Relative Bioavailability Estimates for Dioxins/Furans in Soils

Issue

The Department of Ecology (Ecology) is proposing to establish cleanup levels for mixtures of dioxins/furans in soils using congener-specific profiles that reflect differences in toxicity and bioavailability. Based on the available information, is Ecology's proposal scientifically defensible?

Background

The Model Toxics Control Act (MTCA) Cleanup Regulation provides methods to establish residential (unrestricted land use) and industrial (restricted land use) soil cleanup levels (WAC 173-340-740 through -745). The gastrointestinal (GI) absorption fraction is one of several factors considered when establishing soil cleanup levels. The MTCA rule establishes a default GI absorption fraction of 1.0 which applies to most chemicals including dioxins and furans. This value is based on the assumption that soil-bound hazardous substances are absorbed to the same extent as hazardous substances administered in the studies used to establish the cancer slope factor and/or reference dose[1].

At the October and December 2006 Science Advisory Board (SAB) meetings, Ecology proposed to revise WAC 173-340-740 and -745 to establish a default GI absorption factor of 0.4 that would be used when establishing soil cleanup levels for dioxin/furan mixtures. The current default GI absorption value of 1.0 would continue to be applied for other hazardous substances.

Ecology proposed to use a GI absorption fraction of 0.4 for dioxin/furan mixtures because:

1. The cancer slope factor for TCDD was calculated using the administered dose levels.
2. Environmental Protection Agency (EPA) estimates that the test animals absorbed 80% of the administered dose.
3. Available studies indicate that soil-bound dioxins and furans are not absorbed to the same degree as dioxin and furans in food or when administered in an oil-based vehicle.

The proposed default value (0.4) was calculated by dividing 30% absolute bioavailability (value used to characterize absorption of soil-bound dioxins and furans) by 80% (value used to characterize absolute bioavailability of dioxin/furan in the toxicological studies used to calculate the cancer slope factor).

[1] See Appendix E for clarification of terminology related to absorption and bioavailability.

The Board has reviewed and provided comments to Ecology on the issue of soil bioavailability of dioxins/furans during the October and December 2006 SAB meetings. Several observations have been made by the Board:

- Available evidence suggests that soil-bound dioxins/furans are less bioavailable than dioxins/furans used to assess the health risks from bioassays, epidemiological studies or studies used to assess the toxicity of dioxins/furans in foods and drinking water.
- Although there is uncertainty in assigning congener-specific bioavailability estimates, the available evidence suggests that the higher chlorinated dioxin/furan congeners (hexa-, hepta-, octa-) are less well absorbed, less bioavailable, than the fewer chlorinated congeners (tetra- and penta-).
- Within a range of uncertainty and variability, available evidence suggests that congener-specific differences in bioavailability should be considered when evaluating the toxicity and assessing the risks for mixtures of dioxins/furans.
- Based on available evidence, the Board agreed with the National Academy of Sciences (NAS) that it is reasonable to assume that test animals absorbed 80% of the administered dose in the toxicological study used to establish the cancer slope factor for dioxins and furans[2].

At the December 2006 meeting, the Board requested that Ecology further evaluate the use of a default GI absorption factor of 0.4 when establishing soil cleanup levels for dioxin/furan mixtures. Specifically, the Board requested:

- Ecology should attempt to discern the basis for EPA's conclusion that a 30% absolute bioavailability (40% relative bioavailability) for soil-bound dioxins/furans was appropriate.
- Ecology review the EPA's Science Advisory Board's review comments on the dioxin reassessment with a focus on soil-bound dioxins/furans bioavailability.
- Further evaluate Van den Berg literature regarding information on the bioavailability of dioxin/furan congeners.

Review Methodology & Findings

In collaboration with the Washington State Department of Health (Health) and the U.S. Environmental Protection Agency, Region 10 (EPA, R-10), Ecology reviewed current and earlier EPA dioxin reassessments, the EPA's Science Advisory Board's comments on the dioxin reassessments, and additional Martin Van den Berg literature relevant to the soil-bound bioavailability for dioxins/furans congeners. Also, Craig McCormack (Ecology), Marcia Bailey (EPA, R-10), and Jim W. White (Health) met with Board member Dr. Faustman to discuss their preliminary findings, the scope of the reviews

[2] In their review of the EPA dioxin reassessment, the National Research Council (2006) noted that the values for bioavailability used to determine steady-state body burdens are uncertain with values ranging from 50% to 88%. The NRC panel concluded that "Overall the value proposed and used by EPA to calculate the body burden in humans at steady state (80% absorption) appear reasonable, although the data are limited."

being conducted, and to obtain Dr. Faustman's feedback regarding future directions on the soil-bound bioavailability of dioxin/furan congeners.

