTRODUCTION

Chromium: Background information. Chromium can exist in multiple valence states, with trivalent [Cr(III)] being most common. Chromium (III) is a naturally occurring element which is an essential nutrient for humans and other species (NRC, 1989). Cr(III) is the form found in biological systems and is the form found in foodstuffs and nutritional supplements. Its primary biological role is in the potentiation of insulin; chromium also plays a role in nucleic acid metabolism and gene expression. It has not been shown to be carcinogenic and is associated with a very low degree of toxicity; intakes even 1000-fold higher than the recommended intake level have not been associated with adverse effects (Anderson, 1994).

Concern may be warranted, however, for excessive exposure to hexavalent chromium [Cr(VI)], which is a known human carcinogen by the route of inhalation (EPA, 1996a), can elicit allergic contact dermatitis (ACD) (Menne and Maibach, 1991), and is associated with greater toxicity than the trivalent form (Dourson, 1994). Cr(VI) is a strong oxidizing agent and is found most often linked to oxygen as either the chromate ($Cr_2O_4^{2-}$) or the dichromate ($Cr_2O_7^{2-}$). While Cr(VI) poses more of a human health hazard than its trivalent analogue, it is not typically found to be naturally occurring in the environment. Nevertheless, Cr(VI) is found at high concentrations in some regions of the country, most notably areas in New Jersey where chromite ore processing operations were in existence (Chromium Information Exchange, 1995). These facilities, located in Hudson County, New Jersey, utilized a process to extract chromium from chromite ore. The residue, which can contain up to 5% chromium which cannot be extracted, was often used as fill material in the development of residential, commercial, and industrial sites. The vast majority of the chromium that persisted in the residues was in the trivalent form, but some hexavalent was also present. Because of its use as fill material in construction sites, it is now found throughout regions of Hudson County, and risk managers are posed with the difficult question of determining at what level it is acceptable or, alternatively, to what level it should be removed from soils.

The risk assessment paradigm. The National Research Council (NRC, 1983, 1994) risk assessment paradigm defines the four classical components of the risk assessment process: hazard identification, dose–re-

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sponse assessment, exposure assessment, and risk characterization. Each of these components is described herein to varying extents, with emphasis placed on issues pertaining to dose–response assessment and risk characterization for Cr(VI).

The importance of risk characterization has been highlighted by the 1995 guidance document issued by EPA (1995a). In addition to providing guidance on the process of risk characterization, this document also addresses issues surrounding the division between risk assessment and risk management. Of particular relevance to the case of Cr(VI)-contaminated soils are two guiding principles laid out in this document, which are excerpted at some length below in accordance with their importance to this article:

1. Risk assessors and risk managers should be sensitive to distinctions between risk assessment and risk management.

> For the *generators of the assessment,* distinguishing between risk assessment and risk management means that scientific information is selected, evaluated, and presented without considering issues such as cost, feasibility, or how the scientific analysis might influence the regulatory or site-specific decision. . . .
> For *users of the assessment and for decision-makers* who integrate these assessments into regulatory or site-specific decisions, the distinction between risk assessment and risk management means refraining from influencing the risk description through consideration of other factors—e.g., the regulatory outcome—and from attempting to shape the risk assessment to avoid statutory constraints, meet regulatory objectives, or serve political purposes. Such management considerations are often legitimate considerations for the overall regulatory decision . . ., but they have no role in estimating or describing risk. . . . Matters such as risk assessment priorities, degree of conservatism, and acceptability of particular risk levels are reserved for decision-makers who are charged with making decisions regarding protection of human health.

2. The risk assessment product, that is, the risk characterization, is only one of several kinds of information used for regulatory decision-making.

> As authorized by different statutes, decision-makers evaluate technical feasibility . . ., economic, social, political, and legal factors as part of the analysis of whether or not to regulate, and, if so, to what extent. For this reason, risk assessors and managers should understand that the regulatory decision is usually not determined solely by the outcome of the risk assessment. [For example], assessment efforts may produce an RfD for a particular chemical, but other considerations may result in a regulatory level that is more or less protective than the RfD itself.[1]

HAZARD IDENTIFICATION

Humans may be exposed to soil-borne chromium by multiple routes, including inhalation, oral, and dermal, providing several possible bases for cleanup standards for chromium-contaminated soils. Additional exposures may occur as the result of fate and transport of chromium through environmental matrices (e.g., leaching into groundwater, uptake into vegetation which is consumed). These are considered to be indirect exposures and are not considered here.

Following is a brief description of the potential hazards posed to human health as a consequence of direct exposure by various routes to chromium-contaminated soil. Because of the ability of Cr(VI) to be reduced to Cr(III) in the environment, both forms are discussed with regard to toxicity.

By the oral route, Cr(III) is an essential nutritional element with a very low degree of absorption from the gastrointestinal tract. Donaldson and Barreras (1966) reported a mean absorption efficiency of 0.5 ± 0.3% in human volunteers. Even ingestion of large amounts has not been shown to result in toxicity (EPA, 1996a). Ingested Cr(VI) is associated with a somewhat greater absorption: 2.1 ± 1.5% in the study by Donaldson and Barreras (1966). However, Cr(VI) is readily reduced to trivalent chromium in acidic solutions, so that ingested Cr(VI) which ends up in the acid milieu of the stomach is reduced to Cr(III) prior to uptake (O'Flaherty, 1994). Only intakes that exceed the reducing capacity of the stomach would result in significant absorption of Cr(VI) across the gastrointestinal mucosa. At such large doses, Cr(VI) has resulted in toxicity to the blood, liver, and kidney (Fristedt *et al.,* 1965; Kaufman *et al.,* 1970; Zhang and Li, 1987).

By inhalation, Cr(III) has not been shown to pose a human health hazard. Exposure to Cr(VI) by inhalation, however, can cause both cancer and noncancer toxicity. The noncancer effects include diffuse nasal and bronchopulmonary effects, which are primarily a result of the corrosive properties of Cr(VI) at the site of contact (reviewed in WHO, 1988). Lung cancer incidences have been found to be elevated in workers exposed occupationally to Cr(VI)-containing dusts (Langard, 1983) and is clearly an end point of concern for Cr(VI)-contaminated soils.

By the dermal route, Cr(III) does not appear to pose a hazard. Because of its low water solubility, there is negligible absorption of Cr(III) through the skin (Burrows and Adams, 1990). Cr(VI), on the other hand, has been known for decades to elicit an ACD in sensitive individuals (reviewed in Stern *et al.,* 1993; Paustenbach *et al.,* 1992). Because of the allergic nature of this reaction, it can occur in some individuals at very low concentrations. At higher concentrations, Cr(VI) may elicit dermal effects (of an irritant nature) in the general population; ACD, however is a potential problem for only a small percentage (i.e., 0.1–1%) of the population (Hostynek and Maibach, 1988; Paustenbach *et al.,* 1992; Nethercott *et al.,* 1994).

[1] See also Barnes and Dourson (1988) for a comparison of regulatory doses and reference doses.

DOSE–RESPONSE ASSESSMENT

Oral exposure. As more fully explained in EPA (1996a), the reference dose (RfD) for Cr(III) is 1 mg/kg day, which is equivalent to an intake of 70 mg/day for a 70-kg adult. This assessment is based on a chronic study in rats (Ivankovic and Preussmann, 1975) in which the highest dose, 5% Cr_2O_3 in the diet, was a no observed adverse effect level (NOAEL).[2] Groups of rats (60/sex) were given Cr_2O_3 baked in bread at dietary levels of 0, 1, 2, or 5% for 5 days/week for 120 weeks. The highest concentration was equivalent to a total intake of about 1800 g Cr_2O_3/kg body wt over 600 days. This NOAEL was adjusted to account for the proportion of Cr in Cr_2O_3 (68.5%) and divided by the exposure period of 600 days (×5/7 days to account for a 5 day/week exposure protocol) to result in a NOAEL of 1468 mg Cr(III)/kg day. This NOAEL was divided by an uncertainty factor (UF) of 100 (10-fold each for intra- and interspecies extrapolation) and a modifying factor of 10 to "reflect uncertainties in the NOAEL."[3] The resulting RfD, rounded to 1 significant figure, is 1 mg/kg day; this level is 350- to 1400-fold higher than the estimated safe and adequate daily dietary intake (ESADDI), indicating that Cr(III) does not appear to present a human health risk following ingestion of even significant amounts (EPA, 1996a). In fact, Cr(III) is an essential element for which the majority of Americans have a suboptimal intake. Typical intakes are in the range of 25–33 μg/day (Anderson and Kozlovsky, 1985). This is only about half of the lower end of the daily intake (ESADDI of 50–200 μg/day) recommended by the Food and Nutrition Board of the National Research Council (NRC, 1989). In both humans and laboratory animals, intakes far above the ESADDI have been shown to be without adverse effect.

