Response to Charge Question on

Development of Health-Based Acute Criteria

Summary Report

of the NJDEP Science Advisory Board

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The following report has been issued
by the Science Advisory Board
to the Commissioner
of the New Jersey Department of Environmental Protection

Response to the Charge Question:

Development of Health-Based Acute Criteria: Can a framework be developed to establish health-based acute criteria that address appropriate acute toxicity endpoints, exposure durations and pathways, and a hierarchy of potential data sources?

A report was initially prepared by the Public Health Standing Committee and sent to the Science Advisory Board for review. The Science Advisory Board forwards this approved report.

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Report of the NJ Department of Environmental Protection Science Advisory Board Standing Committee on Public Health in Response to the Charge Questions on Development of Acute Soil Criteria

Introduction

The NJDEP's soil criteria are based on health effects resulting from chronic (greater than 1 year) exposure through the direct contact (ingestion/dermal) and inhalation pathways. Cancer (incremental lifetime cancer risk of 10^{-6}) and/or non-cancer (Hazard Quotient of >1 – defined relative to the Reference Dose) endpoints are considered, as appropriate for each specific contaminant. These chronic criteria have been developed to identify unacceptable levels of contamination in soils, indicating the need for remediation of contaminated sites. Health-based criteria based on chronic exposure are generally considered to be protective for exposures of shorter durations, such as acute and subchronic exposures. This, however, is not necessarily the case and in some instances, health-based soil concentrations based on acute and chronic exposure may need to be identical to protect (e.g.) against allergic or irritative effects.

However, the NJDEP is in need of soil criteria based on acute exposures for purposes other than those for which chronic criteria are applied. These include prioritization of remediation efforts, and the specification of a ceiling level for *in-situ* capping that will be protective in case of cap failure. With respect to the latter need, the NJDEP Site Remediation Program (SRP) has provided examples to the Public Health SAB panel of sites at which remediation under existing regulations was completed by capping leaving exceedingly high concentrations in place. At one site, soil arsenic concentrations exceeded 4,500 mg/kg. At a second site, arsenic levels in soil were up to 360,909 mg/kg, 4,4'DDD up to 1400 mg/kg, and 4,4'DDT up to 2000 mg/kg. At a third site, the highest concentration of toxaphene detected was 750,000 ppm (250,000 times the chronic exposure non-residential Soil Remediation Standard that would have been applied if excavation had been employed in lieu of capping) (NJDEP, 2008)

If caps are breached either through structural design failure, or through physical damage (e.g., unrelated construction damage), even short-term exposures to such levels could result in daily doses greatly exceeding those envisioned under chronic exposure scenarios. Such exposures could lead to risks of adverse health effects that are qualitatively different from those posed by long-term (chronic) exposures at much lower doses.

The SRP identified a suite of 136 chemicals that are routinely analyzed for at hazardous waste sites. While, as discussed in detail below, acute toxicity information exists for some of these chemicals, these criteria rarely address soil exposure. Furthermore, there are no generally recognized default exposure scenarios for acute (i.e., short-term) soil exposure. Thus, the NJDEP is, to some extent, in uncharted territory in seeking to

develop and apply a clear, consistent and reasonably protective approach for the development of acute soil criteria for contaminants of concern.

Charge Questions Addressed by the Public Health Standing Committee

The issue approved by NJDEP Commissioner Martin and submitted to the SAB stated: "Development of Health-Based Acute Criteria: Can a framework be developed to establish health-based acute criteria that address appropriate acute toxicity endpoints, exposure durations and pathways, and a hierarchy of potential data sources?". Based on the initial charge, the SRP drafted a series of charge questions designed to elicit practical guidance for their adoption and application of acute soil criteria. These were reviewed by the NJDEP Office of Science (OS) for scientific clarity and to ensure that the questions were scientific in nature rather than specifically policy-based. The following are the specific charge questions submitted to the Committee:

1. Are other sources of acute toxicity information available that are appropriate as the basis for acute soil ingestion criteria? For example, USEPA has developed Drinking Water Health Advisories to be used as guidance for exposure of short durations. Are there additional sources of such information? Can a hierarchy of sources be established?

2. If non cancer data are not available for a carcinogenic contaminant, is it appropriate and scientifically defensible to use cancer risk resulting from acute exposure as the basis for an acute health hazard value?

3. Is it appropriate and scientifically defensible to use ATSDR's intermediate MRLs as the basis for acute health hazard values?

4. The following exposure scenario is proposed for acute soil exposure:

$$S_{ac} = \frac{THQ * BW}{10^{-6} kg / mg * \frac{1}{MRL_{ac}} * IR}$$

Parameter	*Definition*	*Units*	*Residential Child*	*Nonresidential Construction Worker*
S_{ac}	Acute Soil Health Hazard	mg/kg	Chemical-specific	Chemical-specific
THQ	Target Hazard Quotient	unitless	1	1
BW	Body weight	kg	15	70
MRL_{ac}	Acute Minimum Risk Level	mg/kg-day	Chemical-specific	Chemical-specific
IR	Soil Ingestion Rate	mg/day	200	330

Are the residential and non residential exposure scenarios and assumptions appropriate and scientifically defensible as the basis for acute soil criteria? Should a dermal exposure component be added? Should short-term intra-individual variability in soil ingestion behavior among normal (i.e., non-pica) children be considered in the development of acute criteria?

5. What is the appropriate time frame over which acute (as opposed to chronic or possibly sub-chronic) criteria should be applied?

6. Are the assumptions and approach for the development of the acute soil criteria for lead appropriate and scientifically defensible? For the acute residential soil standard, SRP proposes to apply the current USEPA IEUBK lead model to calculate the soil lead concentration corresponding to no more than 5% of exposed young children having a blood lead concentration exceeding 20 µg/dL. This resulted in a soil concentration of 6,000 ppm. For the acute non-residential standard, the scenario envisions a pregnant worker and the soil lead concentration is based on no more than 5% of exposed fetuses having blood lead concentration exceeding 20 µg/dL. This resulted in a soil concentration of 21,000 ppm.

7. Is there an appropriate and scientifically defensible health based approach available to develop an acute level for elemental mercury? If not, is the narrative requirement of "None Visible" appropriate and scientifically defensible?

Structure of the Committee's Deliberations

The full committee met initially on 10/18/10, at which time, the three groups of charge questions assigned to the Committee (including Perimeter Air Monitoring, and NJ

Biomonitoring as well as Acute Soil Criteria) were presented to the Committee. At that meeting, Committee Chair, Dr. Mark Robson asked for volunteers from among the Committee members to serve on an Acute Soil Criteria Workgroup. The Workgroup was constituted and consisted of Drs. Maddaloni (Workgroup Chair), Johnson, Kipen, Marcus, Mitala, and Zelikoff. The SAB terms of Drs. Mitala and Johnson expired during the deliberations of the Workgroup and at their requests, their appointments to the Committee were not renewed. The Workgroup and the Committee in general was assisted by Drs. Stern and Post (NJDEP-OS liaisons to the Committee and Linda Cullen, the NJDEP-SRP liaison).

The Workgroup met, either in person or by conference, call on 11/23/10, 1/21/11, 2/24/11 and 6/14/11. The full committee met on 10/18/10, 3/18/11, and 7/28/11.

The Workgroup addressed each of the charge questions and, in most cases, reached consensus and presented their recommendations to the full Committee. In some cases, however, the Workgroup did not resolve certain critical aspects of charge questions and deferred the issues to the full Committee for further discussion.

The Committee's Findings and Recommendations

The findings and recommendations of the full Committee are presented below by charge question. Rather than repeat the full charge question, they are represented by a summary of the charge. In each case, the key points of discussion and consideration are presented, followed by the specific response to the charge questions.