Based on this review, the following conclusions can be made (refer to Appendix F for additional details):

- EPA Related Information: Ecology, Health, and EPA Region – 10, can find no information in dioxin reassessment, EPA's Science Advisory Board review of that reassessment and related documentation that provides a scientific – technical rationale for the *assumed* 30% estimate used to derive the soil bioavailability point estimate.
- International Information – Development of Allowable Daily Intakes (ADIs): International organizations recognized a wide range of per cent estimates for the absorption of dioxins and dioxin-like compounds (~30 to 90%) with most organizations using an assumed 50% estimate for the development of ADIs.
- Additional Technical Literature: Additional technical literature reaffirms that soil may influence bioavailability, bioavailability may be congener- and tissue-specific, and percent estimates are provided in a range of ~ 10% to > 40%.

Options Considered by Ecology

Ecology has considered at least three different options for the GI absorption fraction in the proposed rulemaking for dioxins/furans:

- Maintain the current rule language using 1.0 as the GI absorption fraction applicable to dioxin/furan mixtures. The Method B soil cleanup levels would remain at a soil concentration of 6.7 ppt. The industrial soil cleanup levels would remain at a soil concentration of 875 ppt.
- Use previous proposal of 0.4 as the default for mixtures of dioxins/furans. As noted previously, Method B soil cleanup levels would be established at a soil concentration of 17 ppt. Industrial soil cleanup levels would be established at a soil concentration of 2,200 ppt.
- Use a GI absorption fraction that recognizes the differences in the bioavailability for different congeners. A wide range of congener-specific GI absorption fraction values of 0.2 to 0.8 was considered in this analysis.

Ecology's Revised Rulemaking Proposal and Rationale

Ecology is proposing to revise WAC 173-340-740 and -745 to establish soil cleanup levels for dioxin/furan mixtures that takes into account the congener-specific concentrations, the relative toxicity of the congeners, and congener-specific differences in soil bioavailability. Specifically, Ecology is proposing to assign a gastrointestinal absorption fraction for soil (AB1) of 0.7[3] for the tetra- and penta- chlorine substituted dioxin and furan congeners and an AB1 value of 0.4[4] for the hexa-, hepta-, and octa-

[3] Based on average of per cent estimates from Table 4, Appendix D.
[4] Reflects reduced soil bioavailability for higher chlorinated dioxin/furan congeners noted in Van den Berg studies, National Academy of Sciences, and EPA's dioxin reassessment default.

chlorine substituted dioxin and furan congeners (Appendix A). Appendix B provides the formula for calculating a site-specific weighted AB1 for mixtures of dioxins/furans.

Under this proposal, the resulting cleanup levels for mixtures of dioxins/furans will reflect differences in concentrations for the different congeners (composition of the weathered mixture) and reflect differences in toxicity and bioavailability for the congeners. Based on available congener-specific analyses in Washington State, it is expected the weighted GI absorption for most mixtures will fall within the range of 0.4 to 0.6, with the most likely value being 0.5. This results in a 2,3,7,8 TCDD equivalent concentration cleanup level of 11 to 17 ppt, with a value of 14 ppt at most sites for unrestricted land use. For industrial properties, this proposal results in a 2,3,7,8 TCDD equivalent concentration cleanup level of 1500 to 2200 ppt, with a value of 1750 ppt at most industrial sites.

The rationale for the revised proposal for these gastrointestinal absorption fractions is based on the following factors.

Technical/Scientific Considerations-Technical Literature

Available evidence suggests that soil-bound dioxins/furans are less bioavailable than dioxins/furans used to assess the health risks from bioassays, epidemiological studies or studies used to assess the toxicity of dioxins/furans in foods and drinking water.

Van den Berg et. al., 2006 noted the influence of abiotic matrices on bioavailability (page 234): . . . "the issue of matrix-specific bioavailability of these chemicals from abiotic environmental samples leads to a high degree of uncertainty for risk assessment as this is largely dependent upon the organic carbon content and age of the particles."

In addition, Van den Berg et. al., 1994; Poiger and Schlatter, 1980 & 1986; Bonaccorsi et. al., 1984; Lucier et. al., 1986; McConnell et. al., 1984; Dioxins and Health, 2nd Edition; collectively demonstrated that absorption of TCDD from contaminated soils may be influenced by soil type (% carbon content), duration of contact with the soil, and soil characteristics.

Further more, these same studies indicate that although there is uncertainty in assigning congener-specific bioavailability estimates, the available evidence suggests that the higher chlorinated dioxin/furan congeners (hexa-, hepta-, octa-) are less well absorbed, less bioavailable, than the fewer chlorinated congeners (tetra- and penta-).

Technical/Scientific Considerations-Expert Committees and Regulatory Agencies

The National Academy of Sciences, the World Health Organization (Van den Berg et. al., 2006), other international committees and organizations, the U.S. Environmental Protection Agency, and other state agencies recognize that soil will influence the bioavailability of mixtures of dioxins/furans with the higher chlorinated congeners less bioavailable than the more chlorinated congeners. The MTCA Science Advisory Board has agreed with these other expert committees that the bioavailability of dioxins/furans may be influenced by the soil matrix.