As more fully explained in EPA (1996a), the RfD for Cr(VI) is 5×10^{-3} mg/kg day, which is equivalent to an intake of ~0.4 mg/day for a 70-kg adult. This assessment is based on a 1-year drinking water study in Sprague–Dawley rats by MacKenzie *et al.* (1958). The rats (8–10/sex/group) were provided drinking water containing 0, 0.45, 2.2, 4.5, 7.7, or 11 mg/L Cr(VI) (as K_2CrO_4). No adverse effects were apparent in this study in any group of animals. In a second study, the authors provided drinking water containing 25 mg/L Cr as either a hexavalent form (i.e., K_2CrO_4) or a trivalent form (i.e., chromic chloride). Although tissue concentrations of chromium were ~nine-fold higher in the rats administered the Cr(VI) compared with those administered Cr(III), there were no adverse effects observed in either group. The NOAEL from this study, 25 mg/L, serves as the basis for EPA's RfD for Cr(VI). Based on actual body weight and water consumption data, this concentration is equivalent to an intake of 2.4 mg Cr(VI)/kg body wt/day. A total uncertainty factor of 500 (10 for intraspecies variability, 10 for interspecies extrapolation, and 5 for less-than-lifetime exposure) was applied to yield the RfD of 5×10^{-3} mg/kg day.

Inhalation exposure. Cr(III) is not associated with toxicity from the inhalation route, perhaps because it has not been well studied independently of Cr(VI). The authors do not conduct a dose–response assessment for Cr(III) as a result.

Inhalation of Cr(VI) dusts has been associated with both noncancer and cancer effects. The noncancer toxicity is related to the corrosive properties of Cr(VI) and is manifested as diffuse nasal symptoms at the point of contact. Lindberg and Hedenstierna (1983) conducted a study on 100 workers in a chrome-plating operation and reported on the occurrence of nasal mucosal atrophy in workers exposed to Cr(VI) mists. EPA developed a reference concentration (RfC) based on this study, but has since withdrawn this risk value. For noncancer effects, Finley *et al.* (1992) have suggested that the Lindberg and Hedenstierna (1983) study may be useful for setting an RfC for Cr(VI) mists, but not dusts which would be more commonly encountered in environmental exposures. For Cr(VI) dusts, Finley *et al.* (1992) contend that the available human data are not suitable for a quantitative risk assessment, and propose that a multispecies study (i.e., rabbits, guinea pigs, and mice) by Steffee and Baetjer (1965) be used. This study involved inhalation exposures of these three species to Cr(VI) dusts (~3000–4000 $\mu g/m^3$) for 5 hr/day, 4 days/week for a lifetime. Using the concentration of 3000 $\mu g/m^3$ (adjusted to 357 $\mu g/m^3$ for continuous exposure) as a minimal lowest-observed-adverse-effect-level (LOAEL) based on lung and nasal effects in 15–25% of the animals and an UF of 300 (10 for intraspecies extrapolation, 10 for interspecies extrapolation, and 3 for a minimal LOAEL), the authors propose an RfC of 1.2 $\mu g/m^3$.[4]

More recently, Malsch *et al.* (1994) have proposed an RfC for particulate Cr(VI) using benchmark dose methodology. They used two studies in the calculation of benchmark concentrations: Glaser *et al.* (1990), in which male Wistar rats were exposed to sodium dichromate at concentrations of 50 to 400 $\mu g/m^3$ for 22 hr/

[2] It is noted that this is also the predominant form of Cr(III) in the New Jersey soils contaminated with chromite ore processing residue.

[3] The critical study was conducted primarily to investigate the carcinogenic potential of Cr(III) and did not include a complete evaluation of toxicological parameters. Also, the absorption of Cr(III) is influenced by multiple factors, and may be quite variable.

[4] Finley *et al.* (1992) calculated a dosimetric adjustment factor for particle deposition (according to EPA, 1994a; Jarabek, 1994) by the incorporation of a regional deposited dose ratio (RDDR). For this evaluation, the RDDR was determined to be 1.0760 and therefore has little bearing on the quantitative value of the RfC.

day, 7 days/week for up to 90 days, and Glaser *et al.* (1985), which used the same study protocol but with concentrations of 25 to 200 $\mu g/m^3$. Using the data from these two studies combined, Malsch *et al.* (1994) determined a benchmark concentration of 34 $\mu g/m^3$ based on the 95% lower confidence limit on the dose resulting in a 10% increase in lactate dehydrogenase in bronchoalveolar lavage fluid.[5] An UF of 100 (10 for intrahuman variability, 3.16 (half-log) for interspecies, and 3.16 for subchronic-to-chronic extrapolation) was applied, resulting in a proposed RfC of 0.34 $\mu g/m^3$.

Cr(VI) has been shown to be carcinogenic following inhalation by both humans and laboratory animals. The EPA (1996a) has classified Cr(VI) in Group A (known human carcinogen) based on the results of occupational epidemiologic studies of chromium-exposed workers. Chromium-exposed workers are exposed to both Cr(III) and Cr(VI) compounds.[6] However, because only Cr(VI) has been found to be carcinogenic in animal studies, and only Cr(VI) is mutagenic, the EPA concluded that only Cr(VI) should be classified as a human carcinogen.

For cancer effects, dose–response relationships have been established in humans for chromium exposure and lung cancer. As more fully described in EPA (1996a), an inhalation unit risk of 1.2×10^{-2} per ($\mu g/m^3$) was estimated using the multistage (extra risk) extrapolation method based on the study by Mancuso (1975) on occupationally exposed humans. The upper 95% confidence limit on a risk level of one in a million (1 in 10^{-6}) is an air concentration of Cr(VI) of 8×10^{-5} $\mu g/m^3$.

The cancer risk assessment for Cr(VI) results in a 10^{-6} risk level that is about 4000-fold lower than the RfC proposed by Malsch *et al.* (1994), indicating that basing a soil cleanup standard on the carcinogenic risk by the route of inhalation would result in a lower basis for the determination of soil cleanup standards than noncancer end points arising following inhalation exposure.

Dermal exposure. Cr(III) is not associated with dermatitis, nor is it expected to be absorbed in sufficient quantities to evoke systemic toxicity.

Cr(VI) can elicit two types of dermatitis. One type, which may occur in the general population, is a primary irritant dermatitis which results from the direct cytotoxic properties of Cr(VI). The other involves an immunological type IV response in sensitive individuals following dermal exposure to Cr(VI) compounds, i.e., ACD. Elicitation of either dermatitis may serve as an alternative option for setting soil standards for Cr(VI). We investigate more fully the elicitation of ACD as one option here.

The determination of ACD in an individual is made by a standard patch test procedure in which the material is put in direct contact with the skin for 24–48 hr under occlusion. The most commonly used patch test for determining chromium sensitivity utilizes a 0.25% potassium dichromate patch. Recently, a number of dermatologists have suggested that these studies be limited to 24-hr exposures, with an obligatory reading 3 days postexposure to reduce the number of questionable allergic responses (Brasch *et al.,* 1995).

The prevalence of Cr(VI)-related ACD in the general population is fairly low. Peltonen and Fraki (1983) examined 822 Finnish volunteers and found the rate of chromium sensitivity to be 1.7%. This included, however, 110 individuals with known exposure to chromium. Hostynek and Maibach (1988) estimated the rate of chromium sensitivity in the general population to be <1%. Paustenbach *et al.* (1992) gave a comparable estimation of 0.7%, and Nethercott (1990) estimated 0.6%. However, Nethercott *et al.* (1994) estimated that if these studies were reanalyzed while excluding individuals with more than 10 years of experience working with wet cement, the prevalence of Cr(VI) sensitization in the general population would likely be ≤0.1%.

