

Attachment E

Dioxin and Dioxin-Like Compounds in Soil,
Part 2: Technical Support Document for ATSDR Interim Policy Guideline

DIOXIN AND DIOXIN-LIKE COMPOUNDS IN SOIL, PART II: TECHNICAL SUPPORT DOCUMENT FOR ATSDR INTERIM POLICY GUIDELINE

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2. Abbreviations: ATSDR, Agency for Toxic Substances and Disease Registry; AUC, area under the curve; CDDs, chlorinated dibenzo-*p*-dioxins; BDDs, brominated dibenzo-*p*-dioxins; BDFs, brominated dibenzofurans; CCEHRP, The Public Health Service Committee to Coordinate Environmental Health and Related Programs; CDDs, chlorinated dibenzo-*p*-dioxins; CDFs, chlorinated dibenzofurans; EMEGs, environmental media evaluation guides; EPA, U.S. Environmental Protection Agency; FDA, U.S. Food and Drug Administration; LOAEL, lowest-observed-adverse-effect level; MRL, minimal risk level; NOAEL, no-observed-adverse-effect level; PBBs, polybrominated biphenyls; PCBs, polychlorinated biphenyls; TCDD, 2,3,7,8-tetrachlorodibenzo-*p*-dioxins; TEF, toxicity equivalent factor; TEQs, toxicity equivalents.

3. Key words: dioxin, human exposure, risk assessment, soil levels, TCDD, TEQs.

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INTRODUCTION

Dioxin remains at the forefront of public health concerns in the United States and throughout the world. Over the past 20 years, a wide range of federal agencies and other organizations have been involved in developing policy statements, strategies, and assessment methods to address the public health implications of dioxin exposure. These positions were developed in response to issues confronted by those organizations in pursuing their missions, often as a direct function of legislative mandates. Because of distinct differences in perspective, policy, and practice, dictated by the mandated activities of these organizations and the evolving understanding of dioxin toxicity, apparently divergent positions may be reflected in their conclusions.

In pursuing its mandated responsibilities, the Agency for Toxic Substances and Disease Registry (ATSDR) must address public health concerns associated with exposure to dioxin and dioxin-like compounds in the context of all available relevant information. This information includes both technical data and science policy positions adopted by ATSDR and others that are germane to the public health assessment of dioxin and dioxin-like compounds.

The issues outlined previously, coupled with requests from the public, other agencies, the private sector, and agency staff for a statement reflecting the agency's position on science and science policy issues related to dioxin and dioxin-like compounds, prompted the development of this technical support document. This document is intended to serve as technical background and support for the agency interim policy guideline on dioxin and dioxin-like compounds in soil and to harmonize such efforts with those of other federal agencies and relevant organizations to the extent practicable. This document reflects an assessment of current practice within the agency and defines the appropriate roles of professional judgment and emerging scientific principles in ATSDR's public health assessments of exposures to dioxin and dioxin-like compounds.

This document is not intended to supplant the Environmental Protection Agency's (EPA) ongoing reassessment of dioxin and dioxin-like compounds or ATSDR's toxicological profile on chlorinated dibenzo-*p*-dioxins (CDDs), but it will provide technical background support for ATSDR's public health practice at sites contaminated by dioxin and dioxin-like compounds. A central theme of this document is the use of health guidance values in the broader context of biomedical and other scientific judgment to define exposures of concern rather than single numerical conclusions that may convey an artificial sense of precision (ATSDR, 1993; CEQ, 1989).

After reviewing the previously cited issues, ATSDR further considered three specific issues:

- o Issue 1: The relationship between the ATSDR action level of 1 part per billion (ppb) dioxin and dioxin-like compounds in residential soil and ATSDR's environmental media evaluation guides (EMEGs)
- o Issue 2: That current analytic and sampling techniques employed for soil contaminated with dioxin and dioxin-like compounds may not be sufficiently sensitive
- o Issue 3: That ATSDR's action level of 1 ppb dioxin and dioxin-like compounds in residential soil is too high.

Each of these issues is addressed in subsequent sections of this paper. To facilitate its review of these issues ATSDR has

- o developed a glossary of critical terms and concepts to facilitate a consistent use and understanding of terminology in this support document (Appendix 1)
- o identified and evaluated key assumptions underlying the review and evaluation of the ATSDR action level of 1 ppb of dioxin and dioxin-like compounds in residential soil, the ATSDR minimal risk level (MRL), and the ATSDR EMEG (Appendix 2)
- o reviewed and evaluated the documentation for the ATSDR action level of 1 ppb for dioxin and dioxin-like compounds in residential soils, the MRL of 1 picogram/kilogram/day (pg/kg/day) 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), and the EMEG of 50 parts per trillion (ppt) (Appendix 3)
- o reviewed and evaluated ATSDR's use of an action level of 1 ppb (HazDat) for dioxin and dioxin-like compounds, given recent insights into the toxicologic and human health effects of such compounds, particularly those associated with reproductive and developmental toxicities (Appendix 4).