Other Regulatory Agencies

Ecology has previously reviewed for the SAB different state regulations regarding mixtures of dioxins/furans (Appendix C, tables 2 & 3). Generally, using either a TEQ

approach or considering 2,3,7,8-TCDD, Oregon, Massachusetts, West Virginia, Texas, and Florida have cleanup standards approximating or lower than 10 ppt (ng/kg, pg/g). The 10 ppt cleanup levels is based on the administered dose used in the critical studies to develop the TCDD cancer slope factor by EPA which corresponds to an absolute bioavailability factor of 80%. Michigan has a 90 ppt cleanup level which reflects a 50 % estimate for bioavailability. Minnesota cleanup level of 200 ppt reflects a 55% estimate for bioavailability. As noted in Appendix F, the international community uses a 50% estimate for GI absorption when developing allowable daily intakes (ADIs).

Ecology's Risk Policy:

Under MTCA, as clarified by the current rulemaking proposal, the total toxicity equivalent concentration of the mixtures of dioxins/furans is considered a single hazardous substance assigned a 10^{-6} target risk to establish cleanup levels for unrestricted soils. This risk policy, coupled with allowance for bioavailability in soil, results in protective cleanup levels.

Cleanup levels – Reasonable Maximum Exposure /Protectiveness

Ecology establishes soil cleanup levels based on a reasonable maximum exposure. WAC 173-340-200 and -708 defines reasonable maximum exposure as ". . . the highest exposure that can be reasonably expected to occur for a human or other living organisms at a site under current and potential future site use." Determinations of reasonable maximum exposures by EPA and Ecology are based on a combination of upper bound and average values for the individual exposure parameters.

In consideration of the different exposure parameters used to establish soil cleanup levels under MTCA (such as soil ingestion rate and exposure duration & frequency), Ecology believes the current rulemaking for dioxins/furans continues to represent an upper bound exposure estimate that is protective and reflects the reasonable maximum exposure.

Background concentrations

Dioxin concentrations in Washington soils occur at a background level of 0.13 ppt to 19 ppt 2,3,7,8 TCDD equivalent concentrations (Ecology, 1999). This background level is the average presence of dioxin in the environment that cannot be attributed to a point source of pollution. MTCA does not require cleanup sites to perform remediation in excess of the background level of contamination. The proposed rule establishes a cleanup level that is on the high end of the range of background concentrations found in Washington State. This should minimize investigative costs.

Ecological Considerations

MTCA establishes criteria for ecological protectiveness and defines a tiered process for evaluating threats from soil contamination to terrestrial ecological receptors. The terrestrial ecological evaluation (TEE) process is set forth in WAC 173-340-7490 through 173-340-7494. Screening values for the protection of terrestrial ecological receptors at sites that qualify for a simplified assessment are 5 ppt for total dioxins and 3 ppt for total furans for unrestricted (residential) and restricted (industrial) land use (Table 749-2). Screening values for the protection of terrestrial wildlife at sensitive sites are 2 ppt for dioxins and 2 ppt for furans (Table 749-3).

Thus, for those sites exempted from conducting a terrestrial ecological protection, Ecology's approach will still result in a high level of protection for ecological receptors. For sites where protection of ecological receptors must be addressed, the protection of ecological receptors may override human health considerations.

Concluding Remarks

For this rulemaking, Ecology is proposing for mixtures of polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans (dioxins/furans) to use a point estimate of 0.7 as an AB1 value to establish standard or modified Method B and C formula cleanup levels. For site specific evaluations, Ecology proposes to use congener specific AB1 values of 0.7 for the dioxin/furan tetra- and penta- chlorinated congeners and 0.4 for the hexa-, hepta-, and octa- chlorinated congeners. Ecology's proposal addresses the following:

- Recognizes the differences between the absorption of soil bound dioxins/furans compared to the dioxins/furans administered in studies using food, water, and various oil based vehicles.
- Recognizes an abiotic matrix influence on the relative bioavailability of dioxins/furans from soils.
- Recognizes congener-specific differences for the relative bioavailability of dioxins/furans from soils.
- Recognizes a reasonably conservative level of protection for human health and the environment when considering Ecology's proposal in the context of other state, national, and international guidance and regulatory approaches.

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Appendix A
Toxicity Equivalency Factors and Gastrointestinal Absorption Fractions For Mixtures of Dioxins/Furans

Table 1: Toxicity Equivalency Factors and Gastrointestinal Absorption Fractions for Chlorinated Dibenzo-p-Dioxin and Chlorinated Dibenzofuran Congeners