As a general recommendation, the Committee noted that SRP intends that the charge questions address acute non-occupational (children's) exposures only in the context of exposures at or immediately adjacent to the home (i.e., residential exposures). However, the Committee recommends that DEP should consider acute non-residential, non-occupational scenarios (e.g., recreational exposures) where appropriate

Charge Question 1 - What are the appropriate sources of acute toxicity information that can be applied to the development of NJDEP acute soil criteria and how should they be prioritized?

Table 1 lists the 136 chemicals that SRP has identified as commonly occurring on NJ hazardous waste sites. SRP's stated intention is to apply acute soil criteria to exposure occurring over a maximum of 14 days. SRP initially identified two groups of toxicity criteria that are potentially useful for acute soil criteria development. The larger group of these is the ATSDR acute and intermediate MRLs (Minimal Risk Levels), (available at: http://www.atsdr.cdc.gov/mrls/index.asp) the former defined as applicable to 1-14 day exposures and the latter defined as applicable to 15-364 day exposures. The MRLs are parallel in derivation and intent to the USEPA Reference Dose (RfD) with the difference that RfDs address only chronic exposure, while MRLs address acute and intermediate, as well as chronic, exposures. MRLs are derived on the basis of a comprehensive review of

the scientific literature for each chemical and the application of standard risk assessment procedures (LOAEL/NOAEL determination, uncertainty factor adjustments). MRL derivations and justifications are peer-reviewed.

Acute and Intermediate MRLs are available for many, but not all of the 136 chemicals (Table 1). Acute MRLs are available for 41 of the 136 target chemicals. Intermediate MRLs are available for an additional 34 chemicals for which there are no acute MRLs.

The second group of criteria are the USEPA 1-day and 10-day Drinking Water Health Advisory values (http://water.epa.gov/action/advisories/drinking/drinking_index.cfm ; http://water.epa.gov/action/advisories/drinking/upload/dwstandards2011.pdf). Although they are specifically intended for drinking water exposures, they are also applicable to direct contact soil exposures since both are based on the ingestion route. USEPA 1-day and 10-day Drinking Water Health Advisories are available for 58 of the 136 chemicals of interest to SRP, including 17 of those chemicals for which there are no acute or intermediate MRLs.

In the early Workgroup deliberations, two other possible sources of acute toxicity criteria were identified: USEPA PALs (Provisional Advisory Levels (for Hazardous Agents)) (http://www.epa.gov/nhsrc/news/news121208.html) and AEGLs (Acute Exposure Guideline Levels) (http://www.epa.gov/opptintr/aegl/) developed for the USEPA by a committee of the National Academy of Sciences. The Workgroup (with the approval of the full Committee), however, rejected the use of these values for acute soil criteria development for two reasons. First, because they addressed inhalation exposures only, the Workgroup was of the opinion that for short-term exposures, route-to-route extrapolation (i.e., inhalation route to ingestion/dermal route) posed too many uncertainties. And secondly, because both PALs and AEGLs were designed for extremely short-term exposures, such as evacuations, the Workgroup felt temporal extrapolations for the exposure duration of interest for acute soil criteria (up to 14 days) were not appropriate.

In total, 91 of the 136 target chemicals have at least one of an acute or intermediate MRL or 1-day or 10-day Drinking Water Health Advisory value

The Workgroup identified allergic contact dermatitis patch test concentrations as a third possible source of acute soil criteria. Patch testing is used as a tool in the diagnosis and identification of allergic contact dermatitis. Patches are loaded with the potential allergen in liquid form, either in aqueous solution or in petrolatum, and are applied to the skin surface for 24-48 hours. Upon removal, the underlying skin is “read” for evidence of a topical allergic response. The concentration of the chemical applied to the patch is generally standardized in dermatological practice. To avoid irritative responses that might be misinterpreted as allergic responses, patch test concentrations are set at levels that will elicit minimal responses from allergically sensitized individuals but will not result in irritative responses in the general population. Given that the conditions of environmental exposure, occurring through unoccluded contact with soil rather than occluded contact with a liquid, are likely to be shorter in duration and less direct than those experienced in

patch testing, patch test concentrations can provide a concentration that is protective for the general population as well as most allergically sensitized individuals. Additionally, elicitation of allergic contact dermatitis is an inherently acute effect. With the single exception of hexavalent chromium, SRP does not currently use allergic contact dermatitis as the basis for chronic soil criteria. Table 2 presents the patch data obtained for 17 of the 136 target chemicals.

The Committee's recommendation for Charge Question #1

-Acute criteria should protect for up to 14 days. Acute criteria are not intended to be protective for long term exposure. These criteria are only protective if an exposure (e.g., breach) is recognized within the specified 14-day period of time.

-ATSDR acute/intermediate MRLs (Minimal Risk Levels) and USEPA 1-day and 10-day Drinking Water Health Advisory values are appropriate to use as the basis for acute soil criteria. ATSDR intermediate MRLs should be used for acute exposure scenarios only if no acute value is available or if available acute data is deemed outdated or inadequate.

-PALs (Provisional Advisory Levels (for Hazardous Agents)and AEGLs (Acute Exposure Guideline Levels)are not appropriate to use as basis for acute soil criteria.

-Allergic contact dermatitis patch test concentrations are a reasonable approach for chemicals for which there is a significant background of sensitization in the population

- The lowest value among ATSDR Acute MRLs, and the toxicity basis for the USEPA 1-day and 10-day Drinking Water Health Advisories should be used for acute soil criteria. However, as some of the Drinking Water Health Advisories were developed as long ago as the 1980's, they should be reviewed for currency.

- Except for nickel and hexavalent chromium, patch test data on levels that cause allergic contact dermatitis (ACD) should be used only if data from the sources listed above are not available. For nickel and hexavalent chromium, there is a much larger background prevalence of sensitization in the population (several percent) and the patch test concentrations have been well developed over a long period of time.

-There should be provision for flexibility as appropriate in using the hierarchy.

Charge Question 2 - If a non-cancer toxicity factor is not available for a carcinogenic contaminant, is it appropriate and scientifically defensible to use cancer risk resulting from acute exposure as the basis for an acute health hazard value?

For some chemicals that are recognized as carcinogens, cancer potency slope factors have been developed that can be used to make lifetime risk estimates (e.g., 1×10^{-6}) from specified exposures. Cancer potency estimates are based on chronic studies in animals or, less frequently, humans. While there is some evidence that short-term exposure to carcinogens may carry long-term risk, this relationship has not been well defined (except for ionizing radiation). Thus, for cancer potency estimates to be applied to acute exposures, it would be necessary to extrapolate to a small fraction of the chronic exposure. While this can be accomplished in a mathematical sense, there is little or no toxicological basis for such a procedure. For some chemicals, for which there are no acute exposure criteria, cancer potency estimates are available. Recognizing the lack of a toxicological basis for such an extrapolation, the Workgroup recommended and the full Committee approved the recommendation that cancer potency estimates not be used in the derivation of acute soil criteria.

The Committee's recommendation for Charge Question #2

- Cancer potency estimates should not be used for the purposes of deriving acute soil criteria even if no acute toxicity data are available.

Charge Question #3 - Is it appropriate and scientifically defensible to use ATSDR's intermediate MRLs as the basis for acute health hazard values?