DISCUSSION

Issue 1: Relationship between ATSDR's action level and EMEGs

Comparison Values

EMEGs are comparison values used by ATSDR health assessors to select contaminants for further evaluation based on concerns about end points other than cancer. As such, EMEGs represent a starting point for the health assessor to make an initial determination of whether or not a specific contamination level merits further evaluation as a potential health concern. EMEGs are based on ATSDR's MRLs or analogous health guidance values that are thought to be without appreciable risk for a given route and duration of exposure.

Generally, if a concentration of a chemical at a site is less than the EMEG, ATSDR assumes there is little likelihood that the chemical presents a health hazard at the site via a particular environmental medium. In some instances, ATSDR may further consider contaminants present at levels below the EMEG, based on community health concerns. However, if the concentration of a chemical meets or exceeds the EMEG, this does not mean there is a chemical health hazard; instead, this means that the situation merits further evaluation of site-specific information (for example, bioavailability, demographics, on-site activities, climatic conditions, or soil cover). Follow-up evaluation of all available site-specific information may reveal that there is no health threat at the site even though the media concentrations may exceed the EMEG.

Exposure Evaluation and Interdiction Strategies

Levels greater than the EMEG of 50 ppt (0.05 ppb) TCDD in soil are used to determine whether further site-specific evaluation for dioxin is to occur. Because the toxicity of dioxin and dioxin-like compounds is assumed to be elaborated through a common receptor-mediated mechanism, the EMEG is expressed in total toxicity equivalents (total TEQs). An action level of 1 ppb (also expressed as total TEQs) is used to determine the need for public health actions on a site-specific basis and on the basis of the maximum concentration identified at the site.

For these reasons, ATSDR considers source-specific contributions to total exposure and associated body burdens of dioxin and dioxin-like compounds expressed as TEQs in evaluating sites. This requires insight into not only contamination levels in soil, but also into other media as well. In this way the contribution of each potential source of exposure is evaluated and viewed in the context of total exposure and associated body burdens for a given at-risk population.

ATSDR also evaluates exposure levels and potential body burdens in at-risk populations in the context of current knowledge regarding effect levels as identified in both experimental studies and epidemiologic investigations (DeVito et al., 1995; Appendix 4). A full range of strategies to interdict exposures and reduce overall body burden are then considered. These exposure interdiction strategies include restricted land use and access, health education, relocation, and remediation to reduce incremental contributions to body burdens and risks of potential health effects.

Action Levels, EMEGs, and MRLs

ATSDR's health guidance values for dioxin or dioxin-like compounds (MRLs, EMEG, action level) each have their distinct application corresponding to screening, evaluation, or consideration of potential public health actions (Table 1). The use of such a hierarchy or framework of quantitative conclusions for purposes of screening, evaluation, and consideration of action is not intended to serve as a surrogate for professional judgment. Parameters of exposure and toxicity that may serve to either increase or decrease health concerns for at-risk populations should be considered on a site-specific basis. ATSDR's approach is consistent with recommendations of the National Research Council (NRC, 1994) that a tiered or iterative approach be used in health assessment efforts, beginning with relatively conservative screening techniques and subsequently relying on more rigorous data-intensive efforts as suggested by public health concerns.

Limitations, Assumptions, and Uncertainties

Health guidance values reflect the application of a range of default assumptions that are conservative (i.e., protective) and which are believed, in aggregate, to result in protective health guidance values. These assumptions include bioavailability of dioxin and dioxin-like compounds from test vehicles, soil ingestion rates for different at-risk populations (i.e., children, geophagic children, adults), and the use of animal data in the absence of adequate epidemiologic data addressing the health effects in human populations (Appendix 2). Additionally, to account for recognized areas of uncertainty regarding species variability in effect(s) and effect levels, sensitive human populations, and low-dose extrapolation, uncertainty factors are used in developing health guidance values. The application of such uncertainty factors contributes further to the protective nature of health guidance values.

The limitations, assumptions, and uncertainties inherent in health risk assessment are addressed in the National Academy of Sciences report "Science and Judgment in Risk Assessment" (NRC, 1994). In this report, the Academy states that "uncertainty analysis should be an iterative process, moving from the identification of generic uncertainties" to more refined analyses for chemical-specific or industrial plant-specific uncertainties. Implicit in this scenario are site-specific applications addressed in this support document. ATSDR's practice in evaluating sites contaminated with dioxin and dioxin-like compounds is consistent with the position of the National Academy of Sciences (NRC, 1994) in terms of uncertainty analysis.

Issue 2: Analytic and sampling techniques

Analytic Techniques

The EPA 8280 method is currently unable to provide analytical data for levels between the screening level of 50 ppt and the action level of 1 ppb TEQs (EPA, 1995). The EPA 8290 method can provide analytical data in the range of 50 ppt to 1 ppb. The detection limit of Method 8290 has a range of 1–5 ppt. Thus, in those instances where the health assessor has determined that it is necessary to evaluate the site-specific public health implications of exposure to soil levels of dioxin and dioxin-like compounds between 50 ppt and 1 ppb, it may be appropriate to implement the EPA 8290 (EPA, 1994) soil analytic method with the more sensitive detection limit. This decision should be made on a site-specific basis.