ACD is a two-step process involving an irreversible sensitization reaction in which an immune response is induced following absorption of Cr(VI) into the skin and a nonpermanent elicitation reaction in which subsequent exposures elicit a dermal reaction. A general review of contact dermatitis is provided by Polak (1983). Symptoms of contact dermatitis include erythema, swelling, papules, and vesicles, with most Cr(VI)-induced ACD involving portions of the hands (Burrows, 1983). While other allergic dermatitis reactions are transient in nature (e.g., poison ivy), Cr(VI)-induced ACD has been noted for its persistence (Burrows, 1983).

A number of studies have been conducted to determine the threshold concentration for elicitation of ACD in sensitive individuals (see Tables 1 and 2). Several different compounds of Cr(VI) have been studied, the most common being potassium chromate (K_2CrO_4) and potassium dichromate ($K_2Cr_2O_7$). These two compounds exist in equilibrium in aqueous solutions, with the dichromate form predominating at lower pH levels. Therefore, potassium chromate solutions are generally buffered at higher pH levels and potassium dichromate at lower pH levels. As discussed below, an analysis of the dose–response data suggests that pH is an important factor influencing the response rate of ACD in sensitive individuals. Although the number of subjects in these studies is too small to draw definitive conclusions, a higher rate of ACD elicitation from Cr(VI) appears at higher pH levels.

[5] This benchmark concentration incorporates an RDDR of 2.1576.

[6] Cr(III) compounds have not been reported as being carcinogenic by any route of administration.

TABLE 1

Cumulative Percentage of Dermatitis in Sensitive Individuals as a Function of *Dichromate* Exposure via Occluded Patch Tests and pH of the Testing Solution

Zelger, 1964 (n = 33, pH 1.5)	Zelger & Wachter, 1966 (n = 50, pH 1.5)	Anderson, 1960 (n = 15, pH 4.3)	Pirila, 1954 (n = 35, pH 4.3)	Geiser *et al.*, 1960 (n = 53, pH 4.3)	Allenby& Goodwin, 1983 (n = 46, pH 7.0)	Skog & Wahlberg, 1969 (n = 46, pH 7.0)	Wahlberg, 1973 (n = 21, pH 7.0)	Calnan, 1962 (n = 24, pH 7.7)	Calnan, 1962 (n = 24, pH 10)	Skog & Wahlberg, 1969 (n = 46, pH 12)	Wahlberg 1973 (n = 21, pH 12)
									0	—	—
									0	—	—
0	0				–			—	—	—	—
					0			—	—	—	—
0	0						–	—	—	—	—
			3	—	—	—	—	8	4		
0	0						0	—			5
							–	—			
0					–	2	0	—		7	10
					–	2	5			22	29
		33	14	25	—	—	—	29	21		—
	0	—	—	—	—	—	14				43
										39	
					29					—	
6	4					30	24			54	48
		87	—	53		35	48			70	71
		—	86	66		43	57	58	50	91	95
58	54					—					
			97	—	—	—	—	—			
					79	57	67			93	100
100	100										
		—	100	92	100	100	100	100	100	100	

trations as ppm chromium.

TABLE 2

Cumulative Percentage of Dermatitis in Sensitive Individuals as a Function of *Chromate* Exposure via Occluded Patch Tests and pH of the Testing Solution

Concentration (ppm)	Wahlberg, 1973 (n = 31, pH 7.0)	Zelger, 1964 (n = 33, pH 11.7)	Zelger and Wachter, 1966 (n = 50, pH 11.7)	Wahlberg, 1973 (n = 31, pH 12)
0.5	—	0	0	—
1	—	0	0	—
5	3	0	0	10
10	3	9	8	10
20	6	—	—	23
40	13	—	—	39
50	—	36	32	—
80	16	—	—	52
100	—	67	64	—
200	35	—	—	77
300	65	—	—	94
500	—	100	100	—
700	71	—	—	100
1400	100	—	—	100

Note. Concentrations are as ppm chromium.

Zelger (1964) conducted 24-hr patch testing studies in 33 Cr(VI)-sensitive subjects using four different Cr(VI) compounds: potassium chromate (buffered to pH 11.7), potassium dichromate (pH 1.5), chromic acid (pH 11.7), and lead chromate (pH 11.7). The threshold for elicitation of ACD was 10 ppm Cr(VI) for potassium chromate and chromic acid, 50 ppm for lead chromate, and 100 ppm for potassium dichromate. Also, while 100% of the subjects exposed to potassium chromate and chromic acid responded at or below a concentration of 500 ppm Cr(VI), only 58% of the subjects exposed to potassium dichromate responded at or below this concentration.[7]

In a similar study, Zelger and Wachter (1966) studied the reaction of 50 Cr(VI)-sensitive subjects to potassium chromate (pH 11.7) and potassium dichromate (pH 1.5). For the chromate, the threshold for ACD elicitation was 10 ppm Cr(VI) (8% response), with 32% responding to 50 ppm, 64% responding to 100 ppm, and 100% responding at levels of 500 ppm. For the dichromate, the results also support the earlier study by Zelger. The threshold (4% response) for the dichromate was 100 ppm, with 54% responding to 500 ppm and 100% responding to a concentration of 1000 ppm.

Skog and Wahlberg (1969) conducted a study in 46 subjects with potassium dichromate either in distilled water (resulting in a weakly acidic solution) or in a pH 12-buffered solution. There was a clear distinction in the dose–response relationships, with a higher percentage of responders at the higher pH exposed to the same concentration of Cr(VI). At 10 ppm, 7% in the pH 12 group responded while only 2% in the nonbuffered group responded. By 30 ppm, there were no additional responders in the nonbuffered group, while an additional 14% in the pH 12 group had a positive reaction. In the pH 12 group, 90% of the subjects responded at or below a concentration of 400 ppm Cr(VI). At more than twice this concentration [900 ppm Cr(VI)], only 56% of the subjects in the nonbuffered group had responded.

Wahlberg (1973) conducted a similar study using both potassium dichromate (n = 21) and potassium chromate (n = 31) in nonbuffered and pH 12-buffered solutions. Results again showed that a higher response rate resulted from exposure to the pH 12-buffered solution.

Calnan (1962) studied the response rate of 22–24 subjects exposed to patch tests containing potassium dichromate at pH levels of 7.7 and 10.1 but did not observe any difference in response between these two groups (with 5–10% responding at 4 ppm Cr(VI) and 21–29% by 40 ppm). The results of this study suggest that the effect of pH may not be apparent until levels higher than 10.1.

A number of studies were conducted using varying concentrations of potassium dichromate only (not stated to be buffered). Three of these utilized concentrations ranging from 4 to 1800 ppm Cr(VI) as potassium dichromate. Pirilä (1954) reported 1 response (of 35 subjects) at a concentration of 4 ppm Cr(VI) (the lowest concentration tested) and 4 responses at 40 ppm. It was noted by the author, however, that this study

[7] *Note.* Lead chromate was applied at a maximum concentration of 100 ppm. 39% of the subjects responded at or below this concentration.