CAS Number	Dioxin Congeners	Toxicity Equivalency Factor (1) (Unitless)	Gastrointestinal Absorption Fraction (Unitless)
6-01-6	2,3,7,8-Tetrachloro dibenzo-p-dioxin	1	0.7
21-76-4	1,2,3,7,8-Pentachloro dibenzo-p-dioxin	1	0.7
7-28-6	1,2,3,4,7,8-Hexachloro dibenzo-p-dioxin	0.1	0.4
53-85-7	1,2,3,6,7,8-Hexachloro dibenzo-p-dioxin	0.1	0.4
08-74-3	1,2,3,7,8,9-Hexachloro dibenzo-p-dioxin	0.1	0.4
22-46-9	1,2,3,4,6,7,8-Heptachloro dibenzo-p-dioxin	0.01	0.4
8-87-9	1,2,3,4,6,7,8,9-Octachloro dibenzo-p-dioxin	0.0003	0.4
	Furan Congeners		
07-31-9	2,3,7,8-Tetrachloro dibenzofuran	0.1	0.7
17-41-6	1,2,3,7,8-Pentachloro dibenzofuran	0.03	0.7
17-31-4	2,3,4,7,8-Pentachloro dibenzofuran	0.3	0.7
48-26-9	1,2,3,4,7,8-Hexachloro dibenzofuran	0.1	0.4
17-44-9	1,2,3,6,7,8-Hexachloro dibenzofuran	0.1	0.4
18-21-9	1,2,3,7,8,9-Hexachloro dibenzofuran	0.1	0.4
51-34-5	2,3,4,6,7,8-Hexachloro dibenzofuran	0.1	0.4
62-39-4	1,2,3,4,6,7,8-Heptachloro dibenzofuran	0.01	0.4
73-89-7	1,2,3,4,7,8,9-Heptachloro dibenzofuran	0.01	0.4
01-02-0	1,2,3,4,6,7,8,9-Octachloro dibenzofuran	0.0003	0.4

(1) Van den Berg, Martin; Jongh, Joost De.; Poiger, Hermann; and Olson, James R.; 1994. The Toxcokinetic and Metabolism of Polychlorinated Dibenzo-p-Dioxins (PCDDs) and Dibenzofurans (PCDFs) and their Relevance for Toxicity. Critical Reviews in Toxicology, 24 (1): 1-74.

Appendix B

Formula of Calculating a Site-Specific Gastorintestinal Absorption Fraction

Use the congener specific toxicity equivalency factors and gastrointestinal absorption fractions provided in Table 1, Appendix A, and the following equation to calculate a site weighted average gastrointestinal absorption fraction for the soil direct contact exposure pathway cleanup level calculation. This value can be substituted for the default gastrointestinal absorption fraction (AB1) in the standard and modified Method B and C equations (Equations 740-2, 740-5, 745-2, and 745-5).:

$$AB1_w = \frac{1}{n}\sum_{i=1}^{n}\left(\frac{\sum_{j=1}\left[TEF_{(j)} x AB1_{(j)} x C_{(i,j)}\right]}{\sum_{j=1}\left[TEF_{(j)} x C_{(i,j)}\right]}\right)$$

Where:

$AB1_w$ = site weighted average gastrointestinal absorption fraction for soil

i= "i" th soil sample

j = "j" th congener

n = number of soil samples

$TEF_{(j)}$ = toxicity equivalency factor for congener (j) from table 1, Appendix A

$AB1_{(j)}$ = gastrointestinal absorption fraction for congener (j) from table 1, Appendix A

$C_{(i,j)}$ = Congener (j) concentration of a soil sample (i)

Appendix C

Regulations & Guidance Soil Criterion for Dioxin

Table 2: Dioxin Soil Criteria – Cleanup Levels		
Country	**Residential Soil Criteria**	**Comment - Reference**
New Zealand	1,500 ng I-TEQ/kg	Criterion as an interim value in timber treatment. Under review. (Mfe/MoH, 1997)
Germany	1,000 ng I-TEQ/kg	Set as an "action value" by Federal Soil Protection and Contaminated Sites Ordinance
Japan	1,000 ng I-TEQ/kg	Environmental Quality Standard set under the Law Concerning Special Measures against Dioxin (Law No. 105 of 1999, MoE, 2001)
Canada	4 ng I-TEQ/kg	Soil Quality Guideline. Derived using ambient background concentrations; is not effects based criterion. (CCME, 2001)
United States, Environmental Protection Agency	1,000 ng I-TEQ/kg	OSWER Directive 9200.4-26, April 13, 1998
USEPA Region 6	39 ng/kg (for TCDD)	Screening level for 2,3,7,8-TCDD
USEPA Region 9	39 ng/kg (for TCDD)	Preliminary remedial goal for 2,3,7,8-TCDD
Michigan Department of Environmental Quality	90 ng I-TEQ/kg	Direct contact criterion based on 1/100,000 cancer risk (DEQ, 1998)
US Dept of Health and Human Services- ATSDR	≤ 50 ng I-TEQ/kg . . . . >50 but < 1,000 ng I-TEQ/kg . . ≥ 1,000 ng I-TEQ/kg	Screening level Evaluation level Action level*
Dioxin Concentration in Residential Soil, Paritutu, New Plymouth. Prepared for the Ministry for the Environment and The Institute of Environmental Science and Research Limited. Wellington, New Zealand, adapted from Appendix D. 26 September 2002		
The 1,000 ng I-TEQ/kg (1 ppb/1000 ppt) dates back to Times Beach, MO EPA dioxin superfund site; ***assumed*** 30% bioavailability estimate from soil.		
*71 FRN 78441-78442 solicits comments to retain 50 ng as screening level for dioxin TEQ in soil only		
1000 ng/kg = 1000 ppt = 1 ppb		

NOTE: EPA's OSWER Directive 9200.4-26 of 1000 ppt of dioxin in soil is associated with a cancer risk of 2.5E-04 or 2.5 in a population of 10,000. This risk level is approximately 25 times the risk allowed under MTCA for a single hazardous substance in a residential setting. EPA does not consider 1,000 ppt of dioxin in soil as a final "safe" level but as a screening level to help evaluate hazardous waste sites. If a more protective state standard is applicable, then that standard must be used.