Sampling Techniques

ATSDR's position regarding soil sampling strategies is germane to the discussions in this document. ATSDR recommends that appropriate soil sampling methods be determined on a site-specific basis (Emmett and Jordan-Izaguirre, 1994).

TABLE 1. ATSDR's Decision Framework for Sites Contaminated with Dioxin and Dioxin-Like Compounds

Because the toxicity of dioxin and dioxin-like compounds is assumed to be elaborated through a common receptor-mediated mechanism, levels greater than 50 ppt (0.05 ppb) TEQs* are used to determine whether further site-specific evaluation for dioxins is to occur based on the maximum soil concentrations identified at the site. A level of 1 ppb TEQs is used to determine the potential need for public health actions on a site-specific basis and on the basis of adequate sampling and measured or projected human exposure—past, present, or future—as determined by the health assessor.

SCREENING LEVEL	EVALUATION LEVELS	ACTION LEVEL**
≤ 50 ppt (0.05 ppb) TEQs	> 0.05 ppb but < 1 ppb TEQs	≥ 1 ppb TEQs
<ul style="list-style-type: none"> • The EMEG for TCDD is 50 ppt • This is based on an MRL of 1 pg/kg/day for TCDD (ATSDR, 1989). • For screening purposes 50 ppt TCDD is assumed to be equivalent to 50 ppt TEQs 	Evaluation of site-specific factors, such as: <ul style="list-style-type: none"> • Bioavailability • Ingestion rates • Pathway analysis • Soil cover • Climate • Other contaminants • Community concerns • Demographics • Background Exposures 	Potential public health actions considered, such as: <ul style="list-style-type: none"> • Surveillance • Research • Health studies • Community education • Physician education • Exposure investigations

*The toxicity equivalent (TEQ) of TCDD is calculated by multiplying the exposure level of a particular dioxin-like compound by its toxicity equivalency factor (TEF). TEFs are based on congener-specific data and the assumption that Ah receptor-mediated toxicity of dioxin-like chemicals is additive. The TEF scheme compares the relative toxicity of individual dioxin-like compounds to that of TCDD, which is the most toxic halogenated aromatic hydrocarbon.

**A concentration of chemicals at which consideration of action to interdict/prevent exposure occurs, such as surveillance, research, health studies, community education, physician education, or exposure investigations. Alternatively, based on the evaluation by the health assessor, none of these actions may be necessary.

Issue 3: One part per billion of dioxin and dioxin-like compounds as an action level for cleanup

The decision to derive standard action levels for individual chemicals and to further use these values to drive clean-up activities is an EPA risk management decision. Risk management issues are outside the direct mandates of ATSDR.

Historical Background

The 1 ppb level for dioxin has been described as a "reasonable level to begin consideration of action to limit exposure" (Kimbrough et al., 1984); "a level of concern" (Kimbrough et al., 1984; Pohl et al., 1995); and "a soil action level" (Johnson, 1992b). This action level of 1 ppb was originally used in reference to TCDD in soil (see Appendix 5 for a complete chronology regarding the use and application of these terms). More recently, it has been used in reference to TCDD toxicity equivalents or TEQs (CCEHRP, 1992). The TEQ approach is based on the assumption of a common receptor-mediated mechanism of toxic action for dioxin and dioxin-like compounds (Birbaum, 1994; DeVito et al., 1995).

Limitations of Soil Action Level

A key limitation inherent in the use of any soil action level is the incomplete understanding of how such a soil action level would contribute to body burdens in at-risk populations. The extent of contribution of soil dioxin and dioxin-like compounds to body burdens of dioxin is a function of all media-specific levels of the contamination at a given site. Accordingly, a 1 ppb level of dioxin and dioxin-like compounds in residential soil could result in distinctly different contributions to overall body burdens in different populations. For this reason, ATSDR's use of 1 ppb has always been coupled with the recommendation that full consideration be given to site-specific factors such as demographics, on-site activities, climatic conditions, and soil cover.

These site-specific factors provide health assessors with valuable insight into how closely the assumptions associated with health guidance values actually reflect real site conditions. Moreover, such insight and understanding are essential to the determination of whether a site-specific action level other than 1 ppb might be appropriate. As noted by Kimbrough et al. (1984), exposure assessments used to project risk contain assumptions that are unlikely to be actually encountered. These assumptions include uniform levels of contamination, uniform land use patterns, lifetime exposure, and no degradation of dioxin and dioxin-like compounds.

Carcinogenic Versus Other Health Outcomes

A significant point to be considered in regard to 1 ppb as an action level for dioxin and dioxin-like compounds in residential soil is the issue of carcinogenic versus other health outcomes. As discussed previously, 1 ppb dioxin in residential soil was identified by Kimbrough et al. (1984) as a "level of concern," and was recommended as "a reasonable level to begin consideration of action to limit exposure." It is important to note that Kimbrough et al.'s (1984) conclusions were derived in part from an evaluation of the carcinogenic potential of TCDD, based on a 2-year oral chronic toxicity and oncogenicity study in rats (Kociba et al., 1978).