As noted with respect to Charge Question #1, the Committee endorsed the use of the ATSDR Intermediate MRLs in cases where no Acute MRL or 1-day or 10-day EPA Drinking Water Health Advisory is available. However, this charge question also deals with whether it is appropriate and acceptable to adjust an Intermediate MRL to estimate the corresponding Acute MRL for the same chemical. Haber's Law, a general principle of toxicology, states that longer-term exposures require a lower dose than shorter-term exposures to achieve the same toxicological endpoint. Thus, we might expect that an Acute MRL could be estimated from an Intermediate MRL by multiplying the Intermediate MRL by some whole number factor, or "scaling up" of the Intermediate MRL value. In non-cancer risk assessment, an uncertainty adjustment, generally division by 10, is applied to a subchronic NOAEL to estimate the corresponding chronic NOAEL. Conceptually, estimating an Acute MRL from an Intermediate MRL value would follow this procedure in reverse – multiplying an Intermediate MRL by 10. The Committee notes that there is some precedent for "scaling up" in EPA's use of a Hazard Quotient of 10 (rather than 1) for some emergency cleanups.

However, more so than in the case of "scaling down" from a subchronic to a chronic dose, acute and sub-chronic/chronic toxicity may differ qualitatively as well as quantitatively i.e., they may operate through different toxicological mechanisms. Such differences in mechanisms would not necessarily be addressed by scaling. That is, if a different toxicological mechanism comes into play at doses above those producing the

critical intermediate-term effect, there is no *a priori* reason to assume that the high dose effect would differ from the lower-dose effect by a factor of 10 or less. Thus, while dividing a subchronic NOAEL by 10 to estimate the corresponding chronic NOAEL is considered to be health protective and likely conservative, "scaling up" an Intermediate MRL by a standard factor of 10 to estimate the corresponding Acute MRL would not necessarily be conservative and public health protective. Conversely, the Committee also notes that while using a sub-chronic/intermediate value without scaling up would be protective, it could be overly protective (i.e., restrictive).

The Committee's recommendation for Charge Question #3

- As per the Committee's response to Charge Question #1, it is appropriate to use an ATSDR Intermediate MRL if no Acute MRL or 1-day or 10-day Drinking Water Health Advisory value is available. However, in such cases, scaling up of the intermediate duration values is not appropriate.

Charge Question #4 - Should a dermal exposure component be added? Should short-term intra-individual variability in soil ingestion behavior among non-pica children be considered in the development of acute criteria?

The Committee focused on the aspects of exposure relating to the two specific questions posed here – the dermal component of soil exposure and the soil ingestion rate. These are each addressed separately below. The Committee implicitly endorses the other aspects of the acute exposure scenarios given in the equation and table accompanying the full presentation of Charge Question #4 at the beginning of this report.

Dermal Exposure Component

This issue specifically refers to dermal absorption of a chemical from soil and contributing, along with the ingestion dose, to the total internal dose. It does not, however, refer to dermal toxicity resulting from direct contact of chemicals with the skin.

EPA in Part E of its Risk Assessment Guidance for Superfund (http://www.epa.gov/oswer/riskassessment/ragse/pdf/chapter3.pdf) presents values for a chemical specific parameter, the "soil absorption fraction" for 10 specific chemicals/chemical families, as well as a generic value for semi-volatile organic chemicals. This value is a semi-quantitative estimate of the relative trans-dermal absorption potential of a given chemical. It implicitly takes into account a range of likely soil types, loading rates, chemical concentrations, etc. In that document, the USEPA concludes that the dermal absorption contribution to the total internal dose by direct contact (ingestion plus dermal) can exceed the direct ingestion contribution when the soil absorption fraction exceeds a value of approximately 0.1 (10%). For the chemicals for which the USEPA presents dermal absorption fraction values, the following have values ≥0.1: benzo(a)pyrene and other PAHs; Aroclors 1254/1242 and other PCBs;

pentachlorophenol: and semi-volatile organic compounds (as a class). Given that when the soil absorption fraction is ≥0.1, the dermal contribution to the total direct contact dose is approximately equal to the ingestion contribution, it follows that when the soil absorption fraction is ≥0.01, the dermal contribution to the total direct contact dose will be about 10% of the ingestion contribution. With one exception (cadmium), for each of the 136 target chemicals for which there is an applicable soil absorption fraction, the soil absorption fraction is ≥0.03. In other words, in each of these cases the dermal contribution to the total direct contact dose is estimated to be ≥10% of the ingestion contribution. SRP currently adds the trans-dermal component of exposure to the ingestion dose for the purposes of comparing estimated exposure to toxicity criteria under the chronic exposure scenario.

The Workgroup noted that the although there is some uncertainty in the exposure scenarios underlying the derivation of the soil absorption fraction based on its default assumptions, trans-dermal route of absorption is a legitimate and potentially significant contributor to total direct contact exposure. This conclusion was endorsed by the full Committee. However, for purposes of practical application, the Committee recommended that the dermal component be considered only when it contributes approximately 10% of the dose accounted for by the ingestion route.

The Committee also considered whether to apply the dermal component when an intermediate (in lieu of an acute) MRL is used as the toxicity criterion. There was some discussion that the inherent conservatism of using an intermediate MRL for an acute exposure scenario generally, resulting in a lower toxicity criterion than would otherwise be available, could be offset by not including the dermal component. However, the full Committee rejected this approach on the grounds that it was neither logically, nor quantitatively appropriate to address an uncertainty in one parameter by eliminating another, unrelated parameter.

Short-Term Intra-Individual Variability in Soil Ingestion Behavior

The NJDEP chronic residential soil criteria assume that 200 mg/day represents a reasonable maximum exposure (RME) estimate for the mass of soil ingested by a toddler each day. This value applies to children who do not engage in pica behavior (i.e., the intentional ingestion of large quantities of dirt and other non-food items). Given the chronic nature of the exposure scenario it is appropriate that this rate of soil ingestion represents a long-term average for daily intake. However, a long-term average daily value can be composed of widely divergent values for individual daily intake, providing that excursions above and below the mean cancel out. Thus, both logically and experientially, on a given day, a toddler's soil ingestion can be considerably greater than her overall mean ingestion. This may not have significant implications for chronic exposure as the chronic toxicity criteria integrate exposure over period longer than one year. However, excursions above the mean daily soil ingestion rate can have significant toxicological implications for acute exposure given the already elevated levels of contaminants permitted under acute exposure conditions compared to chronic criteria.

In the current version (1997) of the USEPA Exposure Factors Handbook (EFH) (http://www.epa.gov/ncea/efh/pdfs/efh-chapter04.pdf), findings are presented from 7 studies designed to estimate soil ingestion by young children. These findings were derived from studies of children 1-3, 2-4, 2-7, 1-4, and 1-5 years old who were classified as not exhibiting pica behavior. These studies were relatively short in duration, with samples generally collected over 1-7 days. Thus, estimates from these studies reflect both intra- and inter-individual variability in soil ingestion. Furthermore, these studies yield a relatively large range of soil ingestion estimates depending on which soil mineral is used as the basis of the estimate.

From seven studies, the estimates from the EFH of the mean soil ingestion rate range from 65-483 mg/day. The average of these studies is 146 mg/day for soil alone and 191 mg/day for soil plus dust. The "upper percentile" estimates range from 106 -1,432 mg/day with an average among the studies of 383 mg/day for soil alone and 587 mg/day for soil plus dust. The recommended central tendency estimate is 100 mg/day with a conservative (RME) value of 200 mg/day. The current SRP soil ingestion rate of 200 mg/day applied in the chronic exposure scenario is derived from this estimate. From these findings, the USEPA also recommends an "upper percentile" estimate of 400 mg/day for use in acute exposure assessments. The difference between the upper percentile estimate on the one hand and the mean and RME estimates on the other hand is intended to reflect the daily intra-individual variability in the soil ingestion rate.