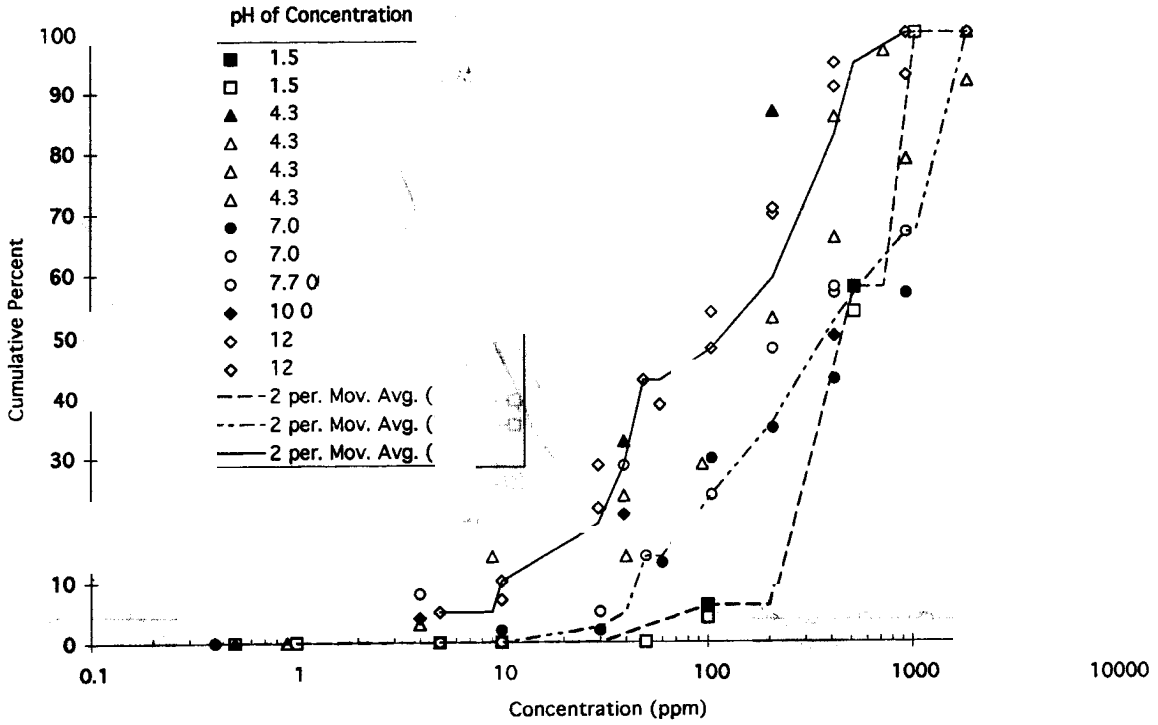

FIG. 1. Percentage of dermatitis as a function of dichromate concentration and pH.

was performed with test material of inferior quality and that quantitative pipettes were not used (Pirilä, 1995). Anderson (1960) reported responses (5 of 15 subjects) at 40 ppm, as did Geiser *et al.* (1960), who reported a positive response in 13 of 53 subjects at 40 ppm. Allenby and Goodwin (1983) conducted a similar study using lower concentrations. Of 7 subjects exposed to 0.9 ppm Cr(VI), 0 responded. Two of 14 subjects (14%) responded to 9 ppm, and an increasing response rate was recorded for even higher concentrations [with 29% responding at 90 ppm, 79% at 900 ppm, and 100% at 1800 ppm Cr(VI)].

Stern *et al.* (1993) did a statistical analysis of these nine separate patch test studies (data from these studies are shown in Tables 1 and 2). Stern *et al.* (1993) plotted data together from patch test studies utilizing different forms of Cr(VI) at different pH levels. They determined the elicitation of ACD in sensitized individuals to be concentration dependent with an effective threshold of ~10 ppm Cr(VI) in solution (10 mg/L). Stern *et al.* (1993) emphasize that in calculating the threshold concentration of Cr(VI) in soil for elicitation of ACD, the extractability of Cr(VI) into solution must be addressed.

The present analysis of these same data led the authors to agree with Stern *et al.* (1983) that the toxicity data on occluded patch tests is concentration dependent. However, the toxicity also appears to be pH dependent. For example, Fig. 1 suggests that the cumulative percentage of dichromate-induced dermatitis increases from 0% at between 1 and 10 ppm to near 100% at concentrations of about 1000 ppm. In general, low pH's serve to increase the concentration needed to achieve a given level of dermatitis. However, a statistical analysis of these data was not conducted, primarily due to the difficult interpretation of the studies from which the data arise.

Figure 2 suggests that the chromate-induced dermatitis is also both concentration and pH dependent. The cumulative percentage of dermatitis increases from 0% at between 1 and 10 ppm to 100% at concentrations of about 1000 ppm. In general, low pH's again serve to increase the concentration needed to achieve a given level of dermatitis, as an analysis of these data using a regression based on moving averages for pH's of 7 and 12 suggests.

Although Tables 1 and 2 and Figs. 1 and 2 suggest that the response to chromium-induced dermatitis is pH dependent, this is even more apparent when one plots the concentrations associated with a 10% dermatitis response rate, estimated from Figs. 1 and 2, as a function of pH. These concentrations are shown in Table 3 and Fig. 3. Figure 3 also shows a power function regression ($y = 99.817x^{-1.0352}$) of the dichromate data. The implications of these findings seem clear: ACD response depends on pH.

Nethercott *et al.* (1994) conducted a study of Cr(III)- and Cr(VI)-induced ACD in 54 volunteers to determine

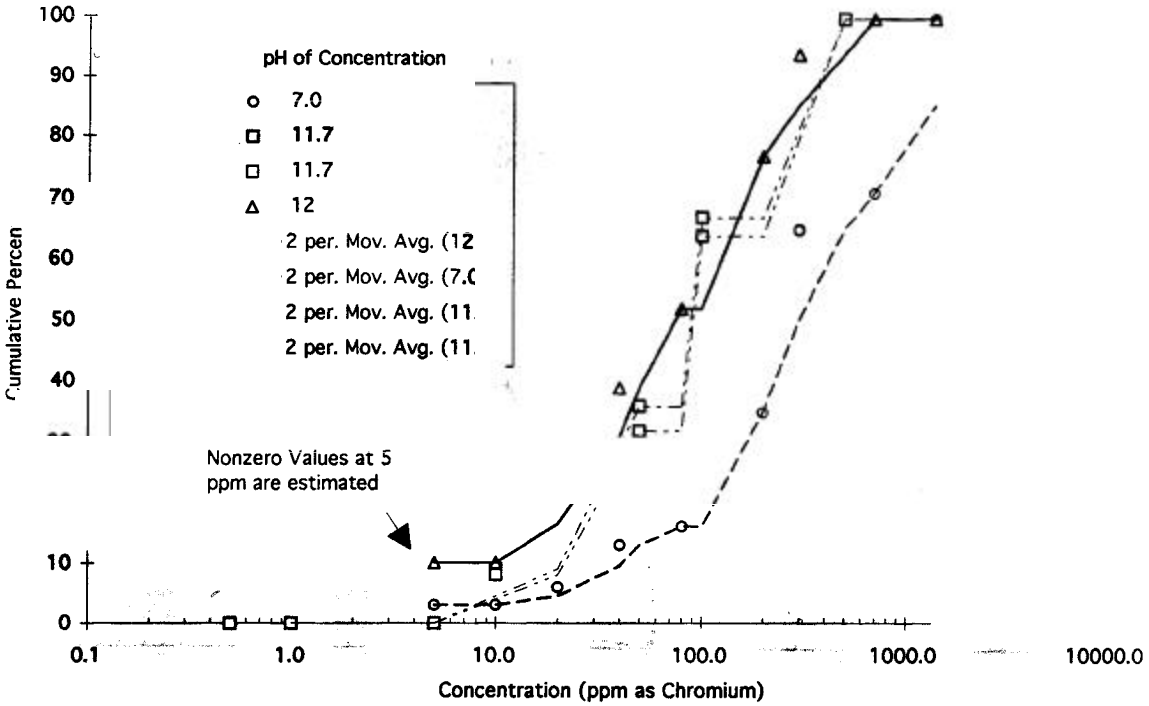

FIG. 2. Percentage of dermatitis as a function of chromate concentration and pH.

the minimum elicitation threshold (MET) for both species of chromium by patch-testing techniques. The authors contend that earlier studies involving patch testing were of limited use for quantitative analysis because the data were reported in terms of concentration of chromium in the patch test as opposed to mg Cr/cm^2 skin. In this study, 54 Cr-sensitized volunteers were patch tested with serial dilutions of Cr(VI) (0.018 to 4.4 μg/cm^2 skin) and Cr(III) (0.66 to 33 μg/cm^2 skin) under occlusion for 48 hr. The minimum elicitation threshold (10% response rate) for Cr(VI) was determined to be 0.089 μg/cm^2 skin. For Cr(III), with the exception of one equivocal response to the highest concentration tested, the results were all negative.