The Kociba et al. (1978) study also served as the basis for the Food and Drug Administration's (FDA's) derivation of a risk-specific dose of 0.057 pg/kg/day dioxin for a 1 in a million (10^{-6}) upper-bound risk estimate for cancer (FDA, 1990). Using typical default values of 70 kilograms (kg) for average body weight, and 100 milligrams/day (mg/day) for soil consumption, FDA's 0.057 pg/kg/day risk-specific dose corresponds to a soil concentration of 40 ppt, a value marginally lower than, but essentially equivalent to (from a risk assessment perspective), the ATSDR screening EMEG of 50 ppt (0.05 ppb). EPA's 0.006 pg/kg/day risk-specific dose corresponds to a soil concentration of 4 ppt, a value about one order of magnitude below the FDA level. In contrast, Paustenbach et al. (1992) reexamined human exposure to dioxin and dioxin-like compounds from soil. In residential areas, soils containing 20 ppb of TCDD were calculated to pose a lifetime cancer risk no greater than 1 in 10^{-5} . Assumptions used for estimating exposure from soil differed from previous evaluations of soil ingestion, dermal contact, dust inhalation, fish consumption, and in the cancer slope factor for TCDD. Exposure through dermal contact was discussed.

As noted previously, ATSDR's EMEG is based on the MRL of 1 pg/kg/day TCDD, which is approximately two orders of magnitude below any human effect levels demonstrated either experimentally or in epidemiologic studies for both cancer and noncancer health end points. The

conservative (i.e., protective) nature of both the MRL and the EMEG reflects adjustments made for recognized areas of uncertainty perhaps spanning two to three orders of magnitude (Appendix 2). As such, the EMEG and the MRL (on which the EMEG is based) are below levels of exposures associated with demonstrated health effects and are therefore considered protective of human health. A 1000-fold uncertainty factor was used in the derivation of the MRL, reflecting the range of currently recognized areas of scientific uncertainty. The EMEG of 50 ppt is at the low end of this range, which is approximately 50–50 000 ppt (0.05–50 ppb). The level calculated by Paustenbach of 20 000 ppt (20 ppb) is closer to the mid-point of the range of scientific uncertainty.

In the case of the FDA's risk-specific dose, it should be noted that this dose is based on an upper-bound estimate of risk in the 95% confidence limit sense. This means that there is a 95% chance that actual risk is less (CCEHRP, 1992) and could be as low as zero. This places the low end of ATSDR's range of evaluation (> 0.05 ppb but < 1 ppb TEQs) approximately two orders of magnitude below health effect levels demonstrated experimentally or in epidemiologic studies.

CONCLUSIONS

Protection of Public Health

The issues discussed previously indicate that (1) ATSDR's EMEG and MRL are approximately two orders of magnitude below effect levels in experimental and epidemiologic studies, (2) cancer risk-specific doses and screening values for end points other than cancer are essentially equivalent from a risk assessment perspective, (3) ATSDR's EMEG of 50 ppt (0.05 ppb) and action level of 1 ppb are not inconsistent, and (4) a 1 ppb action level for dioxin and dioxin-like compounds in residential soil, when coupled to a site-specific context of evaluation for the range of greater than 50 ppt to less than 1 ppb (TEQs) in residential soil, is protective of public health. Similarly, a cleanup level of 1 ppb (TEQs) for dioxin and dioxin-like compounds in residential soil is considered to be generally protective of human health if coupled with a full evaluation of site specific factors.

Site-Specific Parameters

A range of site-specific parameters, e.g., soil type, soil cover, media-specific contamination levels, and demographics, affect body burdens of dioxin and dioxin-like compounds in at-risk populations. Because these parameters vary on a site-specific basis, it is not currently feasible to identify, for all sites, a single numerical value to appropriately guide cleanup or other public health actions. For this reason, ATSDR uses a hierarchy of health guidance values (Table 1) for purposes of screening, evaluation, and consideration of the potential need for further action to interdict exposures, extending to and possibly including cleanup. Alternative actions may include, but are not limited to, health education, restricted access, deed restrictions, and relocation.

Evaluation of Recent Literature

Based on ATSDR's evaluation of more recent literature (Appendix 4), ATSDR has determined that the agency's MRL of 1 pg/kg/day (ATSDR, 1989) is approximately two orders of magnitude below effect levels in experimental and epidemiologic studies. Accordingly, ATSDR concludes that this MRL and the EMEG of 50 ppt, which is based on the MRL, continue to be reasonable and protective, although geophagic children and those with elevated body burdens of dioxin and

dioxin-like compounds may represent special at-risk populations. Such an approach is consistent with the current public health conclusions and practices reflected in a recent publication by the Health Council of the Netherlands (1996), in which a health-based exposure limit of 1 pg/kg/day dioxin and dioxin-like compounds was also recommended based on the council's own independent reassessment of dioxin.