Based on the Workgroup's recommendation, the Committee discussed the application of a rate of soil ingestion for the acute exposure scenario that is larger than the 200 mg/day used as the basis for chronic soil criteria. The Committee agreed that it was appropriate to address short-term intra-individual variability in soil ingestion in children in deriving acute soil criteria and recommended the USEPA "upper percentile" value of 400 mg/day. SRP expressed concern with the practical implications of applying this rate as, in some cases, the value of the acute soil criterion would fall below the chronic standard. The Committee acknowledges that this could present practical problems with implementing acute soil criteria based on this approach. However, the Committee was firmly of the opinion that short-term intra-individual variability in soil ingestion leading to excursions above the chronic exposure soil ingestion rate is real, relatively common, and potentially of toxicological significance at levels of likely acute soil criteria. Thus, if application of the higher rate of soil ingestion for acute exposure results in soil concentrations for some chemicals that are below their corresponding chronic soil criteria, this likely reflects the inadequacy of the chronic exposure scenario to be protective of ingestion of greater amounts of soil over a short time period, rather than an inappropriate approach to acute soil criteria.

<u>The Committee's recommendation for Charge Question #4</u>

- The trans-dermal exposure dose should be added to the ingestion dose when the appropriate trans-dermal data are available and when the trans-dermal contribution is at least 10% of the ingestion dose.

- The application of the trans-dermal contribution should occur when either an acute or intermediate MRL is used.

- Residential acute soil criteria should be on an assumed child soil ingestion rate of 400 mg/day as opposed to the rate of 200 mg/day that SRP (The NJDEP Siter Remediation Program) applies to the chronic soil criteria.

<u>Charge Question #5</u> What is the appropriate time frame over which acute (as opposed to chronic or possibly sub-chronic) criteria should be applied?

SRP describes the default acute exposure scenario as an exposure resulting from the failure or disturbance of a cap that was designed to prevent exposure to high concentrations of contaminants. As a result of such a breach in the cap, the contaminated soil is exposed on the surface and residents and/or workers can be exposed to those contaminants. Under this scenario, exposure can occur until the breach is discovered and access is restricted. Other, less distinct, scenarios can also be envisioned. These include the unintentional exposure to previously buried contaminated soils during construction, landscaping, etc. In such cases, the contaminated soil may be detected at the time that it is exposed and the appropriate response would be to immediately restrict access to the area. However, it is also possible that the contamination would not be identified until some time after it is exposed. In addition to scenarios under which contaminated soil is exposed through an event such as cap breach or construction, SRP has also stated that it envisions that acute soil criteria will be used to prioritize the remediation of sites where acutely toxic levels of contamination exist. The establishment of acute levels may also limit the maximum concentration that is allowed to be left at a site with capping. If remediation to these levels cannot be achieved, then justification will be required prior to approval granted by the Department.

Given these anticipated uses of acute soil criteria, and the nature of the toxicological criteria that are available to apply to the derivation of acute soil criteria, the Committee recommends that acute soil criteria should be used with the understanding that they are designed to be protective for a maximum of 14 days. Beyond this period of potential exposure, they should not be viewed as protective. This requires that surveillance be in place and capable of recognizing events that can lead to the onset of exposure.

<u>The Committee's recommendation for Charge Question #5</u>

- Acute criteria should protect for up to 14 days. Acute criteria are not intended to be protective for long term exposure. These criteria are only protective if an exposure (e.g., breach) is recognized within the specified period of time.

<u>Charge Question #6</u> Are the assumptions and approach for the development of the acute soil criteria for lead (Pb) appropriate and scientifically defensible?

Residential Exposure Scenario

SRP initially proposed that acute soil criteria for Pb for both the residential and non-residential exposure scenarios be based on a target blood Pb concentration of 20 µg/dL (i.e., not more than 5% of the exposed target population having a total blood Pb concentration exceeding 20 µg/dL). The target receptor for the residential soil criterion was a young child (6 months-7 years old). The target receptor for the non-residential soil criterion is a fetus whose mother is occupationally exposed outdoors on a site. SRP proposed to calculate the corresponding soil concentration using the USEPA IEUBK (Integrated Exposure Uptake Biokinetic) model (http://www.epa.gov/superfund/lead/products.htm). The combination of this target concentration and the IEUBK model along with an assumed soil ingestion rate of 200 mg/day for the residential scenario resulted in proposed soil concentrations of 6,000 ppm The current residential SRP chronic soil standard for Pb is based on the same target populations as originally proposed for the acute soil criterion and a blood Pb concentration of 10 µg/dL. The chronic soil standard is 400 ppm and 800 ppm for the residential and non-residential scenarios, respectively.

The 20 µg/dL target blood Pb concentration proposed by SRP was based on an interpretation by the NJDHSS of 2002 CDC guidance for managing elevated blood Pb in young children ("Managing Elevated Blood Lead Levels Among Young Children: Recommendations from the Advisory Committee on Childhood Lead Poisoning Prevention" http://www.cdc.gov/nceh/lead/CaseManagement/caseManage_chap1.htm). As part of that guidance, the CDC advises that for blood Pb levels in the range of 20-44 µg/dL a home visit should be initiated by a public health agency within 24 hours of the referral from a physician. This is in contrast to the response recommended with the report of blood Pb in the range of 15-19 µg/dL where a home visit is initiated only with persistent elevation as defined by two consecutive blood Pb measurements taken more than 3 months apart. NJDHSS interpreted this guidance to mean that 20 µg/dL as a short-term elevation in blood Pb concentration is an approximate threshold for acute adverse effects.

The question of the appropriate acute soil criteria for Pb engendered considerable discussion by the Committee. In that discussion, the Committee addressed three separate aspects of the derivation of acute residential soil criteria for Pb that, together, result in an approach and a standard different from that initially proposed by SRP: the soil ingestion rate; the appropriate model for relating soil Pb concentration to blood Pb concentration; and the appropriate blood Pb target concentration. These are addressed here separately

Soil ingestion rate

Although there was some discussion among the committee members that the previously recommended soil ingestion rate of 400 mg/day may not be adequately inclusive when considering Pb, the Committee ultimately concluded that soil ingestion rate under the acute exposure scenario should be independent of the nature of the soil contamination. Having previously recommended that, in contrast to the chronic soil ingestion rate of 200

mg/day, a soil ingestion rate of 400 mg/day for the residential scenario is appropriate for acute exposure, the Committee recommends that a soil ingestion rate of 400 mg/day also be applied to the derivation of the acute soil standard for Pb.

Modeling of the relationship between soil Pb and blood Pb

SRP initially proposed that this relationship be modeled using the IEUBK model as had previously been done in the derivation of the chronic soil standard for Pb. The Committee notes, however, that the IEUBK model is a steady-state kinetic model. That is, it assumes that Pb exposure is constant and that levels in the various body compartments are determined by the resulting equilibrium between intake and elimination. This is an appropriate model for a chronic exposure scenario where it is reasonable to assume that the conditions of exposure will remain constant over an indefinite period of time. For acute exposure, however, the conditions of exposure are, by definition, not constant. Rather, exposure increases dramatically with the onset of the availability of the contaminated soil through cap breach, etc., and continues for a maximum of 14 days (as defined by the acute exposure scenario). Under this exposure scenario, steady-state conditions are not achieved. Therefore, the IEUBK model is not appropriate for use under the acute exposure scenario.

The Committee identified the All-Ages Lead Model (AALM) approach currently under development by the USEPA as a more appropriate basis for estimating the relationship between soil Pb and blood Pb under the acute exposure scenario. This model is also referred to as the Leggett model (Pounds and Leggett, 1998). This model is a dynamic physiologically-based pharmacokinetic (PBPK) model that calculates Pb concentration in various tissues from a variety of media as a one-day step function. It is, therefore, able to predict the blood Pb concentration resulting from short-term exposures. Although the USEPA has not finalized several exposure related aspects of the overall model package, the PBPK portion of the model is well established (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=139314). Consistent with SRP's intended time frame of a maximum of 14 days over which acute soil criteria are to be applied, the Committee requested that the USEPA provide predictions from the AALM for the acute scenario, specifically; a 14-day exposure duration, 400 mg soil ingestion /day by a 2-year old child and a background blood Pb concentration = 1.5 µg/dL. Although the model can accommodate Pb exposures from multiple environmental media and routes of exposure, the model calculations in this case were restricted to ingestion of soil. For these conditions, the model predicts a linear relationship between soil Pb concentration and blood Pb concentration.