Nethercott *et al.* (1994) also conducted a supplemental study to assess whether the concentration of Cr(VI) in the patch [mg Cr(VI)/kg patch] or the mass of Cr(VI) per surface area of the patch [mg Cr(VI)/cm^2 patch] was the determining factor for whether dermatitis could be elicited. Two different sets of patches were prepared, with the second being $\frac{1}{7}$ as thick as the first. Each patch had the same mass of Cr(VI) per mass of patch (i.e., 175 ppm). The thin patch, then, contained $\frac{1}{7}$ the amount of Cr(VI) per surface area in contact with the skin: 0.13 μg/cm^2 compared with 0.88 μg/cm^2 for the thick patch. These patches were tested in volunteers who had previously shown a positive response to 0.88 μg/cm^2 (using the thick patch). Of nine subjects tested, six had a positive response to the thick patch, and none responded to the thin patch. This indicates that the mass of Cr(VI) per unit area of skin is a more appropriate measure of dose than the concentration of Cr(VI) applied to the patch.

In a second supplemental study, Nethercott *et al.* (1994) exposed volunteers who had previously shown a positive response to 0.88 μg Cr(VI)/cm^2 to the same total amount of Cr(VI) spread over a larger surface

TABLE 3

Estimated Chromium Concentration Associated with a 10% Cumulative Percentage of Dermatitis in Sensitive Individuals as a Function of pH of the Testing Solution

pH	Dichromate (ppm)	Chromate (ppm)
	110	
	120	
	15	
	5	
	50	28
	40	
	5	
	9	
		11
		12
	12	10
	10	

Note. Concentrations are as ppm chromium from Figs. 1 and 2.

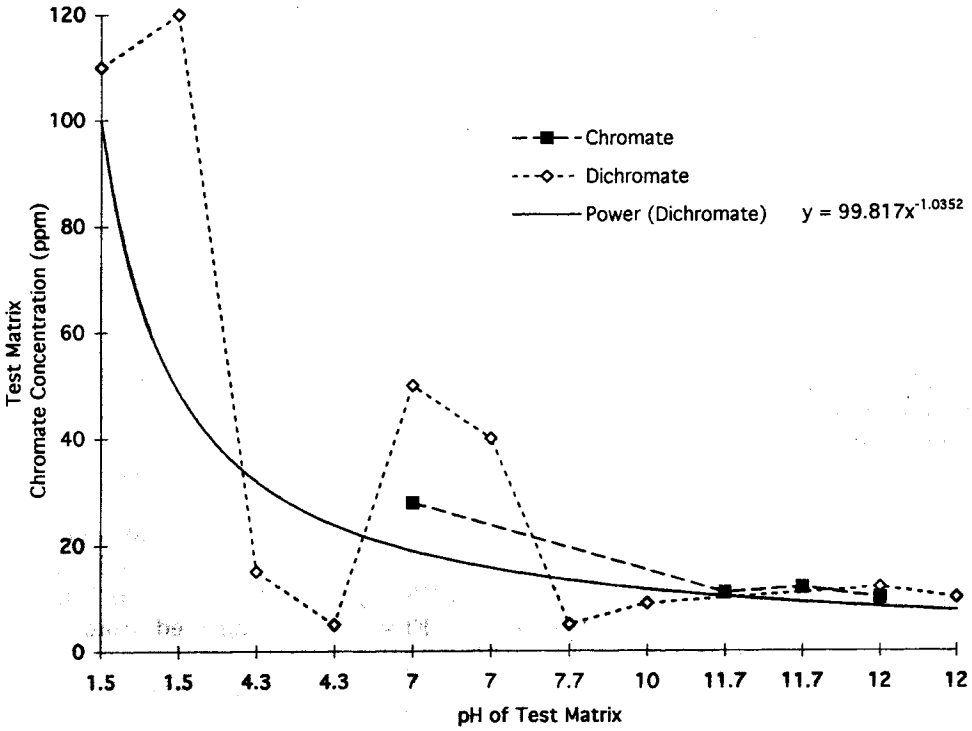

FIG. 3. Chromate and dichromate exposure associated with an estimated 10% dermatitis response.

area: five 0.18, μg Cr(VI)/cm^2 patches placed side by side. None of the four subjects had a positive response, indicating that subthreshold concentrations of Cr(VI) applied over a larger skin surface area do not result in a positive response. In summary, the studies by Nethercott *et al.* (1994) demonstrate that the amount of Cr(VI) delivered to the target organ (the Langerhans cell) in a given area of skin is an appropriate measure of dose to be used in dose–response assessment for allergic contact dermatitis.

In summary, ACD may be induced in sensitive individuals (0.1 to 1% of the general population) following dermal exposure. Many dose–response studies have been conducted with varying results and interpretations. Factors that should be considered in using ACD as an end point for a risk assessment include:

- pH: When chromium is administered at higher pH levels (i.e., >pH 10), Cr(VI)-sensitive individuals have been shown to develop ACD from dermal exposure at lower concentrations of Cr(VI). In developing a dose–response relationship for ACD, then, we suggest that data from studies utilizing different pH levels should not be combined. Furthermore, in determining which dose–response relationship for ACD should be used in a risk assessment, the exposure-specific conditions should be taken into account. For example, if exposures from Cr(VI)-contaminated soils are in a pH range of less than 10, then the dose–response data for ACD elicitation at pH levels greater than 10 should not be used as the basis for a risk assessment.
- Effect of 24- to 48-hr occlusion in patch test studies: The available patch test studies for Cr(VI) were conducted by placing a Cr(VI)-containing patch in direct contact with the skin, and leaving it in place for 24 to 48 hours, under occlusion. The relevance of this sort of exposure to those that might occur under environmental conditions is questionable. Indeed, many dermatologists have recently recommended that such patch tests not be conducted for longer than 24 hr (Brasch *et al.*, 1995). Unfortunately, data are not available for shorter durations or for exposures not under occlusion. It is reasonable to assume that exposures of shorter duration without occlusion would be less likely to pose a risk of ACD than the conditions used in patch testing. These data not being available, however, a risk assessment for the ACD end point can only include these as areas of uncertainty.
- Most appropriate measure of Cr(VI) exposure [ppm vs μg Cr(VI)/cm^2 skin]: As highlighted by Nethercott *et al.* (1994), all of the patch studies conducted previously (see Tables 1 and 2) did not actually measure the amount of Cr(VI) in contact with a given area of skin. Rather, the data were reported as a concentration of Cr(VI). The results of some of these studies are at odds, which may reflect differing amounts of Cr(VI) applied.

The Nethercott *et al.* (1994) study allows an estima-

tion of a likely minimum elicitation threshold for ACD and this threshold has important implications for determining environmental criteria. Allergen loading into the dermis is an operative concept in chromium-induced dermatitis. With unlimited environmental reservoirs (such as lakes), concentrations can perhaps be used as surrogates for allergen loading. However, a reservoir must be sufficiently large in order to maintain its concentration as absorption through the skin occurs. No one would disagree that a 500,000 ppm chromium solution *could not* evoke a dermatitis response if the solution was only 10 molecules (5 chromium and 5 water), because the high concentration quickly drops as chromium enters the skin and equilibrium is reached. It follows that at some point, concentration in the environmental medium is not important, and the dose to the target cell must be estimated by some other means.

The use of μg Cr(VI)/cm^2 skin as a measure of exposure is also consistent with the assessment of exposure described in EPA's *Risk Assessment Guidance for Superfund* (EPA, 1989) and as also briefly described in the next sections.

EXPOSURE ASSESSMENT

Where available, actual exposure data can be used in conjunction with dose–response information to actually characterize the risk to people exposed. The purpose of this text, however, is to lay out a strategy to determine acceptable soil concentrations for Cr(VI) that would not result in toxicologically excessive exposures for the relevant routes: oral, inhalation, and dermal. To determine acceptable soil concentrations, one has to first start with an assumption that a given exposure to Cr(VI) is acceptable. For example, by the oral route it is typical to assume that an intake equivalent to or less than the RfD or a 10^{-4} to a 10^{-6} upper limit, excess lifetime cancer risk, is acceptable. Likewise, by the route of inhalation it is typical to assume that an intake equivalent to or less than the RfC, or an intake of an upper limit between 10^{-4} or 10^{-6}, excess lifetime cancer risk, is acceptable. For dermal exposures, however, little guidance is available in setting acceptable risks, particularly for allergic end points. In the following section on risk characterization, options are presented for how a risk assessor may calculate soil concentrations which are considered to be protective for toxicity following each of the potential routes of exposure.