With specific reference to the issues outlined in this paper, ATSDR further concludes the following:

- o ATSDR's action level of 1 ppb of dioxin and dioxin-like compounds (TEQs) in residential soil is consistent with ATSDR's EMEG. These values are used for distinctly different purposes in the evaluation of dioxin-contaminated sites (Table 1).
- o Currently used soil analytic methods may not be sufficiently sensitive. Determination of an appropriate analytic method should be made on a site-specific basis. Specific knowledge of different dioxin-like compounds at a given site is required to evaluate the adequacy of a soil sampling protocol.
- o ATSDR's action level of 1 ppb for dioxin and dioxin-like compounds (TEQs) in residential soil is not too high. Whether to use the 1 ppb action level should be decided on a site-specific basis in which residential soil levels greater than 50 ppt and less than 1 ppb are further evaluated in the context of site-specific parameters.

Health Guidance Values

While health guidance values represent an important frame of reference in public health assessment, they are not surrogates for biomedical and other technical judgments in public health assessments. For this reason, health guidance values, including those used for screening, evaluation, and consideration of action, are used by ATSDR in the context of all relevant site-specific parameters. In this site-specific context of evaluation for levels of dioxins in soil greater than 50 ppt and less than 1 ppb, ATSDR concludes that the 1 ppb level in residential soil continues to represent a level at which consideration of health action to limit exposure should occur. ATSDR considers this action level to be both reasonable and protective.

The identification of a threshold body burden/blood serum level, below which adverse health effects are not anticipated, would help to better define potential health risks at sites contaminated with dioxin and dioxin-like compounds. However, since significant uncertainties remain regarding such levels, especially for at-risk populations by virtue of exposure or physiologic sensitivity, a threshold level cannot be identified at present.

RECOMMENDATIONS

Evaluation of Hazardous Waste Sites

ATSDR's approach to the evaluation of hazardous waste sites, including those contaminated with dioxin and dioxin-like compounds, places preeminent emphasis on biomedical and other technical judgment. In the exercise of such a judgment, health guidance values serve as a frame

of reference to guide agency practice at sites. In this frame of reference, values of ≤ 50 ppt (0.05 ppb) TEQs, > 50 ppt (0.05 ppb) but < 1 ppb TEQs, and ≥ 1 ppb TEQs continue to be the agency's best estimate of appropriate health guidance values for purposes of screening, evaluation, and consideration of health action to limit exposure, respectively (Table 1).

Based on the foregoing frame of reference, the dioxin workgroup's recommendations are as follows:

Issue 1: Relationship between ATSDR's action level and EMEGs

- o That ATSDR continue to use the EMEG of 50 ppt as TEQs for soil contaminated with dioxin and dioxin-like compounds for purposes of screening
- o That 1 ppb dioxin and dioxin-like compounds expressed as TEQs in soil continue to be used by ATSDR as an "action level" (Johnson, 1992b), which has been characterized as "a reasonable level to begin consideration of action to limit exposure" (Kimbrough et al., 1984) to dioxin from residential soil.

Issue 2: Analytic and sampling techniques

- o That ATSDR and EPA continue their efforts to assure earlier consultation at sites
- o That the adequacy of analytic and sampling techniques be assessed on a site-specific basis.

Issue 3: One part per billion of dioxin and dioxin-like compounds as an action level for cleanup

- o That ATSDR continue to consult with EPA regarding the appropriateness of 1 ppb of dioxin and dioxin-like compounds as an action level for cleanup or other actions to interdict exposure and protect human health on a site-specific basis.

ATSDR Draft Profile for CDDs

It is recommended that ATSDR complete its draft profile on CDDs in coordination with EPA's dioxin reassessment.

Further Evaluation of Dioxin and Dioxin-Like Compounds

Finally, once ATSDR's toxicological profile has been completed, the health guidance values for dioxin and dioxin-like compounds should be further evaluated when new information becomes available.

APPENDICES FOR TECHNICAL SUPPORT DOCUMENT
FOR ATSDR INTERIM POLICY GUIDELINE

APPENDIX 1 - GLOSSARY

Action level	A concentration of chemicals at which consideration of action to interdict/prevent exposure occurs, such as surveillance, research, health studies, community education, physician education, or exposure investigations. Alternatively, based on the evaluation by the health assessor, none of these actions may be necessary.
"At-risk" population	A population at a potentially elevated risk due to physiological sensitivity and/or increased exposure to a hazardous chemical.
BDDs	Brominated dibenzo- <i>p</i> -dioxins
BDFs	Brominated dibenzofurans
CDDs	Chlorinated dibenzo- <i>p</i> -dioxins
CDFs	Chlorinated dibenzofurans
Comparison value	A concentration used to select contaminants of concern at hazardous waste sites that are taken forward in the health assessment process for further evaluation (The terms comparison value and screening level are often used synonymously.)
Dioxin	A term used interchangeably with 2,3,7,8-tetrachlorodibenzo- <i>p</i> -dioxin or TCDD
Dioxin-like compounds	Compounds from a group of halogenated aromatic hydrocarbons that have molecules shaped like TCDD and produce similar toxic effects, such as certain other chlorinated dibenzo- <i>p</i> -dioxins (CDDs) and certain chlorinated dibenzofurans (CDFs), polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs), brominated dibenzo- <i>p</i> -dioxins (BDDs), and brominated dibenzofurans (BDFs).
Dioxins	A term used interchangeably with chlorinated dibenzo- <i>p</i> -dioxins
EMEG	An environmental media evaluation guide (EMEG) is a media-specific comparison value that is used to select contaminants of concern at hazardous waste sites.
HazDat	ATSDR's Hazardous Substance Release/Health Effects Database