The default absolute bioavailability assumption for ingestion by children of Pb in soil in the AALM model is 0.3 (i.e., 30% bioavailability). There was some discussion within the Committee as to the basis for this assumption. The USEPA recommends a default absolute bioavailability of 50% (0.5) for uptake of soluble Pb in children (USEPA 2007). In addition, the USEPA, based on research in young swine (USEPA, 2007) and on limited data from dosing of adults with Pb-containing soil (Maddaloni et al., 1998) suggests an overall estimate of 60% for the relative bioavailability of Pb in soil (USEPA, 2003). That is, it is assumed that Pb in soil is 60% as bioavailable to children as soluble

Pb. Thus, the absolute bioavailability of Pb in soil is assumed to be 0.6 x 0.5 = 0.3 (30%). This is the basis for the default value of 30% absolute bioavailability of Pb in soil for children in the AALM model.

The AALM can be run to predict the Pb intake (and associated soil Pb concentration) corresponding to either a given mean Pb concentration (i.e., area-under the curve, or the harmonic mean) or a given peak blood Pb concentration. For the same duration of exposure and the same target blood concentration, the mean blood Pb concentration is achieved with a higher soil concentration than the peak blood Pb concentration. This is because with relatively short-term exposures, the rate of accumulation of Pb in blood is greater than the rate of elimination and the blood Pb concentration therefore increases during the course of exposure. Thus, at the time that the peak blood concentration is achieved, the mean concentration reflects the lower concentrations at each time point leading up to the peak concentration. The Committee endorses using the area-under the curve approach. The Committee is of the opinion that the peak value is an unstable prediction because it is intended to predict a concentration at a single point in time. In contrast, the area-under the curve, is more stable given that it expresses an integration over time. Further, the Committee believes that the approach of modeling to a peak target Pb blood concentration is unnecessarily conservative (i.e., resulting in a lower acceptable soil Pb concentration) given the already conservative application of short-term target Pb blood concentration of 10 µg/dL.

Figure 1 shows the predicted blood Pb concentrations for a 2-year old over a range of Pb daily intakes for an exposure of 14 days assuming 30% absolute bioavailability.

Target Pb concentration

There was considerable discussion among the committee members on this topic. Most of the Committee felt that the 20 µg/dL target recommended by the NJDHSS and initially proposed by SRP had little or no basis in risk or health outcome. At the same time, the Committee also acknowledged that there is little clinical or toxicological basis on which to identify a short-term blood Pb concentration that reflects short-term adverse health effects. The Committee believes that this is largely a function of the lack of research on the effects of short-term Pb exposure rather a function of a lack of effect. The Committee noted that since the time that the CDC issued its guidance for management of elevated blood Pb levels, evidence has come to light indicating that a blood Pb concentration of 10 µg/dL was not adequate to prevent neurodevelopmental deficits with fetal and possibly with post-natal exposure. The Committee also noted that Pb clearance is 50-60 µg/day. Since the blood volume of a 2-year old is approximately 1 L (Nathan and Orkin, 1998), with a blood Pb concentration of 20 µg/dL (200 µg/L), a 2-year old would have a blood mass of Pb of 200 µg. Assuming that Pb exposure ceased entirely at the time that the peak concentration was reached, the child's blood Pb concentration would remain above 10 µg/dL for about two additional days. However, if Pb that had been deposited in bone and other tissues is taken into account, the child's blood Pb concentration would remain above 10 µg/dL for at least several days. Further, the Committee noted that although the acute exposure scenario envisions a maximum of 14 days of exposure, there is no clear limit as to the true duration of the acute exposure in any given case. Although not

unanimous, there was strong consensus within the Committee that a target blood Pb concentration of 20 µg/dL was not protective for acute exposures, and the majority of the Committee recommends a target blood Pb concentration of 10 µg/dL.

Soil Pb Concentration for Acute Exposure Under the Residential Scenario

Based on the modeling specifications above (and detailed in the legend to Figure 1), the soil Pb concentration that would result in, but not exceed a blood Pb concentration of 10 µg/dL in a 2-year old child is approximately 400 ppm. The Committee recommends that this value be applied to acute soil exposure guidelines under the residential exposure scenario.

The Committee is aware that this is the same value as the *chronic* residential lead soil standard. The Committee does not intend, however, to suggest that it believes that exposure to Pb in soil for an acute exposure is as hazardous as chronic exposure to the same concentration of Pb in soil. Rather, the Committee emphasizes that this acute value is based on exposure assumptions appropriate to the range of acute exposure possibilities, that differ from exposure assumptions appropriate for chronic exposure. Further, given the lack of knowledge about the effects of acute Pb exposure during early childhood development, conservative assumptions are appropriate. The application of these conservative assumptions coincidentally results in a similar acute exposure soil criterion to that used by SRP for chronic exposure. The Workgroup also noted that background levels of lead in soil in NJ, particularly in urban areas, may be above 400 ppm.

Non-Residential Exposure Scenario

For the non-residential exposure scenario, the target receptor (as defined by SRP) is the fetus of a pregnant woman who is exposed in an outdoor occupational setting. SRP's chronic soil standard for Pb under the non-residential scenario is 800 ppm. This value was calculated using the USEPA All-Ages Lead Model under the assumption of a mean soil intake rate of 200 mg/day and a target fetal blood Pb concentration of 10 µg/dL. For the acute non-residential exposure scenario, SRP proposed an acute soil ingestion rate of 330 mg/day based on the USEPA Exposure Factors Handbook recommended soil ingestion rate for construction work. This is in contrast to the soil ingestion rate in the non-residential exposure scenario that assumes light outdoor work such as landscaping. Although the Committee has reservations about the reasonableness of assuming that a pregnant woman would be engaging in construction work, we accept the possibility that such a scenario could reasonably occur during the first trimester of pregnancy. The Committee feels that the third trimester is likely to be the most sensitive period for Pb exposure, but we do not feel that there is sufficient information on the developmental toxicity of Pb during the various fetal stages to rule out first trimester exposure as relevant. Therefore, the Committee recommends the construction worker soil ingestion scenario (330 mg/day) be applied to acute, non-residential soil exposure.

Consistent with the Committee's recommendation for acute residential (i.e., toddler) exposure to Pb in soil, the Committee recommends that the non-residential acute exposure scenario should address exposure during a 14-day period. The Committee also

recommends that a 10 ug/dL target blood lead level (calculated as the area-under-the curve) should be applied to the entire period of pregnancy, including first trimester.

In contrast to the assumption of 50% absolute bioavailability of soluble Pb in children (see above), the USEPA assumes a 20% (0.2) absolute bioavailabilty for soluble Pb in adults (USEPA, 2003). Given an assumed relative bioavailability of Pb in soil of 60% (as in model for the 2-year old child), the default assumption employed by the USEPA for the absolute bioavailability of Pb in soil for adults in the AALM is 12% (i.e., 0.6 x 0.2). This is in contrast to the default absolute bioavailability of Pb in soil of 30% employed in the AALM modeling assumptions for the 2-year old child used for the residential scenario (see above).

Figure 2 shows the predicted fetal blood Pb concentrations over a range of maternal daily Pb intakes for an exposure of 14 days, assuming 330 mg soil ingested/day, and the relevant AALM model defaults.