Table 3: State Soil Dioxin Criterion	
State	**Residential Soil Criterion – Cleanup Level,** ppt (parts per trillion, µg/mg; ng/kg)
Oregon*	< 10
Massachusetts*	< 10
West Virginia*	< 10
Washington*	< 10
Florida*	< 10
Iowa	14
Arizona	38
Michigan**	90
Pennsylvania	120
Minnesota**	200

Source: Michigan Department of Environmental Quality. Dioxin Contamination in the Midland Area. July 02, 2004. Found at: www.deq.state.mi.us/documents/deq-whm-hwrp-dowfactsfinal.pdf.

* Reflects 80% absolute bioavailability estimate of administered dose used in the critical studies to develop the TCDD cancer slope factor by EPA

** Reflects 50% bioavailability for Michigan criterion and 55% for Minnesota criterion

Appendix D

Table 4: Consolidation of the Dioxin Bioavailability Data			
Overall (1) (%)	**As Measured by Liver Content (%)**	**As Measured by AHH Induction (%)**	**As Measured by P-450 Induction (%)**
48	48	54	117
19	19	112	91
62	62	49	90
70	70	92	76
67	67	56	105
60	60	121	65
67	67	113	71
52	52	81	84
57	57	103	
14	14	60	
54	22	61	
112	45	106	
49	32		
92	71		
22	56		
45	66		
56	44		
121	0.25		
113	24		
81			
103			
60			
61			
106			
117			
91			
90			
76			
105			
65			
71			
84			
32			
71			
56			
44			
0.25			
24			
# of Studies 39	19	12	8
Average (2) 66	46	84	87
(1) Overall represent the % bioavailability/absorption estimates of dioxin as measured by tissue levels, enzyme induction or other measures of absorption.			
(2) Arithmetic average of ***overall*** % bioavailability/absorption estimates is 66 which rounded off approximates 70% bioavailability used in Table 2, Appendix A			

Appendix E

Terminology & Units of Measure

Absorption is the process by which chemicals cross the body membranes and enter the bloodstream. Absorption usually occurs from the gastrointestinal tract (ingestion), lungs (inhalation), and skin (dermal). Absorption is necessary for a chemical contaminant to exert biological effects. Exposure is the contact a person has with environmental contaminants. The magnitude of exposure is determined by measuring or estimating the amount of the chemical available at the exchange surfaces of the gastrointestinal tract, lungs, and skin. Evaluation of a person's exposure to environmental contaminants is based on the magnitude, frequency, duration, and route of exposure. For most environmental contaminants there are three primary routes of exposure: ingestion, inhalation, and dermal contact. An exposure pathway describes the pathway a chemical takes from its source to the person that is exposed.

The absorption of a chemical is usually expressed as a percentage as an estimation of absorption efficiency. There is a distinction between absorption and bioavailability. For example, the oral absorption refers to the disappearance of the chemical from the gastrointestinal lumen. While the oral bioavailability refers to the amount of the chemical that reaches systemic circulation unchanged. The bioavailability of a chemical accounts for both absorption and metabolism. The bioavailability of a chemical is expressed as absolute or relative bioavailability. The absolute bioavailability is the ratio of the amount of the chemical absorbed compared to the amount ingested. The relative bioavailability is the ratio of the chemical in some medium compared to the absolute bioavailability of the chemical. Accounting for potential differences in absorption between different exposure media may be important for dioxins/furans because the toxicity values (cancer potency factor) are generally expressed in terms of ingested dose (rather than absorbed dose) and the absorption may vary depending on the congener and congener profiles in different media. Hence, since the oral cancer potency factor for dioxins/furans is based on studies using the contaminant in food or water, then adjustment may be necessary to account for the influence of soil on the absorption or bioavailability of dioxins/furans.

- Ecology currently uses 100% as the gastrointestinal absorption factor to establish cleanup levels for dioxins in soil. The Risk Assessment Guidance for Superfund (RAGS, 1989) emphasizes that in the absence of reliable scientific information on relative absorption efficiencies for different media assume that the relative absorption efficiency between food or soil and waster is one. The cleanup level is therefore based on administered dose, but does address fractional absorption through an absolute bioavailability factor of 80% (which is incorporated into the slope factor) that is applied by default when the slope factor is used. (So in an unusual twist for risk assessors, this bioavailability factor is part of the toxicity side of the equation instead of the exposure side.)