MRL	A minimal risk level (MRL) is an estimate of the daily human exposure to a hazardous substance that is likely to be without an appreciable risk of adverse noncancer health effects over a specified route and duration of exposure.
PBBs	Polybrominated biphenyls
PCBs	Polychlorinated biphenyls
Screening	The process of initially identifying potentially important chemical contaminants and exposure pathways by eliminating those of known lesser significance.
TCDD	2,3,7,8-Tetrachlorodibenzo- <i>p</i> -dioxin
TEFs	Toxicity equivalency factors (TEFs) are based on congener-specific data and the assumption that the toxicity of dioxin and dioxin-like compounds is mediated by the Ah receptor and is additive. The TEF scheme compares the relative toxicity of individual dioxin-like compounds to that of TCDD, which is the most toxic halogenated aromatic hydrocarbon.
TEQs	Toxicity equivalent (TEQ) is defined as the product of the concentration, C_i , of an individual "dioxin-like compound" in a complex environmental mixture and the corresponding TCDD toxicity equivalency factor (TEF_i) for that compound. The total TEQs is the sum of the TEQs for each of the congeners in a given mixture:

$$\text{Total TEQs} = \sum_{i=1}^n (C_i \cdot TEF_i)$$

APPENDIX 2 - ASSUMPTIONS, LIMITATIONS, AND UNCERTAINTIES IN DEVELOPING HEALTH GUIDANCE VALUES

Regulatory and policy decisions regarding contaminant levels must constantly be made in the face of scientific and technical uncertainties. In establishing health-based benchmarks such as minimal risk levels (MRLs) and environmental media evaluation guides (EMEGs), multiple assumptions are made about the nature of these uncertainties, depending on the specific question or issue being addressed. In interpreting and using health-based benchmarks to make general and/or site-specific decisions, these assumptions must be identified and addressed to avoid underestimating or overestimating actual risks. Some of these assumptions are made routinely during the development of health-based guidance values, and the conservatism they introduce into the final estimate is explicitly prescribed in the appropriate guidance documents.

Minimal Risk Level

An ATSDR MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects for a specified route and duration of exposure. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors and other responders to identify contaminants and potential health effects that may be of concern at hazardous waste sites. It is important to note that MRLs are not intended to define clean-up or action levels for ATSDR or other agencies.

MRLs are intended to serve as a screening tool to help public health professionals decide where to further evaluate the potential for health effects. They may also be viewed as a mechanism to identify those hazardous waste sites that are not expected to cause adverse health effects. MRLs contain some degree of uncertainty because of the lack of precise toxicological information on the people who might be most sensitive (e.g., infants, elderly, individuals with liver disease, and nutritionally or immunologically compromised) to the effects of hazardous substances. ATSDR uses a conservative (i.e., protective) approach to address these uncertainties consistent with the public health principle of prevention. Although human data are preferred, MRLs often must be based on animal studies because relevant human studies are lacking. In the absence of evidence to the contrary, ATSDR assumes that humans are more sensitive than animals to the effects of hazardous substances and that certain persons may be particularly sensitive. Thus, the resulting MRL may be as much as two orders of magnitude below levels shown to be effect levels in laboratory animals.

Environmental Media Evaluation Guide

The EMEG is a media-specific concentration below which exposure is unlikely to pose a health threat. The EMEG is calculated by multiplying the MRL by the body weight and dividing by the ingestion rate. No site-specific assumptions are used in deriving the EMEGs. Because they are not site-specific, they are not clean-up levels.

Assumptions used in developing the ATSDR EMEGs include (1) exposure occurs 24 hours a day for every day of the exposure period, (2) body weight, 10 kilograms for a child (22 pounds) and 70 kilograms for an adult (154 pounds), (3) ingestion rate for drinking water is 2 liters per day for adults and 1 liter for children, and (4) ingestion rate for soil is 100 milligrams per day for adults, 200 milligrams per day for children, and 5 grams per day for the geophagic child.

EMEGs should not be used to suggest or predict adverse health effects or to set clean-up levels. Their purpose is to provide health assessors with a means of selecting environmental contaminants for further evaluation (ATSDR, 1992).

Exposure to Dioxin-like Compounds

Dioxin-like compounds or "related chemicals" are other compounds containing chlorine or bromine whose molecules are shaped like TCDD and produce similar toxic effects, including some other dioxin congeners, some furan compounds, some polychlorinated biphenyls (PCBs), and some polybrominated biphenyls (PBBs) (Schierow, 1995). (See also Table 2-1 and Table 2-2.) As explained in Appendix 1, TEQs are used to estimate toxicity of dioxin-like compounds.