Target PB Concentration

Consistent with the Committee's recommendation for acute residential (i.e., toddler) exposure to Pb in soil, the Committee recommends that a target fetal blood concentration of 10 ug/dL should be used as the target for modeling the corresponding Pb soil concentration. The Committee is aware that the AALM models fetal blood Pb concentration relative to the third trimester of gestation while the exposure scenario likely addresses maternal exposure (through construction work) during the first trimester. However, given the lack of data relating fetal blood Pb concentrations at earlier stages of gestation and postnatal outcomes, the Committee believes that the appropriate public health-protective approach is to apply the AALM modeling results to the total period of pregnancy, including first trimester.

Soil Pb Concentration for Acute Exposure Under the Non-Residential Scenario

Based on the modeling specifications above (and detailed in the legend to Figure 2), the soil Pb concentration required to achieve, but not exceed a blood Pb concentration of 10 µg/dL in fetal blood resulting from a 14-day maternal soil exposure through construction work is approximately 4,000 ppm. The Committee recommends that this value be applied to acute soil exposure guidelines under the non-residential exposure scenario.

The Committee's recommendation for Charge Question #6

Residential exposure

- The 400 mg/day soil ingestion rate recommended by the Committee in general for acute criteria for young children should be applied to the acute residential scenario for Pb.

- The target blood Pb concentration for the residential scenario (2 year-old child) should be 10 µg/dL.

- The soil concentration corresponding to 10 µg/dL should be calculated using the AALM (All Ages Lead Model)/Leggett/ model.

- The exposure duration should be 14 days.

- The model should be interpreted to yield a mean (i.e., area-under-the-curve) blood concentration of 10 µg/dL.

- This approach yields a soil Pb concentration of approximately 400 ppm.

Non-residential exposure

- The fetus of a mother engaged in outdoor construction work is a reasonable receptor for acute exposure to soil Pb assuming first semester exposure.

- The 330 mg/day soil ingestion corresponding to construction work should be applied to the non-residential exposure scenario.

- The exposure duration should be 14 days.

- The target fetal concentration should be 10 µg/dL.

- The soil concentration corresponding to 10 µg/dL should be calculated using the AALM/Leggett/ model.

- The model should be interpreted to yield a mean (i.e., area-under-the-curve) blood concentration of 10 µg/dL.

- This approach yields a soil Pb concentration of approximately 4,000 ppm.

Charge Question #7 Is there an appropriate and scientifically defensible health based approach available to develop an acute level for elemental mercury? If not, is the narrative requirement of "None Visible" appropriate and scientifically defensible?

While SRP is concerned with acute soil criteria for the ingestion route of exposure, it appears that all of the available acute soil criteria for elemental mercury are based on inhalation. Elemental Hg is very poorly absorbed through the gastrointestinal tract and thus has little toxicity when ingested. Even if it were appropriate to develop an acute soil criterion for elemental Hg based on inhalation, the acute soil criteria are intended to address only outdoor exposure. Because of its density, elemental Hg vapor does not mix readily in the air column. Thus standard assumptions for modeling the concentration of a gas or vapor in the air column above contaminated soil would not be useful for elemental Hg.

The chronic EPA Reference Concentration (RfC) for elemental Hg in air is 0.3 $\mu g/m^3$ and homes have been evacuated at indoor air levels of 1-10 $\mu g/m^3$. The RfC is based on several epidemiologic studies of neurologic effects in workers, such as tremors, EEG abnormalities, and memory and behavioral changes. These studies are based on average durations of exposures 2-16 years. There does not appear to be a clear toxicological link between these chronic effects and effects from shorter-term exposures to elemental Hg.

The Committee concludes that there is no clearly defined exposure scenario that can be used to quantitatively derive a risk-based acute soil standard for elemental Hg. However, the Committee recognizes that the presence of significant elemental Hg contamination in soil could, under certain circumstances, pose an acute hazard, particularly if exposure were to occur in confined spaces or if a large surface area of contaminated soil were exposed near a residence such as might occur if large piles of contaminated soil were created during excavation/construction.

To address such scenarios, the Committee recommends that two field criteria be applied to acute exposure to elemental Hg: no visible Hg contamination of the soil; and no Hg vapor greater than 10 $\mu g/m^3$ detectable at the soil surface or below.

<u>The Committee's recommendation for Charge Question #7</u>

- At contaminated sites, exposure should be restricted if either of the following conditions occur: visible elemental Hg in the soil or; elemental Hg vapor at a concentration greater than 10 $\mu g/m^3$ at the soil surface or in the soil gas.

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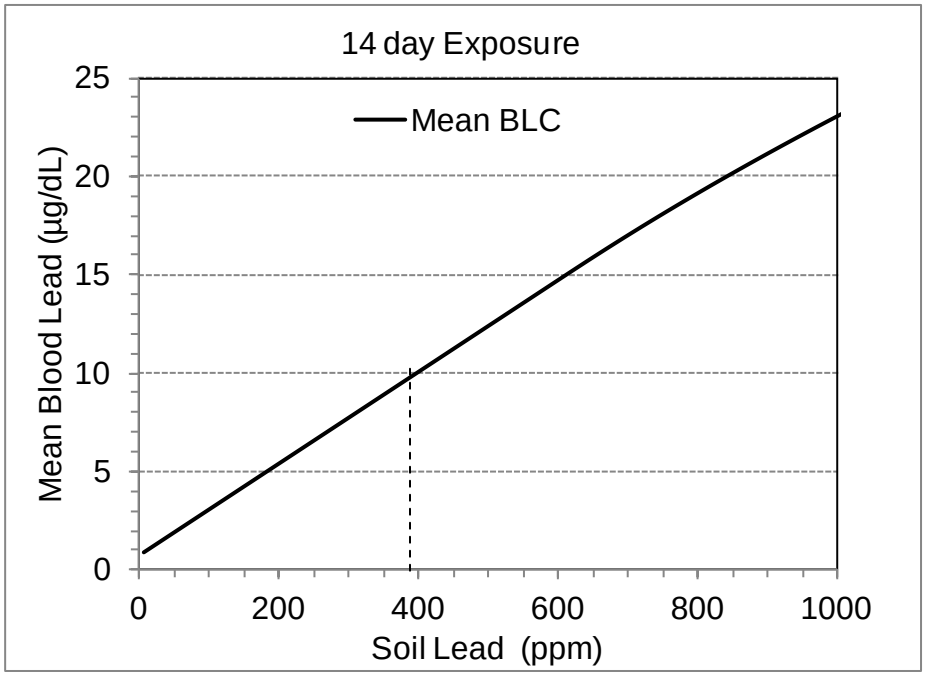
USEPA (2007). Estimation of Relative Bioavailability of Lead in Soil and Soil-Like Materials Using *In Vivo* And *In Vitro* Methods. OSWER 9285.7-77 May 2007 (http://www.epa.gov/superfund/bioavailability/lead_tsd_main.pdf).

Figure 1.