- The use of 80% is a somewhat hidden absolute bioavailability factor (reflective of absorbed dose) that EPA incorporated into the slope factor to account for the difference between administered dose and absorbed dose in the toxicity studies used to develop the slope factor.
- The use of 30% is EPA's published choice for absolute oral bioavailability (or absorbed dose) of dioxins from soil. Ecology, Health, and EPA, R-10 have not been able to find the policy or scientific rationale for choosing this number.

The 40% estimate is based on EPA's published choice for oral bioavailability of dioxins from soil relative to the oral bioavailability of dioxins in toxicity studies used to establish the slope factor. The proposed default value (0.4) was calculated by dividing 30% absolute bioavailability (value used to characterize absorption of soil-bound dioxins and furans) by 80% (value used to characterize absolute bioavailability of dioxin/furan in the toxicological studies used to calculate the cancer slope factor).

Units of Measure			
Milligram	10^{-3}	One thousandth	0.001
Microgram	10^{-6}	One millionth	0.000001
Nanogram	10^{-9}	One billionth	0.000000001
Picogram	10^{-12}	One trillionth	0.000000000001
Parts per million = ppm = µg/g = mg/kg = ng/mg			
Parts per billion = ppb = µg/kg = ng/g = µg/L			
Parts per trillion = ppt = pg/g = ng/kg			

Appendix F

Summarization of:

- **EPA Related Information**
- **International Information Development of ADIs**
- **Additional Technical Literature**

EPA Related Information

- **November 28, 1989 EPA/SAB (EPA-SAB-EC-90-003)** correspondence that reviews an EPA 1988 DRAFT dioxin assessment. Section 4.2.9, page 18, directs EPA to include information on the low bioavailability of 2,3,7,8-TCDD on fly ash as compared to soil in those situations which assess exposures to fly ash – cited is the Van den Berg articles (1983 & 1985) that suggests lower bioavailability of 2,3,7,8-TCDD from fly ash than from soil. Another note related to bioavailability is given on page 19, Section 4.2.11 directing the Agency to consider the inclusion of an absorption factor to account for "fractional bioavailability."
- **Appendix C: Bioavailability of Dioxins From Estimating Exposure to Dioxin-Like Compounds. Volume II: Properties, Sources, Occurrence and Background Exposures. June 1994.** This appendix responds to the concerns of the EPA SAB 1989 review. Table C-1 reviews the available information, though in less detail than Jim's table on bioavailability. Ecology, Health, and EPA, R-10, do not believe there is any science-based information from this appendix that directs one to the 30% absorption and subsequent 40% relative bioavailability. Appendix C summarized the results of available studies (page C-17) noting the estimated relative bioavailability of 2,3,7,8-TCDD from soil is 25% to 50%, and, compared to corn oil provides an estimated GI absorption of 20% to 40% of ingested 2,3,7,8-TCDD in soil.
- **EPA's Dioxin Reassessment – An SAB Review of the Office of Research and Development's Reassessment of Dioxin. Review of the Revised Sections (Dose Response Modeling, Integrated Summary, Risk Characterization, and Toxicity Equivalency Factors) of the EPA's Reassessment of Dioxin by the Dioxin Reassessment Review Subcommittee of The EPA Science Advisory Board (SAB).** Page 48 provides information on the input parameters used for the one-compartment steady-state pharmacokinetic model used to evaluate the relationship between estimating exposures from dietary intake and body burdens. One parameter for the model is the point estimate of 80% of ingested dioxin is absorbed. This is the same description of the model and absorption estimate provided in the article: A Pharmacokinetic model for estimating exposure of Americans to dioxin-like compounds in the past, present, and future. By Matthew Lorber. The Science of the Total Environment 288 (2002) 81-95.

- Two EPA 2003 Dioxin Reassessment Documents – NAS Review Drafts: Chapter 1/Part 2 – Disposition and Pharmacokinetics; and Chapter 2 / Part 1 – Estimating Exposures and Risks. Chapter 2 / Part 1 – Estimating Exposures and Risks, pages 2-16 to 2-17 clearly identifies the derivation of the 0.4 estimate for soil bioavailability. The derivation is based on an ***assumed 30%*** estimate. Sections 1.1.1.2 and 1.1.1.3 discuss GI absorption in humans and bioavailability following oral exposure, respectively. Ecology, Health, and EPA, R-10, can find no information in these sections or other sections of the document that directs one to a scientific-technical rationale for the assumed 30% estimate used to derive the soil bioavailability point estimate.

International Information – Allowable Daily Intakes (ADIs)

Ecology reviewed information from international organizations responsible for establishing threshold concentrations (tolerable or allowable daily intakes) for dioxins/furans. The focus of Ecology's review was to identify per cent estimates of absorption/bioavailability used by these organizations to help establish their tolerable or allowable daily intakes.