TABLE 2-1. Recommended Toxicity Equivalency Factors (TEFs) for CDDs and CDFs

CDDs	EPA current recommended values	CDFs	EPA current recommended values
monoCDDs	0	monoCDFs	0
diCDDs	0	diCDFs	0
triCDDs	0	triCDFs	0
2,3,7,8-TCDD	1	2,3,7,8-tetraCDF	0.1
other tetraCDDs	0	other tetraCDFs	0
2,3,7,8-pentaCDD ^a	0.5	1,2,3,7,8-pentaCDF	0.05
other pentaCDDs	0	2,3,4,7,8-pentaCDF	0.5
		other pentaCDFs	0
2,3,7,8-hexaCDD ^a	0.1	2,3,7,8-hexaCDF ^a	0.1
other hexaCDDs	0	other hexaCDFs	0
2,3,7,8-heptaCDD ^a	0.01	2,3,7,8-heptaCDF ^a	0.01
other heptaCDDs	0	other heptaCDFs	0
octaCDD	0.001	octaCDF	0.001

^aAny isomer that contains chlorine in the 2,3,7,8-positions

CDDs = chlorinated dibenzo-*p*-dioxins; CDFs = chlorinated dibenzofurans;

TCDD = tetrachlorodibenzo-*p*-dioxin.

Source: derived from EPA (1989a).

Some of the assumptions for using the TEQ approach include a well-defined group of chemicals, a broad database of information, consistency across end points, additivity of the effects, and a common mechanism of action (EPA, 1989a). According to EPA guidelines for risk assessment of complex mixtures, potency-weighted additivity is assumed for mixtures in the absence of information to the contrary (EPA, 1987).

The limitations associated with the use of TEQs must be considered in developing health guidance values. TEQs are derived using toxicity equivalency factors (TEFs) that are constants determined from experimental studies for each congener. Although TEFs are considered a constant, they are dependent on the specific study (end point, dose, and duration of exposure). As defined, TEQs are assumed to be additive and not synergistic or antagonistic. In actual mixtures of dioxin and dioxin-like compounds, competitive inhibition may occur at sufficiently high doses. As with MRLs and EMEGs, biomedical judgment must be used in considering site-specific conditions that would reasonably modify estimates applicable for an individual site.

TABLE 2-2. Recommended Toxicity Equivalency Factors (TEFs) for Dioxin-Like PCBs

PCB	WHO proposed interim values	PCB	WHO proposed interim values ^a
3,3',4,4'-TCB	0.0005	2,3,3',4,4',5-HxCB	0.0005
3,3',4,4',5-PeCB	0.1	2,2,3',4,4',5'-HxCB	0.0005
3,3',4,4',5,5'-HxCB	0.01	2,3',4,4',5,5'-HxCB	0.00001
2,3,3',4,4'-PeCB	0.0001	2,3,3',4,4',5,5'-HpCB	0.0001
2,3,4,4',5-PeCB	0.0005	2,2',3,3',4,4',5-HpCB	0.0001
2,3',4,4',5-PeCB	0.0001	2,2',3,4,4',5,5'-HpCB	0.00001
2',3,4,4',4-PeCB	0.0001		

^aInterim values proposed by World Health Organization/International Programme on Chemical Safety
 PCB = polychlorinated biphenyl; TCB = tetrachlorinated biphenyl; PeCB = pentachlorinated biphenyl;
 HxCB = hexachlorinated biphenyl; HpCB = heptachlorinated biphenyl
 Source: derived from Ahlborg et al. (1994).

Bioavailability

Bioavailability is an integral factor in the estimation of the internal dose (or dose at target tissue) of the chemical. The gastrointestinal absorption of TCDD and related compounds is variable, incomplete, and congener- and vehicle-specific. More lipid-soluble congeners, such as 2,3,7,8-tetrachlorodibenzofuran, are almost completely absorbed, while the extremely insoluble octachlorodibenzodioxin is less well absorbed depending on the dosing regimen; high doses may be absorbed at a lower rate, whereas low repetitive doses may be absorbed at a greater rate. The only study of TCDD bioavailability in humans was reported by Poiger and Schlatter (1986) and was based on a single male in which the gastrointestinal absorption was > 87% when TCDD was administered in corn oil.

Laboratory data suggest that there are no major interspecies differences in the gastrointestinal absorption of CDDs and CDFs. However, absorption of TCDD is dependent on conditions and characteristics of the soil medium; in animals, absorption of TCDD from different soils ranged from 0.5% (Umbreit et al., 1986a, 1986b) to 50% (Lucier et al., 1986). Absorption from a diet was 50% to 60% in rats (Fries and Marrow, 1975). Therefore, exposure with food as a vehicle, rather than with oil as a vehicle, relates more closely to exposure from soil. Bioavailability has to be considered when calculating the hypothetical ingestion dose.

If assumed that 100% of TCDD is bioavailable, risk may be overestimated. The health assessor should recognize that others used various assumptions in their calculations. Kimbrough et al. (1984) assumed 30% bioavailability from ingestion of soil, but pointed out that animal studies with contaminated Missouri soil indicated absorption up to 30% to 50% (McConnell et al., 1984). Pohl et al. (1995) assumed 40% bioavailability from soil. In contrast, Paustenbach et al. (1986) estimated bioavailability of 10% to 30%. Unless toxicokinetic studies that use soil samples from the specific site are available, it is difficult to speculate on how much TCDD and related compounds will be absorbed. Therefore, the estimate of the actual intake has limitations.