Relationship between blood Pb concentration and soil Pb concentration for a 2-year old child based on the USEPA All-Ages-Lead Model (AALM)



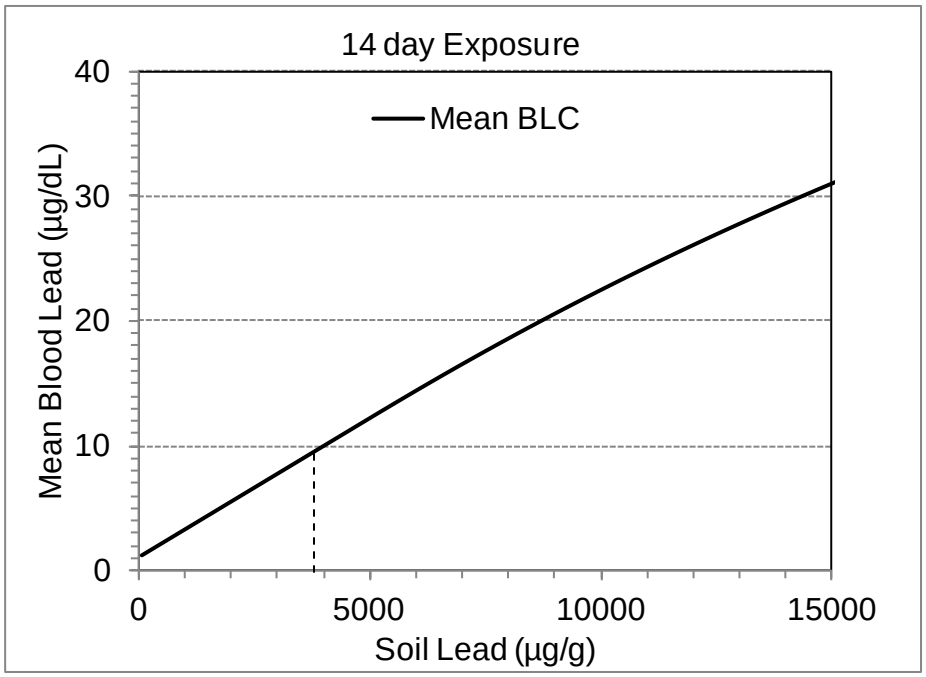
Plot shows predicted relationship between soil Pb concentration (ppm) and blood Pb concentration (µg/dL) for a 14 day exposure beginning at age 730 days.
Mean BLC: mean blood Pb (age 730-744 days)

ICRP model specifications

Air exposure: zero
Ingest baseline: 3.2 µg/day (blood Pb concentration at age 730 days = 1.5 µg/dL)
Short-term exposure: 0-500 (+3.2) µg/day
Short-term exposure duration: 14 days (age 730-744 days)
Absorption fraction: 0.3
Soil Ingestion Rate: 400 mg/day
Soil Pb Concentration = total Ingestion (baseline + short-term exposure)/soil ingestion rate

Figure 2.

Relationship between blood Pb concentration and soil Pb concentration for a fetus- based on the USEPA All-Ages-Lead Model (AALM)



Plot shows predicted relationship between soil lead (µg Pb/g soil) and fetal blood Pb concentration for a 14 day maternal exposure beginning at age 14600 days (40 years)
Soil ingestion rate: 330 mg soil/day
Mean BLC: mean blood Pb (age 14600-14614 days)
Fetal BLC=maternal*0.90

ICRP model specifications

Air exposure: zero
Ingest baseline: 21 µg/day (blood Pb concentration at age 40 years 1.4 µg/dL; NHANES 2005-2006 GM)
Short-term exposure: 0-1000 (+21) µg/day
Short-term exposure duration: 14 days (age 730-760 days)
Absorption fraction: 0.12
Soil Ingestion Rate: 330 mg/day
Soil Pb Concentration = total Ingestion (baseline + short-term exposure)/soil ingestion rate

Table 1. Target Chemicals for Acute Soil Criteria and Available Short-Term Toxicity Information

Chemical	*CAS No.*	*2011 Acute (1-14 days) Oral MRL (mg/kg-day)*	*2011 Intermediate (15-364 days) Oral MRL (mg/kg-day)*	*2011 One-day Drinking Water Health Advisory*	*2011 Ten-day Drinking Water Health Advisory*
Acenaphthene	83-32-9	NA	0.6		
Acenaphthylene	208-96-8	NA	NA		
Acetone (2-Propanone)*	67-64-1	NA	2		
Acetophenone	98-86-2	NA	NA		
Acrolein*	107-02-8	NA	0.004		
Acrylonitrile*	107-13-1	0.1	0.01		
Aldrin	309-00-2	0.002	NA	0.00003	0.00003
Aluminum (total)	7429-90-5	NA	1		
Anthracene	120-12-7	NA	10		
Antimony (total)	7440-36-0	NA	NA	0.001	0.001
Arsenic (total)	7440-38-2	0.005	NA		
Atrazine	1912-24-9	0.01	0.003		
Barium (total)	7440-39-3	NA	0.2		
Benzaldehyde	100-52-7	NA	NA		
Benzene*	71-43-2	NA	NA		0.02
Benzidine	92-87-5	NA	NA		
Benzo(a)anthracene (1,2-Benzanthracene)	56-55-3	NA	NA		
Benzo(a)pyrene	50-32-8	NA	NA		
Benzo(b)fluoranthene (3,4-Benzofluoranthene)	205-99-2	NA	NA		
Benzo(ghi)perylene	191-24-2	NA	NA		
Benzo(k)fluoranthene	207-08-9	NA	NA		
Beryllium	7440-41-7	NA	NA	0.3	0.3
1,1'-Biphenyl	92-52-4	NA	NA		
Bis(2-chloroethyl)ether*	111-44-4	NA	NA		
NAME PROBLEMBis(2-chloroisopropyl)ether (2,2'-oxybis(1-chloropropane)) should be bis(2-chloro-1-methylethyl) ether	108-60-1	NA	NA		0.4
Bis(2-ethylhexyl)phthalate	117-81-7	NA	0.1		
Bromodichloromethane (Dichlorobromomethane)*	75-27-4	0.04	NA		
Bromoform*	75-25-2	0.7	0.2	0.5	0.02
Bromomethane (Methyl bromide)*	74-83-9	NA	0.003		0.01
2-Butanone (Methyl ethyl ketone) (MEK)*	78-93-3	NA	NA	8	8

Butylbenzyl phthalate	85-68-7	NA	NA		
Cadmium	7440-43-9	NA	0.0005	0.004	0.004
Caprolactam	105-60-2	NA	NA		
Carbazole	86-74-8	NA	NA		
Carbon disulfide*	75-15-0	0.01	NA		
Carbon tetrachloride*	56-23-5	0.02	0.007	0.04	0.02
Chlordane (alpha and gamma forms summed)	57-74-9	0.001	0.0006	0.006	0.006
Chlorobenzene*	108-90-7	NA	0.4	0.6	0.6
Chloroethane (Ethyl chloride)*	75-00-3	NA	NA		
Chloroform*	67-66-3	0.3	0.1	0.4	0.4
Chloromethane (Methyl chloride)*	74-87-3	NA	NA	0.9	0.04
2-Chlorophenol (o-Chlorophenol)*	95-57-8	NA	NA	0.05	0.05
Chrysene	218-01-9	NA	NA		
Cobalt (total)	7440-48-4	NA	0.01		
Copper (total)	7440-50-8	0.01	0.01		
Cyanide	57-12-5	NA	0.05	0.01	0.01
4,4'-DDD (p,p'-TDE)	72-54-8	NA	NA		
4,4'-DDE (p,p'-DDX)	72-55-9	NA	NA		
4,4'-DDT	50-29-3	0.0005	0.0005		
Dibenz(a,h)anthracene	53-70-3	NA	NA		
Dibromochloromethane (Chlorodibromomethane)*	124-48-1	0.1	NA	0.06	0.06
1,2-Dibromo-3-chloropropane	96-12-8	NA	0.002	0.02	0.005
1,2-Dibromoethane (Ethylene dibromide)*	106-93-4	NA	NA	0.0008	0.0008
1,2-Dichlorobenzene (o-Dichlorobenzene)*	95-50-1	0.7	0.6	1	1
1,3-Dichlorobenzene (m-Dichlorobenzene)*	541-73-1	0.4	0.02		
1,4-Dichlorobenzene (p-Dichlorobenzene)*	106-46-7	NA	0.07	2	2
3,3'-Dichlorobenzidine	91-94-1	NA	NA		
Dichlorodifluoromethane (Freon 12)*	75-71-8	NA	NA	4	4
1,1-Dichloroethane*	75-34-3	NA	NA		
1,2-Dichloroethane*	107-06-2	NA	0.2	0.07	0.07
1,1-Dichloroethene (1,1-Dichloroethylene)*	75-35-4	NA	NA	0.2	0.2
1,2-Dichloroethene (cis) (c-1,2-Dichloroethylene)*	156-59-2	1	0.3	0.4	0.1
1,2-Dichloroethene (trans) (t-1,2-Dichloroethylene)*	156-60-5	NA	0.2	2	0.2
2,4-Dichlorophenol	120-83-2	NA	0.003	0.003	0.003
1,2-Dichloropropane*	78-87-5	0.1	0.07		0.009