- Opinion of the Scientific Committee on Food on the Risk Assessment of Dioxins and Dioxin-Like PCBs in Food, Adopted on 30 May 2001. European Commission, Health & Consumer Protection Directorate-General. Scientific Committee on Food. Committee reviewed study estimated maternal body burden in pregnant rats where tritiated TCDD measure in tissue at GD 16 following administration by gavage - average maternal body burdens were reported along with % absorption - range of 48% to 65% (page 3). To develop an ADI the Committee used 50% for the absorption of 2,3,7,8-TCDD from a dietary matrix; net absorption was found to be 50-55% when 2,3,7,8-TCDD was contained in normal rat and cow diets. To estimate fetal and maternal body burdens of rats simple first-order kinetics is used, assuming 50% absorption of 2,3,7,8-TCDD from the diet. For the estimated human daily intake derivations the Committee used default uncertainty factors to account for interindividual variations with regard to absorption, biotransformation, accumulation and elimination of 2,3,7,8-TCDD within human populations.
- Gies, Adreas, et. al.; Risk Assessment of Dioxin and Dioxin-Like PCBs in Food - Comments by the German Federal Environmental Agency. Organohalogen Compound - Volume 66. 2004. page 3468: "In calculating the associated estimated daily intake (EHDI), the SFC used 50% as the fraction of dose absorbed. Studies indicate however a significantly higher absorption rate of 89 percent. It should also be considered that infants and children absorb higher rates and that small doses are more readily and effectively absorbed. In addition, uncertainty is also inherent in the use of a half life of 7.5 years (2,3,7,8-TCDD) for the calculation of the EHDIs, because it does not take into account the real mixture of PCDD/PCDF in the food and in fatty tissue."
- Department for Environment, Food and Rural Affairs and the Environment Agency. Contaminants in Soil: Collation of Toxicological Data and Intake Values for Humans. Dioxins, Furans and Dioxin-Like PCBs.

Published by Environment Agency, BRISTOL, England. Section 3.7, page 5, ...human volunteer more than 87% of a single oral dose of TCDD in corn oil was absorbed with 90% of body burden sequestered in fat (Poiger and Schlatter, 1986) A lower absorption would be expected from other matrices with the assumption of 50% absorption of TCDD from the GIT of humans. Section 3.8, page 6 . . . TCDD in diet or in an oil carrier results in absorption between 50% and in excess of 90% of the administered dose. OCDD poorly absorbed with % value ranging from 2 to 15%. Section 3.9, page 6 Rodent feeding studies absorption of TCDD dependent on formulation in which it is administered; Absorption is greatest from oil vehicles (<80%) and lowest from aqueous solutions (<30%).

- Dioxins: Recommendation for A Tolerable Monthly Intake for Australians. 24 October 2002. National Health & Medical Research Council. Uncertainty factors were applied to a LOEL in animal studies associated with the most sensitive adverse effects (hormonal, reproductive and developmental effects) an uncertainty factor(s) was applied to account for toxicokinetic differences between species (absorption).

Additional Technical Literature

Three additional articles [5]were identified considered relevant to the issue of soil bioavailability for dioxins/furans.

(1) Van den Berg, et. al., 1994 was an extensive review article with relevant conclusions summarized below:

- Absorption of 2, 3, 7, 8-TCDD or related compounds (congeners, isostereomers) is variable, incomplete, vehicle dependent, and congener-specific.
- GI absorption is predominantly limited by molecular size and solubility – hepta- and octachlorinated congeners exhibit decreased absorption in mammals and fish
- 2378 substituted tetra-and pentachlorinated congeners are well absorbed from GI tract
- OCDD poorly absorbed from intestinal tract;
- Differences in bioavailability among soil types contaminated with 2378-TCDD explained by: soil composition; duration of contact with soil; method of

(1) Van den Berg, Martin; Jongh, Joost De.; Poiger, Hermann; and Olson, James R.; 1994. The Toxcokinetics and Metabolism of Polychlorinated Dibenzo-p-Dioxins (PCDDs) and Dibenzofurans (PCDFs) and their Relevance for Toxicity. Critical Reviews in Toxicology, 24 (1): 1-74.
(2) Wendling, Jay; Hileman, Fred; Orth, Robert; Umbreit, Thomas; Hesse, Elizabeth; Gallo, Michael. 1989. An Analytical Assessment of the Bioavailablity of Dioxin Contaminated Soils to Animals. Chemosphere, Vol. 18, Nos 1-6, pages 925-932.
(3) Jurgen Wittsiepe, Bibiane Erlenkamper, Peter Welge, Alfons Hack, Michael Wilhelm. Bioavailability of PCDD/F from Contaminated Soil in Young Goettingen Minipigs. Chemosphere. 2007. [in press] Also published under same article title in the book Organohalogen Compounds, Volume 66, 2004, pages 2945-2951.

application.with increase molecular size, ranging from 80% for 2378-TCDD/TCDF to 20 to 40% for OCDD/OCDF.