The chronic MRL is based on studies where food was the vehicle. Results from animal studies indicate that bioavailability of TCDD from soil varies between sites because dioxin and dioxin-like compounds bind tightly to soil, and increasingly so with the passage of time (Gough, 1991) and clay content of soil. Therefore, TCDD content alone may not be indicative of the potential for human health hazard from contaminated environmental materials, and site-specific evaluation is essential.

Soil Ingestion

Soil ingestion rates are assumptions included in the derivation of EMEGs (see previous section). ATSDR (1992) uses assumptions based on consumption of 100 mg/day for adults and 200 mg/day for children. The soil ingestion for children is based on a number of studies (Binder et al., 1986; Clausing et al., 1987) estimating the average soil ingestion in populations of normal children. Kimbrough et al. (1984) assumed in their calculations that children between 1.5 and 3.5 years of age ingest about 10 g of soil daily, and their risk assessment was based on "extreme total daily dose estimates." This estimate was later disputed, and several studies were conducted to evaluate the daily intake of soil by children. One of the reports suggested that an average child ingests only about 25–40 mg of soil daily (Gough, 1991). However, about 1% to 2% of children are geophagic and ingest from 5 g to 10 g of soil daily (EPA, 1989b). Uncertainties associated with this issue are acknowledged, but ATSDR (1992) views ingestion rates of 100 mg/day and 200 mg/day for adults and children, respectively, to be reasonable. In the event that geophagic children are at risk, ATSDR considers this issue further in the public health assessment.

Background Exposure

EMEGs represent an estimation of exposure dose from one source only. All relevant sources of exposure from the hazardous waste site and all possible background exposures should be included in the final evaluation of actual exposure.

Dioxin and dioxin-like compounds are known to readily enter the food chain. It has been estimated that about 98% of exposure occurs through food. It should be noted that the average background intake of dioxin and dioxin-like compounds and of all TEQs of TCDD for adults in the general population were estimated as 0.35 pg/kg/day and 1.9 pg/kg/day, respectively (WHO, 1991).

Further, it is important to consider the background level of dioxin and dioxin-like compounds in contaminated soil. The U.S. background TCDD soil levels ranged from nondetected to 10 ppt in industrialized areas of groups of midwestern and mid-Atlantic states (Nestrick et al., 1986).

Exposure from Soil by Different Routes

Kimbrough et al. (1984) estimated that the lifetime uptake of TCDD from soil will consist of 95% from soil ingestion, 3% from soil dermal exposure (assuming 1% dermal absorption), and 2% from inhalation. Paustenbach et al. (1986) indicated that the 1% dermal absorption proposed for TCDD-contaminated soil may be too high. Similarly, he further lowered the estimates of inhalation intake, speculating that 2% from inhalation may be too high.

Unless indicated otherwise by the specific on-site circumstances, exposure by routes other than oral can be considered insignificant.

Use of Body Burdens to Compare Health Effects in Humans and Animals

Levels of exposure to dioxin and dioxin-like compounds that produce toxicity in experimental animals cannot be directly compared with levels associated with adverse health effects in humans because most epidemiologic studies do not provide adequate data to estimate the exposures in the studied cohort. However, body burden history can sometimes be estimated from reported serum or adipose concentrations and empirically based assumptions regarding whole-body elimination kinetics. Comparisons between estimated body burdens of dioxin and dioxin-like compounds associated with adverse health effects in experimental animals and humans have shown that humans and animals appear to respond to similar body burdens (DeVito et al., 1995).

By definition, the body burden of a chemical is the total amount of chemical present in the whole body at a particular time (Hodgson et al., 1988). Body burden of a chemical is determined by its toxicokinetics. It has been demonstrated that absorption, distribution, and elimination of dioxin and dioxin-like compounds are congener-specific (Flesch-Janys et al., 1996; Van den Berg et al., 1994). Further, parameters such as increased age of the exposed individual, increased body fat, and smoking may influence toxicokinetics (Flesch-Janys et al., 1996). Assumptions made regarding toxicokinetics of dioxin and dioxin-like compounds may result in limitations of the body burden method.

ATSDR acknowledges that other approaches may be used to estimate internal dose such as the area-under-the-curve (AUC) approach (Aylward et al., 1996). AUC is the total area under the curve that describes the concentration of a chemical in the systemic circulation as a function of time (from zero to infinity). AUC is equal to external dose divided by clearance (i.e., elimination rate divided by concentration in body fluid). As some authors have speculated (DeVito et al., 1995), it is possible that, in addition to dose and body burden, length of exposure may also play a significant role in the toxicity of dioxin and dioxin-like compounds. As such, it may be advantageous in some instances to use the AUC method. However, since information about length of exposure and external dose is often missing or inaccurate, the use of body burdens remains the method of choice to describe dose-response relationship. The body burden approach is employed by other ATSDR programs (e.g., in epidemiologic studies executed by the Division of Health Studies), by other U.S. governmental agencies (EPA, FDA), and by international agencies (WHO, IARC).