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SUBJECT: Derivation of Interim Guidance Level for 1,2,4-Trimethylbenzene in Soil

Dear Elizabeth:

Per your request, I have been working on deriving an interim guidance level for use in evaluating reported levels of 1,2,4-trimethylbenzene in soil. I understand that this level will be used to evaluate 1,2,4-trimethylbenzene detected in surface soils around a surface impoundment.

An "official" screening action level for 1,2,4-trimethylbenzene cannot be calculated at this time. Data for this substance were not available from the EPA's Integrated Risk Information System (IRIS; EPA 1992b) as of 10/1/92, and it was not on the list of substances under review at that time. The EPA's Health Effects Assessment Summary Tables (HEAST), Annual FY 1992 (EPA 1992a) lists trimethylbenzene data as "inadequate for quantitative risk assessment"; the FY 1993 version of HEAST has not yet been released.

The ER program's Installation Work Plan (LANL 1992) states that "toxicology studies must be scientifically valid and must be conducted in accordance with the good-laboratory-practice standards set forth in 40 CFR 272. Because the verification of these requirements is labor-intensive, screening action levels will be based, when possible, on toxicity values available from ...IRIS or HEAST. ... When IRIS or HEAST do not provide toxicity values for a constituent, other toxicological data may be used."

In order to determine a soil screening action level for a systemic (i.e., non-carcinogenic) substance, a valid chronic oral or inhalation reference dose (RfD) is needed. This RfD is generally obtained from chronic (2 year) animal studies, although sometimes data from subchronic (usually 90 day) studies are used. If no chronic or subchronic data exist, the data are deemed inadequate for quantitative risk assessment. However, methods for using more widely available acute toxicity data to estimate chronic oral RfDs have been suggested (Layton et al. 1987; Venman and Flaga 1985). For substances with both chronic oral RfD data and oral LD₅₀ data (dose lethal to 50 percent of the tested animals) available, the suggested method compares these data and allows derivation a conservative value that can be used to convert oral LD₅₀ data to estimated RfD values. Layton et al. (1987) suggest multiplying oral LD₅₀ values (expressed in mg/kg of body weight) by a factor in the range of 5×10^{-6} to $1 \times 10^{-5} \text{ day}^{-1}$ to convert to estimated oral RfD values. This estimation method is likely to give a value below the "true" RfD 95 percent of the time it is employed (Layton et al. 1987). However, this method has not been acknowledged or approved in EPA risk assessment guidance released to date.

Even acute toxicity data for 1,2,4-trimethylbenzene are scarce. A common source for summaries of toxicity data was consulted (Lewis 1992). No information on carcinogenicity or mutagenicity was provided; since these data are generally given if in existence, 1,2,4-trimethylbenzene will not be considered a carcinogen in this assessment. Lewis (1992) cited an oral LD₅₀ value for rats of



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8,970 mg/kg for mixed isomers of trimethyl benzene. An LD_{LO} value for rats of 1,752 mg/kg by the intraperitoneal route was cited specific to the 1,2,4-trimethylbenzene isomer. (LD_{LO} values are defined as the lowest dose which causes lethality in any test animal).

An oral RfD for 1,2,4-trimethylbenzene in soils was estimated using the LD_{LO} value for intraperitoneal administration. Use of this value probably results in a conservative (i.e., low) estimate of the RfD, because intraperitoneal administration very likely results in higher absorbed dose than ingestion. Therefore, intraperitoneal toxicity would occur at a lower dose. Additionally, levels inducing death in any test animal (LD_{LO} levels) are by definition lower than level inducing 50% mortality (LD_{50} values), so using an LD_{LO} value also results in a lower estimated RfD value. Use of the intraperitoneal LD_{LO} value in estimating the RfD is also preferable because it is specific to the isomer of interest.

As an additional conservative assumption, the low end of the range of multiplying factors suggested by Layton et al. (i.e., 5×10^{-6}) was used to convert the LD_{LO} to an estimated RfD value of 0.0088. Assumptions given in Appendix A to the Proposed Subpart S to RCRA (EPA 1990) were used to derive an interim guidance value based on the estimated RfD. Proposed Subpart S suggests assuming an incidental soil ingestion rate of 200 mg/day by a 16 kg child to calculate soil guidance levels. Using these assumptions results an interim guidance value of 700 mg/kg 1,2,4-trimethylbenzene in soil (see the attached Table).

Volatilization of 1,2,4-trimethylbenzene from soil is not likely to be a significant environmental pathway, because this substance has a low vapor pressure as compared with atmospheric pressure (e.g., vapor pressure of 1,2,4-trimethylbenzene at 25°C is 302 Pa, as compared with an atmospheric pressure of 101,325 Pa). Therefore, inhalation of this substance from the soil medium need not be considered in deriving the interim guidance level.

It must be emphasized that the interim guidance value is based on somewhat speculative, although conservative, extrapolations from acute exposure to chronic exposure situations. Ideally, a soil screening action level would be based on an RfD derived from chronic or subchronic studies in humans or animals. However, based on the available toxicity data, the interim guidance value is probably a conservative estimate of the actual screening action level that would be calculated if RfD data were available (i.e., a screening action level based on actual RfD data is likely to be higher than 700 mg/kg).

Please contact me if you have any questions regarding the derivation of this interim guidance value for 1,2,4-trimethylbenzene.

Sincerely,



Heidi M. Hartmann
Environmental Assessment and
Information Sciences Division

HH:lmg

Attachment

cc: A. Dorries, LANL

J. Ditmars, ANL

J. Butler, ANL

E. Faillace, ANL

im Guidance Level for 1,2,4-Trimethyl Benzene in Soil

CAS #	Acute Toxicity Data (mg/kg)	Chronic Oral RfD (mg/kg-d)	Possible Interim Guidance Level (mg/kg)
1,2,4-Trimethyl- benzene 95-63-6	8970	4.5E-02	3,588
	1752	8.8E-03	701

*Method to calculate interim guidance level from acute toxicity data obtained from

Layton et al., 1987, Regulatory Toxicology & Pharmacology 7, 96-112.

States that oral LD50 data should be multiplied by factor in range of 5×10^{-6} to 1×10^{-5}

to estimate RfD value. Chose low end of range to be more conservative.

Acute Toxicity Data from SAX's Dangerous Properties of Industrial Materials, 8th ed., 1992 (Lewis, RJ ed)

Value of 8970 mg is oral rat LD50 for mixed isomers of trimethylbenzene.

Value of 1752 is intraperitoneal rat LDLO for 1,2,4-TMB isomer.

Use ipr LDLO because it is for the correct isomer, although it requires route-to-route extrapolation.

There is no data regarding carcinogenicity for 1,2,4-trimethylbenzene.

Equation used to calculate Interim Guidance Level for Soil:

For systemic toxicant:

$IGL = ((THI \times eRfD \times BW \times CF)/(I \times A))$, where:

IGL = interim guidance level (mg/kg).

THI = target hazard index; 1

eRfD = estimated chronic reference dose (mg/kg/day);
estimated from acute toxicity data.

: body weight; 16 kg for child

CF = conversion factor; 1,000,000 mg/kg

I = intake assumption; 200 mg/day (child)

A = absorption factor; 1

DATE: 4-21-93 FILE: C:\123R3\DOC\LANL\IGL-TMB.WK3

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