RISK CHARACTERIZATION

[Or Setting Criteria for Cr(VI) in Soil]

Oral. Following oral exposure, Cr(VI) has not been associated with a carcinogenic risk. Therefore, non-cancer end points are used in determining acceptable soil concentrations for oral exposure. The U.S. EPA has developed methodology for the calculation of acceptable soil concentrations for toxic chemicals in its *Risk Assessment Guidance for Superfund* (RAGS) manual (EPA, 1989). The following equation for the determination of an oral intake level from contaminated soil in residential scenarios is taken from RAGS Exhibit 6–14:

$$\text{Intake (mg/kg day)} = \frac{\text{CS} \times \text{IR} \times \text{CF} \times \text{FI} \times \text{EF} \times \text{ED}}{\text{BW} \times \text{AT}}$$

where

CS = chemical concentration in soil (mg/kg)
IR = ingestion rate (mg soil/day)
CF = conversion factor (10^{-6} kg/mg)
FI = fraction ingested from contaminated source (unitless)
EF = exposure frequency (days/year)
ED = exposure duration (years)
BW = body weight (kg)
AT = averaging time (period over which exposure is averaged—days).

EPA (1989) offers the following default values for use in this calculation:

CS = site-specific measured value
IR = 200 mg/day (children, 1 through 6 years of age)
= 100 mg/day (age groups greater than 6 years of age)
CF = 10^{-6} kg/mg
FI = pathway-specific value
EF = 365 days/year[8]
ED = 70 years (lifetime)
= 30 years [national upper-bound time (90th percentile) at one residence]
= 9 years [national median time (50th percentile) at one residence]
BW = 16 kg (child average)
= 70 kg (adult average)
AT = Pathway-specific period of exposure for noncarcinogenic effects (i.e., ED × 365 days/year) and 70-year lifetime for carcinogenic effects (i.e., 70 years × 365 days/year)

For the determination of a soil concentration that is

[8] It is noted that Superfund risk assessors often use an exposure frequency of 350 days/year (assuming a 2-week period each year when the individual is not residing at this residence). Incorporation of a value of 350 days/year as opposed to 365 days/year does not change the outcome of the calculation.

protective for children, the intake is set equal to the RfD for Cr(VI) (i.e., 5×10^{-3} mg/kg day) and the equation is solved for "CS":

$$5 \times 10^{-3} \text{ mg Cr(VI)/kg day} = \frac{(\text{CS})(200 \text{ mg soil/day})(10^{-6} \text{ kg soil/mg soil}) \times (100\%)(365 \text{ days/year})(6 \text{ years})}{(16 \text{ kg BW})(365 \text{ days/year})(6 \text{ years})}$$

$$5 \times 10^{-3} \text{ mg Cr(VI)/kg BW day} = \frac{(\text{CS})(2 \times 10^{-4} \text{ kg soil/day})}{(16 \text{ kg BW})},$$

$$\text{CS} = \frac{(5 \times 10^{-3} \text{ mg Cr(VI)/kg BW day})(16 \text{ kg BW})}{(2 \times 10^{-4} \text{ kg soil/day})},$$

$$\text{CS} = 400 \text{ mg Cr(IV)/kg soil [400 ppm Cr(VI)]}.$$

This is essentially equivalent to the risk-based concentration of 390 ppm Cr(VI) recommended by U.S. EPA's Region III (EPA, 1996b). EPA Region III uses the same equation and default values except a slightly lower body weight for children (15 kg).

Calculation of acceptable soil concentration for Cr(VI) for adults based on an RfD of 5×10^{-3} mg/kg day is done using the same equation, but assuming an ingestion rate of 100 mg soil/day and a body weight of 70 kg. The resulting soil concentration is 3500 mg Cr(VI)/kg soil.

Inhalation. For inhalation exposures, a similar process is used. As described earlier, however, the carcinogenic risk following inhalation of Cr(VI) dusts is estimated to be greater than the risk of noncancer effects. The inhalation unit risk for cancer was calculated by U.S. EPA to be 1.2×10^{-2} per $\mu g/m^3$ (EPA, 1996a). At a *de minimis* excess risk level of one in a million, the associated concentration of Cr(VI) is calculated as follows,

$$\frac{1.2 \times 10^{-2} \text{ excess risk}}{1 \ \mu g/m^3} = \frac{1 \times 10^{-6} \text{ excess risk}}{x \ \mu g/m^3},$$

and is determined to be 8.3×10^{-5} $\mu g/m^3$ for continuous exposure for a lifetime. In order to calculate an acceptable soil concentration, then, one must have site-specific data or make a number of assumptions regarding the creation of dusts and the duration of exposure. The U.S. EPA determined a level of 270 mg Cr(VI)/kg soil based on cancer risk following inhalation (EPA, 1996c).

In order to reduce the cancer risk to a *de minimis* level (i.e., one in a million), the State of New Jersey recommended that soil levels should not exceed 130 ppm Cr(VI) in residential areas and 190 ppm Cr(VI) for nonresidential areas (NJDEP, 1995a,b). These values were calculated on the basis of both the upper-bound carcinogenic risk (as above) and a number of assumptions regarding exposure scenarios, which would vary with different sites. These soil criteria are slightly lower than that recommended by the U.S. EPA mentioned above of 270 ppm (EPA, 1996c).

Dermal. The determination of a soil concentration of Cr(VI) that is protective for ACD following dermal exposure is also a consideration for a risk assessor. In conjunction with the dose–response information, the risk assessor must evaluate the conditions under which one might be exposed to see how these relate to the experimental conditions used in the studies used to support the dose–response assessment. For the case of Cr(VI), several issues should be considered, three of which have been described previously: site-specific pH conditions, the relevance of 24- to 48-hr occluded exposures to environmental conditions, and the most appropriate measure of Cr(VI) exposure [ppm vs μg Cr(VI)/cm^2 skin]. Several of the existing estimates of Cr(VI) soil criterion described below address some, but not all of these issues.

Bagdon and Hazen (1991) proposed a cleanup level for total Cr[Cr(III) + Cr(VI)] in soil of 75 ppm to "avoid undue risk of contact dermatitis." This recommendation was made based on their analysis of several patch test studies for which they determined a threshold ($\leq$10% response incidence) for ACD of 10 ppm Cr(VI) in solution. Bagdon and Hazen made the assumption that 10 ppm Cr(VI) in solution is equivalent to 10 ppm in soil. Then, using data from soil samples taken from 40 sites in Hudson County, New Jersey, they determined the 95th percentile of the ratio of Cr(VI):total Cr to be 0.14. Using this upper limit on the ratio, a soil concentration of 10 ppm Cr(VI) is equivalent to a total chromium concentration of 75 ppm (10 ppm/0.14).

Paustenbach *et al.* (1992) also evaluated multiple patch test studies in an effort to establish a cleanup level for Cr(VI) in soil. They determined a 10% threshold response for ACD of 54 ppm Cr(VI), although they considered this estimate to be conservative. Citing unpublished data from Wainman *et al.* (1992) and Sheehan and Bono (1990), they used a value (again thought to be conservative) of 10% for the extractability of Cr(VI) from soil. Based on their analysis, Paustenbach *et al.* (1992) recommended a cleanup standard of 350–500 ppm Cr(VI), which they suggest is protective of >99.84% of the general population.

The State of New Jersey recently developed documents for the risks of ACD following dermal exposure to Cr(VI) (NJDEP, 1995c,d). The State recommended that, in general, soil levels should not exceed 15 ppm Cr(VI) (NJDEP, 1995d). This preliminary value was based on an estimated 10% elicitation threshold for ACD and an assumption that 100% of the chromium

VI in soil may be solubilized on human skin. The State acknowledged that consideration of site-specific situations, or the use of different assumptions, might lead to a higher recommendation (NJDEP, 1995f).