(2) The second article, Wendling et. al., 1989, fed guinea pigs a gum acacia suspension of contaminated soils from Times Beach, MO and Newark, NJ (Wendling et. al., 1989). As indicated in the previous literature the per cent bioavailability varied with soil and dose with decreased bioavailability associated with the higher chlorinated congeners.

(3) The third article, Wittsiepe et. al., 2007, concluded that the soil matrix has a significant influence on oral bioavailability, the bioavailability is congener- and tissue-specific, and the estimated soil bioavailability (I-TEQ) for dioxins/furans is 13%. The relative bioavailability of 2378-chlorosubstituted congeners from soil in relation to administration by solvent was in the range of 2% to 42%.

Appendix G

Summary Tables of Technical Studies –Absorption/Bioavailability Mean Estimates of Relative Oral Bioavailability of TCDD from Soil (Based on liver concentrations, unless otherwise noted)

	Author	Animal	Relative Bioavailability	Notes
Times Beach				
	McConnell	Guinea Pig	<48%	1 μg/kg dose
	McConnell	Guinea Pig	19%	3 μg/kg dose (dead animals only)
	Shu	Rat	63% (reported as 43%)	43% from inappropriate adjustment (real range 52-70%)
Minker Stout				
	McConnell	Guinea Pig	<57%	1 μg/kg dose
	McConnell	Guinea Pig	14%	3 μg/kg dose (dead animals only)
	McConnell	Rat	45%	5 μg/kg dose
	McConnell	Rat	49 – 112%	Based on AHH induction
	Lucier	Rat	22 – 45%	Dose range 0.015 – 5.5 μg/kg
	Lucier	Rat	56 - 121%	Based on AHH induction
	Lucier	Rat	65 - 117%	Cytochromes P450 induction
Seveso				
	Bonaccorsi	Rabbit	32%	
Seveso (recontaminated)				
	Bonaccorsi	Rabbit	56 – 71%	
	Poiger	Rat	44 – 66%	
Newark manufacturing				
	Umbreit	Guinea Pig	~0.25%	
Newark salvage				
	Umbreit	Guinea Pig	24%	

Soil From	Reference	Relative Bioavailability	Endpoint Measured	Animal	Gavage Dose (µg TCDD/kg body weight)	Soil Concentration (µg TCDD/kg soil)	Particle Size	Notes
Times Beach, MO								
	McConnell	<48%	Liver content	Guinea Pig	1.3	770 µg/kg	< 250 µm	Dead animals
		19%	Liver content	Guinea Pig	3.8			
	Shu	62%	Liver content	Rat	0.0032			
		70%	Liver content	Rat	0.007			
		67%	Liver content	Rat	0.04			
		60%	Liver content	Rat	0.037			
		67%	Liver content	Rat	0.175			
		52%	Liver content	Rat	1.45			
Minker Stout, MO								
	McConnell	<57%	Liver content	Guinea Pig	1.1	880 µg/kg	< 250 µm	
		14%	Liver content	Guinea Pig	3.3			Dead animals
		54%	AHH induction	Rat	0.22			
		112%	AHH induction	Rat	0.44			
		49%	AHH induction	Rat	1.1			
		92%	AHH induction	Rat	5.5			
	Lucier	22%	Liver content	Rat	1.1	880 µg/kg	< 250 µm	
		45%	Liver content	Rat	5.5			
		56%	AHH induction	Rat	0.015			
		121%	AHH induction	Rat	0.044			
		113%	AHH induction	Rat	0.1			
		81%	AHH induction	Rat	0.22			
		103%	AHH induction	Rat	0.5			
		60%	AHH induction	Rat	1.1			
		61%	AHH induction	Rat	2.0			
		106%	AHH induction	Rat	5.5			
		117%	P450 induction	Rat	0.015			
		91%	P450 induction	Rat	0.044			
		90%	P450 induction	Rat	0.1			
		76%	P450 induction	Rat	0.22			
		105%	P450 induction	Rat	0.5			
		65%	P450 induction	Rat	1.1			

		71%	P450 induction	Rat	2.0			
		84%	P450 induction	Rat	5.5			
Seveso, Italy								
	Bonaccorsi	32%	Liver content	Rabbit	0.56	81 µg/kg	30-74 µm	7 x 80 ng/kg doses
Seveso								
(recontaminated)	Bonaccorsi	71%	Liver content	Rabbit	0.28	30 day soil contact		7 x 40 ng/kg doses
		56%	Liver content	Rabbit	0.56	30 day soil contact		7 x 80 ng/kg doses
	Poiger	66%	Liver content	Rat	0.11	15 hour soil contact		
		44%	Liver content	Rat	0.11	8 hour soil contact		
Newark mfg site								
	Umbreit	~0.25%	Liver content	Guinea Pig	12	Mghing site:1500 to 2500 ppb; Salvage yard: ~180 ppb	For both sites: medium dense, black, coarse to fine-grained sand fill with some medium to fine gravel, traces of silt, organic matter & cinders	
Newark salvage site								
	Umbreit	24%	Liver content	Guinea Pig	0.32			