1,3-Dichloropropene (total)*	542-75-6	NA	0.04		0.03
Dieldrin	60-57-1	NA	0.0001		
Diethylphthalate	84-66-2	7	6		
2,4-Dimethylphenol	105-67-9	NA	NA		
Di-n-butyl phthalate	84-74-2	0.5	NA		
4,6-Dinitro-2-methylphenol	534-52-1	0.004	0.004		
2,4-Dinitrophenol	51-28-5	0.01	NA		
2,4-Dinitrotoluene	121-14-2	0.05	NA	0.1	0.1
2,6-Dinitrotoluene	606-20-2	NA	0.004		0.4
2,4-Dinitrotoluene/2,6-Dinitrotoluene (mixture)	25321-14-6	NA	NA		
Di-n-octyl phthalate	117-84-0	3	0.4		
1,2-Diphenylhydrazine	122-66-7	NA	NA		
Endosulfan I and Endosulfan II (alpha and beta) (summed)	115-29-7	NA	0.005		
Endosulfan sulfate	1031-07-8	NA	NA		
Endrin	72-20-8	NA	0.002	0.003	0.002
Ethylbenzene*	100-41-4	NA	0.4	3	3
Fluoranthene	206-44-0	NA	0.4		
Fluorene	86-73-7	NA	0.4		
alpha-HCH (alpha-BHC)	319-84-6	NA	NA		
beta-HCH (beta-BHC)	319-85-7	0.05	0.0006		
Heptachlor	76-44-8	0.0006	0.0001	0.001	0.001
Heptachlor epoxide	1024-57-3	NA	NA		
Hexachlorobenzene	118-74-1	0.008	0.0001	0.005	0.005
Hexachloro-1,3-butadiene	87-68-3	NA	0.0002	0.003	0.003
Hexachlorocyclopentadiene	77-47-4	NA	0.1	1	0.4
Hexachloroethane	67-72-1	1	0.01	0.5	0.5
Indeno(1,2,3-cd)pyrene	193-39-5	NA	NA		
Isophorone	78-59-1	NA	3	1.5	1.5
Lead (total)	7439-92-1	NA	NA		
Lindane (gamma-HCH)(gamma-BHC)	58-89-9	0.003	0.00001	0.1	0.1
Manganese (total)	7439-96-5	NA	NA		
Mercury (total)	7439-97-6	NA	NA		
Methoxychlor	72-43-5	NA	0.005	0.6	0.2
Methyl acetate*	79-20-9	NA	NA		
Methylene chloride (Dichloromethane)*	75-09-2	0.2	NA		
2-Methylnaphthalene	91-57-6	NA	NA		
2-Methylphenol (o-cresol)	95-48-7	NA	NA		
4-Methylphenol (p-cresol)	106-44-5	NA	NA		
Methyl tert-butyl ether (MTBE)*	1634-04-4	0.4	0.3		
Naphthalene**	91-20-3	0.6	0.6	0.05	0.05

Nickel (total)	7440-02-0	NA	NA	0.1	0.1
2-Nitroaniline	88-74-4	NA	NA		
Nitrobenzene	98-95-3	NA	NA		
N-Nitrosodimethylamine	62-75-9	NA	NA		
N-Nitrosodi-n-propylamine	621-64-7	0.095	NA		
N-Nitrosodiphenylamine	86-30-6	NA	NA		
Pentachlorophenol	87-86-5	0.005	0.001	0.1	0.03
Phenanthrene	85-01-8	NA	NA		
Phenol	108-95-2	1	NA	0.6	0.6
Polychlorinated biphenyls (PCBs)	1336-36-3	NA	0.03		
Pyrene	129-00-0	NA	NA		
Selenium (total)	7782-49-2	NA	NA		
Silver (total)	7440-22-4	NA	NA		
Styrene*	100-42-5	0.1	NA	2	0.2
Tertiary butyl alcohol (TBA)**	75-65-0	NA	NA		
1,1,2,2-Tetrachloroethane*	79-34-5	NA	0.5	0.3	0.04
Tetrachloroethene (PCE) (Tetrachloroethylene)*	127-18-4	0.05	NA	0.2	0.2
Thallium (total)	7440-28-0	NA	NA		
Toluene*	108-88-3	0.8	0.02	2	
Toxaphene	8001-35-2	0.05	0.002	0.5	0.004
1,2,4-Trichlorobenzene	120-82-1	NA	0.1		0.01
1,1,1-Trichloroethane*	71-55-6	NA	20	1	5
1,1,2-Trichloroethane*	79-00-5	0.3	0.04	0.06	0.04
Trichloroethene (TCE) (Trichloroethylene)*	79-01-6	0.2	NA		
Trichlorofluoromethane (Freon 11)*	75-69-4	NA	NA		
2,4,5-Trichlorophenol	95-95-4	NA	NA		
2,4,6-Trichlorophenol	88-06-2	NA	NA	0.003	0.003
Vandium (total)	7440-62-2	NA	0.01		
Vinyl chloride*	75-01-4	NA	NA	0.3	0.3
Xylenes (total)*	1330-20-7	1	0.4	1	0.8
Zinc (total)	7440-66-6	NA	0.3		

* Volatile Organics

Table 2
Allergic contact dermatitis patch test concentrations

Unless otherwise noted, these are compounds that would be expected to result in an allergic response in sensitive individuals at the patch test concentration, but not an irritative response. Patch tests are generally intended to elicit a response in sensitive individuals at a concentration at or close to the minimum concentration necessary to produce the response. Therefore, the patch test concentrations can be considered as a rough estimate of a lower bound concentration that can produce an acute response in sensitive individuals. All values are taken from Fisher's Contact Dermatitis (6 ed.) [1] unless otherwise specified.

Patch test concentrations designated with a '?' indicate that allergic sensitivities are known, but a patch test concentration was not located.

Compound	**patch test conc.**
acrylonitrile	0.10%
aldrin/dieldrin	1%
antimony	?
arsenic	10%
arsenic pesticides	1%
atrazine	1%
beryllium	1% (as $BeS0_{4)}$
Caprolactam	5%
cobalt	1% (as cobalt chloride)
DDD	1%
DDT	1%
Di-n-octyl phthalate	2% (irritative response only) http://toxnet.nlm.nih.gov/cgi-bin/sis/search/a?dbs+hsdb:@term+@DOCNO+1345
manganese	1% as manganese chlroide) Menezes LM et al. Am J Orthod Dentofacial Orthop. 2004 Jul;126(1):58-64.
mercury	0.05% (as mercuric chloride) (NOTE: 0.05% appears to be standard, but reactions were seen at lower concentrations) Marzulli and Maibach's dermatotoxicology 7 ed.
nickel	5% (as nickel sulfate) http://dermnetnz.org/dermatitis/standard-patch.html
pentachlorophenol	3%
selenium	0.1% (as sodium selenite) Richter G et al. Derm Beruf Umwelt. 1987 Sep-Oct; 35(5):162-4.

[1] Fisher's Contact Dermatitis (6th editition). Rietschel RL and Fowler JF eds. BC Decker Inc., Hamilton, Ontaria, Canada. (2008).