The issue of the most appropriate measure of Cr(VI) exposure was brought to the forefront by Nethercott *et al.* (1994) who argue that estimating the dose that will be in contact with a given area of skin (i.e., μg Cr(VI)/cm^2 skin) is more appropriate than using concentrations of Cr(VI) applied in patch-test studies (e.g., Tables 1 and 2). This is because the former can be used to determine dose to the target organ and a minimum elicitation threshold of toxic response. However, the idea of reservoir is an important addition to the discussion of Nethercott *et al.* (1994). In the case of bathing or swimming, for example, the Cr(VI) water concentration might be used directly as the determining factor for eliciting dermatitis. Since the reservoir in these situations is essentially unlimited, the controlling factors in eliciting ACD might be related to the concentration and the length of exposure from which equilibrium with the target tissue could be reached. However, certain environmental exposures of concern, splashes and soil contact, would not generally represent exposures to media of unlimited reservoirs. Therefore, if one can determine the likely threshold dose for evoking the dermatitis in sensitive individuals by way of the Nethercott *et al.* (1994) or similar studies, one can estimate the "safe" soil concentration by dividing this threshold by the upper limit of soil loading. A similar analysis can be done for skin exposures from splashes.

For example, Nethercott *et al.* (1994) calculated a soil concentration that would be equivalent to the 10% minimum elicitation threshold for Cr(VI) using the equation

$$\text{soil concentration} = \frac{\text{MET (mg allergen/cm}^2\text{ skin)} \times \text{CF (}10^6\text{ mg soil/kg soil)}}{\text{SA (mg soil/cm}^2\text{ skin)} \times \text{BVA}}$$

where

MET = minimum elicitation threshold [determined to be 0.000089 mg/cm^2 skin for Cr(VI)]
CF = conversion factor
SA = soil adherence factor of 0.20 mg soil/cm^2 skin (EPA, 1996c; average value)
BVA = bioavailability (assumed to be 100%; authors note the conservative nature of this assumption and state that lower degrees of bioavailability would result in higher acceptable soil concentrations).

Using this equation, Nethercott *et al.* (1994) calculate an acceptable soil concentration of ~450 ppm Cr(VI), which they suggest should not pose an ACD hazard for at least 99.99% of the population [assuming that 0.1% of the population is sensitive to Cr(VI) and the MET protects 90% of those who are sensitive].

Another exposure-related issue exists as well for dermal effects: the extractability of Cr(VI) from soil and the degree to which Cr(VI) in soil can be solubilized upon contact with skin. Horowitz and Finley (1993) conducted a study to evaluate the efficiency by which human sweat can extract Cr(VI) from chromite ore processing residue. The samples of residue were sieved to obtain a uniform particle size of <500 μm, and these samples were mixed with human sweat at 30°C for 12 hr. The sweat was then filtered and analyzed for chromium content. No chromium was detected in sweat incubated with residue containing 16 ppm Cr(VI). At higher concentrations of 136 and 1240 ppm Cr(VI) in residue, <0.1% of the Cr(VI) was extracted into sweat yielding sweat concentrations of 0.133 ppm Cr(VI) or less. The authors suggest that if a minimum of 10 ppm (Bagdon and Hazen, 1991) to 54 ppm (Paustenbach *et al.*, 1992) Cr(VI) in sweat is necessary to elicit an ACD reaction, these would require residue concentrations of at least 10,000–54,000 ppm Cr(VI) (assuming a maximum solubilization into sweat of 0.1%). They conclude, therefore, that ACD is unlikely to occur as a result of dermal exposure to chromite ore processing residue in the environment.

Risk characterization summary. Risk characterization, in essence, serves to bring together all of the information gleaned from the processes of hazard identification, dose–response assessment, and exposure assessment into a cohesive description of plausible risks, including a full discussion of the assumptions made and the uncertainties inherent to the various aspects of the assessment. Risk characterization also takes into account site-specific considerations which may have a bearing on projected risk levels. As discussed previously, this article is focused more on the dose–response and risk characterization components of the risk assessment for Cr(VI). An exposure assessment, other than the default assumptions used herein, can only be done when site-specific data are provided.

By the oral route, toxicity has been observed in laboratory animals chronically exposed to chromium, but not in humans. Therefore, some uncertainty exists for both the hazard identification and the dose–response elements of a risk assessment for ingested Cr(VI) to humans. Using standard EPA methodology (EPA, 1989), soil criteria are estimated as 400 ppm for children and 3500 ppm for adults. These values appear to be conservative, for they are based on animal experiments that have not demonstrated toxicity at the highest dose tested.

As a result of inhaling Cr(VI) dusts, lung cancer has

been shown to occur in humans. EPA has applied its traditional quantitative risk assessment methodology to Cr(VI), the linearized multistage (LMS) model, resulting in a 10^{-6} risk level for inhaled Cr(VI) at 8×10^{-5} $\mu g/m^3$. EPA derived a screening soil level of 270 ppm based on this value (EPA, 1996). NJDEP (1995a,b) estimated an equivalent soil concentration of 130 ppm Cr(VI) for a residential exposure scenario and 190 ppm for a nonresidential exposure scenario, using different exposure assumptions than EPA. All of these estimated soil criteria are similar.

The results of any of these soil criteria are expressed as the 95% upper confidence limit on the slope of the linear portion of the dose–response curve in the low-dose region. While this is a generally accepted method for expressing low-dose risk, the risk assessor should acknowledge that the use of the 95% upper confidence limit likely introduces a fair degree of conservatism into the resulting estimate. Ideally, the results of the cancer risk assessment should be presented in a way that includes the maximum likelihood estimate of the slope as well as the 95% upper confidence limit. Of course, the use of the LMS model as opposed to any other model which fits the data is also a default assumption which likely results in a conservative estimate of the risk. Biologically based models are not available for Cr(VI)-induced cancer, so it is reasonable for a risk assessor to use the LMS model. Nonetheless, it must be made clear to the risk manager, as well as to those involved in risk communication to the public, that the results of applying the LMS model to the tumor incidence data for Cr(VI) do not imply that the 1×10^{-6} risk calculated to be associated with a certain soil concentration is an expression of actual carcinogenic risk, but rather that it is believed to be an upper bound on the possible degree of carcinogenic risk. The true risk from exposure to soil containing Cr(VI) at the level of these soil criteria may, in fact, be as low as 0.

For the end point of ACD following dermal exposure, several areas of uncertainty should be highlighted in any risk characterization. These have been described previously, and include the effect of pH, the effect of occlusion, the usefulness of patch-test studies that reported the exposure as a concentration of Cr(VI) applied to the patch as opposed to the mass of Cr(VI) per unit area of skin, which in many cases is a more toxicologically relevant measurement, and the degree to which Cr(VI) in soil may be solubilized on skin. The recommended Cr(VI) soil levels for the protection of ACD have been calculated by various investigators as ranging from 15 to up to 54,000 ppm.

For example, the State of New Jersey (NJDEP, 1995d), Bagdon and Hazen (1991), Paustenbach *et al.* (1992), Nethercott *et al.* (1994), and Horowitz and Finley (1993) recommend that in general, soil levels need not exceed 15, 75 (total chromium), 350 to 500 [Cr(VI)], 450 [Cr(VI)], and 10,000 to 54,000 [Cr(VI)] ppm, respectively. The wide variation in these numbers is due primarily to assumptions of bioavailability [i.e., degree to which Cr(VI) is extracted from soil and from which it may be solubilized on human skin] and the appropriate measure of exposure in patch-test studies, whether concentration (ppm) or applied dose (mg/cm^2 skin). Clearly, this range is indicative of a significant degree of uncertainty in the risk assessment for ACD.

THE ROLE OF RISK MANAGEMENT IN SETTING CLEANUP STANDARDS FOR HEXAVALENT CHROMIUM

A review of the available toxicity and carcinogenicity data for Cr(VI) indicates end points of potential concern following exposure to hexavalent chromium-contaminated soils through ingestion (blood, liver, and kidney toxicity), inhalation (cancer), or dermal exposure (ACD). The natures of these effects are quite different and the ultimate determination of an acceptable cleanup level raises many questions that pertain to risk management as well as to risk assessment. Table 4 shows how soil criteria based on effects following these three routes of exposure compare.

The Cr(VI) soil criteria that have been developed for the protection against adverse effects are not dissimilar for exposures by the oral route (400 ppm) and inhalation route (130 ppm). For protection against adverse effects following dermal exposure, however, calculations of acceptable soil levels have varied by several orders of magnitude, with the most conservative screening-level assessment proposing soil concentrations of 15 ppm. Given that this proposal is 10- to 30-fold lower than those protecting against more severe effects from Cr(VI) (e.g., lung cancer), it is appropriate to reevaluate the data supporting the screening level assessment for dermal effects and to decrease the uncertainty wherever possible. By substituting data for default assumptions (e.g., measuring actual bioavailability rather than assuming 100%), the assessment of risk posed by dermal exposure has been shown to be much lower than previously estimated. Soil criteria based on these data-supported dermal assessments are still variable (350 to 54,000 ppm), but are all higher than the criterion based on protection against cancer following inhalation exposure.

The Federal EPA currently has no standards or even guidelines for the protection of dermal effects following exposure to Cr(VI). EPA has addressed immunologically based effects with nickel, however, that may offer some guidance for chromium. As with chromium, nickel is a common sensitizing agent which has been shown to elicit ACD following both dermal exposure and ingestion in sensitized individuals. With nickel, EPA decided that the oral RfD, based on decreased body and organ weights as the critical effects, "is believed to be set at

TABLE 4
Potential Criteria for Cr(VI)-Contaminated Soil Based on Prevention of Adverse Effects Following Oral, Inhalation, or Dermal Exposures

End point	Proportion of population at risk	Severity of effect	Soil criteria
Systemic toxicity	100%	Cr(VI) has been shown to cause toxicity to blood, liver, and kidney at high oral doses.	Using standard EPA methodology (EPA, 1989), soil criteria can be estimated as 400 ppm for children and 3500 ppm for adults.
Lung cancer	100%	Cr(VI) is a known human carcinogen, inducing potentially fatal lung cancer.	EPA estimated a soil criterion of 270 ppm (EPA, 1996c). NJDEP (1995a,b) estimated soil criteria of 130 or 190 ppm for residential or nonresidential exposure scenarios, respectively.
Allergic contact dermatitis	0.1–1%	ACD is limited to dermal involvement. Severity ranges from mild to severe.	Published criteria for Cr(VI) in soil based on ACD are varied, including 15, 75 (total chromium), 350 to 500, 450, or 10,000 to 54,000 ppm.

a level which would not cause individuals to become sensitized to nickel; however, those who have already developed a hypersensitivity (e.g., from a dermal exposure) may not be fully protected." The rationale for this comes from the fact that, while EPA is committed to protecting sensitive subpopulations, it is virtually impossible to reduce levels of metals in the environment which may evoke a response in some hypersensitive individuals. With nickel, for example, the amounts found in a standard soil maybe sufficiently high to evoke a response. Individuals having this degree of hypersensitivity cannot be fully protected and must take it upon themselves to reduce exposure.

This example could prove relevant to the difficult question of whether chromium dermatitis should be considered a critical effect and used as a basis for developing a cleanup standard. Another possibility would be to set a standard using sensitization (rather than the elicitation of ACD in already sensitized individuals) as a critical effect. In other words, a standard would be set that is believed to be sufficiently low to prevent sensitization of individuals exposed, but those already sensitized (e.g., from occupational or other exposure) would not necessarily be protected against recurrences of ACD as a result of subsequent exposure. The currently available data do not appear to be sufficient to answer the question of what degree of exposure is necessary to invoke sensitization, but this alternative might be considered if these data become available.

As described previously, the State of New Jersey has developed several documents on health end points for Cr(VI) that might serve as the basis for cleanup standards. The documents, however, end at the point of risk characterization and are not meant to provide the answers for how to most appropriately *manage* the risks posed by Cr(VI) in soil. It is up to the risk manager to take into consideration the information provided by the risk assessor, but to also take into consideration many other factors when making a decision regarding actual cleanup standards. Excerpts from EPA's *Guidance for Risk Characterization* (1995a) were highlighted at the outset of this paper. The importance of the material quoted earlier is emphasized again here:

> . . . decision-makers evaluate technical feasibility . . ., economic, social, political, and legal factors as part of the analysis of whether or not to regulate, and, if so, to what extent. . . . For this reason, risk assessors and managers should understand that the regulatory decision is usually not determined solely by the outcome of the risk assessment.

ACD is clearly an adverse effect that occurs in some humans exposed dermally to Cr(VI). Cancer and noncancer toxicity are also of concern and potentially affect more people. Appropriately, risk assessors have attempted to develop dose–response relationships for these end points, with results that are consistent in part. However, given that ACD is an allergic reaction that is relevant to only 0.1 to 1% of the general population, the risk manager must ask if this an appropriate end point for the determination of a cleanup standard, or if the focus should be on cancer or noncancer end points. If the former, then what percentage of sensitive individuals should be protected? 100% (likely an impossibility given the nature of allergic reactions)? 90%? 50%? At what cost? And with what degree of certainty?

Herein lies the job of the risk manager: to weigh "risk assessment priorities, degree of conservatism, and acceptability of particular risk levels . . ." (EPA, 1995a). A job that is difficult, and one in which the best available risk characterizations are needed to support the final decision.

CONCLUSIONS

The identification of hazard from Cr(VI)-contaminated soil is complicated by different critical effects resulting from exposure by each of the three routes: inhalation, oral, and dermal. Dose–response relation-

ships are also different among these routes, although overlap does occur in the estimated soil criteria.

Oral exposure does not appear to be of great concern because of the reducing capacity of the stomach which results, to a large extent, in the formation of Cr(III), an essential nutritional element. The resulting soil level of 400 ppm based on potential toxicity by this route is conservative since it is based on an RfD in the absence of a critical effect and a child's exposure scenario.

By the inhalation route, estimates of soil criteria of 130 to 270 ppm based on upper limits of cancer risk lie very close to one another and to that derived for noncancer toxicity by the oral route. These criteria are also conservative because they are based on low-dose linear extrapolations that yield upper limits to the excess lifetime cancer risk. Actual risks are likely to be smaller, and may, in fact, be zero.

By the dermal route, soil criteria ranging over 3 orders of magnitude (from 15 to 54,000 ppm) have been suggested as being protective for allergic contact dermatitis. Clearly, some discussion and review is needed for these values. We suggest that since the problem of Cr(VI)-contaminated soil is not one of an unlimited reservoir, every attempt should be made to confirm the minimum elicitation threshold of Nethercott *et al.* (1994). The resulting threshold can be used to determine the likely soil criterion by way of U.S. EPA (1989). Alternatively, a soil criterion can be estimated by establishing the dose likely to initiate the allergic response. This would necessitate some additional work, but it would be entirely consistent with existing decisions by EPA on other compounds that evoke ACD and systemic toxicity.

Inherent in each of these criteria is a significant amount of uncertainty. This uncertainty is from the dose response and the exposure assessments individually and from both when these assessments are folded together to estimate criteria.

Severity of effect and proportion of the population at risk must be described in any risk characterization. For example, the noncancer oral toxicity of Cr(VI) is not well described, but is potentially severe and affects 100% of the population. Lung cancer is potentially fatal, and up to 100% of exposed individuals may be at risk at high enough concentrations. ACD is a transient dermal effect of varying severity, which at most will affect 1% of the exposed population.

While it is incumbent upon the risk assessor to describe uncertainties in a risk characterization for Cr(VI), it is the job of the risk manager to weigh the potential benefits of cleanups against the costs incurred and other considerations.

Risk assessment is an iterative process whereby a risk assessor may give a first assessment using the most conservative default assumptions [e.g., assuming 100% dermal bioavailability of Cr(VI) in soil]. These screening assessments are justified because they are relatively simple to perform, and practically guarantee a "safe" level because of the degree of conservatism built in. However, exceeding of these screening levels does not imply that the exposed population is at risk. Rather, it provides justification for a closer examination of the data by the risk assessors in an effort to better characterize potential risk.

This iterative process of risk assessment is well illustrated by the case of Cr(VI) in soil, and in particular, the potential for elicitation of ACD in sensitive individuals. This has been the subject of initial screening assessments that have resulted in recommendations for cleanups to very low levels; this in turn has provided the impetus for researchers to conduct more in-depth analyses and replace default assumptions with data wherever possible. The result is a more data-rich description of risks, which are associated with a lesser degree of uncertainty. All of the risk assessment analyses—based on possible effects from all routes of exposure and ranging from first-level screening analyses to more intensive data-supported analyses—are available for the risk manager to use and integrate with information on technical feasibility, economic, social, political, and other factors.

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