Attachment A

Petition Letter to ATSDR dated May 1, 2001

John Steward
Draft response due
OHAC 5/24/01
Due OAA 5/30/01

May 1, 2001

Dr. Henry Falk
Assistant Administrator
Agency for Toxic Substances and Disease Registry (ATSDR)
1600 Clifton Road, NE (E28)
Atlanta, GA 30333

Dear Dr. Falk,

We are writing on behalf of our organizations to petition for a public health assessment of the population of Midland, Michigan, because of chronic and serious dioxin contamination. The primary source of this contamination is the Dow Chemical Company.

Our petition is prompted by the following facts, which have emerged over the last two decades:

- Results of soil sampling by the state Department of Environmental Quality (DEQ) in Midland have been surprising, and alarming. Although the state's residential cleanup criteria for dioxins in soil is 90 parts per trillion, of 37 samples taken in the community in 1996, almost a third had dioxin above that level. The areas that exceeded the residential cleanup standard included two elementary schools, an intermediate school, a high school and parks. **These are areas where the public has access and children play.** After release of these results, DEQ promised to resample community areas and determine potential human exposures.

- Instead of carrying through on its commitment, DEQ agreed with Dow's suggestion to use soils inside Dow's corporate center as a "surrogate" for the community. Levels found in 1998 sampling at the corporate center ranged from 66 to 476 parts per trillion, with an average of 136 parts per trillion. One particularly high dioxin hot spot was adjacent to a residential area east of the Dow facility.

- DEQ and Dow *still* refuse to keep commitments to characterize human exposures to dioxins and take appropriate protective actions – more than four years after the first sampling was done.

- There are other routes of exposure to dioxins in Midland. Dioxin contamination of fish in the Tittabawasee River below Midland is chronically high. According to the *Michigan Fish Contaminant Monitoring Program: 2000 Annual Report* issued by DEQ this winter, dioxin TEQ concentrations exceeded the "trigger level" for fish consumption warnings in all 10 carp collected in 1999 and in all 11 carp collected since 1992, and in 2 of 5 smallmouth bass. As a result, the state has tightened its advisory to warn against eating more than 1 meal per week

for smallmouth bass from the river due to dioxin, and advises that women and children eat no smallmouth basis from the river due to elevated levels of dioxins and PCBs.

This data is simply the latest in a long line of disclosures about dioxin contamination of the community. For example, a 1985 multi-media risk assessment by the U.S. Environmental Protection Agency pointed to birth defects and cancer data suggesting elevated health effects in the Midland community, noted that the highest levels of dioxin in the nation were found in Tittabawasee River fish, and called for a comprehensive health study. To date, no such study has ever been done. Further, rather than taking action to protect the public from the serious soil contamination documented in the two most recent rounds of soil testing, the State of Michigan has continued to engage in private discussions with Dow Chemical Company about how to manage public relations. Despite repeated requests from our organizations for an independently-funded, state-commissioned health study and a plan to protect citizens from exposure to excessive levels of dioxins, the state has taken no such action.

It is abundantly clear that significant levels of dioxins and other hazardous materials, including PCBs, are present in the Midland community and in adjacent communities, where contaminants are transported from Dow via water and air. These contaminants may be ingested through fish, consumed in other food, absorbed through dermal contact with soils, and inhaled. The science supporting the link between dioxins and human health effects is strong and growing. It is time for a public health assessment by ATSDR and appropriate protective actions by federal, state and local agencies to prevent further exposures to dioxin and to study health impacts in the community.

Sincerely,

Attachment B

Petition Scoping Report for Dow Chemical Company Midland

Petition Scoping Report
August 31, 2001

Site/City/State: Dow Chemical Company/Midland/Michigan
Region: 5
Scoping Team:

A. Petitioner's Concern(s)

- Dioxins, reported as total equivalent concentrations (TEQs) of 2,3,7,8-TCDD, have been detected in soil in Midland at concentrations above the Michigan Department of Environmental Quality residential cleanup criterion. Levels of dioxins detected in soil adjacent to the eastern perimeter of the Dow plant site and along a road-way (haul route) in the community exceed 1 ppb.
- Dioxins have been detected in fish taken from the Tittabawassee River. Levels detected exceed the State of Michigan trigger levels for fish consumption warnings. In 1985, the U.S. EPA noted that the highest national levels of dioxins in fish were found in the Tittabawassee River.
- In 1985, the U.S. EPA "called for a comprehensive health study" of dioxin exposures and the resulting health effects in the Midland community. No such comprehensive study has ever been performed.

B. Brief Site Background

The Dow Chemical, founded in 1897, operates a chemical manufacturing facility in the city of Midland, Michigan. The facility encompasses approximately 1900 acres on the southern perimeter of the city. The Tittabawassee River forms the southern boundary of the facility and flows east to the Saginaw Bay of Lake Huron.

Chemicals produced at the Midland plant include; styrene, butadiene, picric acid, mustard gas, Saran wrap, Styrofoam, Agent Orange, napalm, and various pesticides including Dursban and 2,4,5-T. Chlorophenol production began in 1915. Wastes generated from this process were initially disposed of in 600 acres of on-site waste ponds. During high flow periods in the early 1900's, wastes from these ponds would be released to the Tittabawassee River. Dow currently operates it's own wastewater treatment plant on-site.

Two rotary kiln incinerators are used for treatment of liquid and solid hazardous and non-hazardous wastes generated from manufacturing activities at the facility. Ambient air dispersion modeling and monitoring indicates that the north-eastern quadrant of the city of Midland have been affected by emissions from the incinerators.

C. Key Previous Actions Related To The Site

The Dow property is currently part of the RCRA corrective action program delegated by the U.S. EPA to the MDEQ Waste Management Division. The EPA sampled soil in the city of Midland in the 1980's and found elevated concentrations of 2,3,7,8-TCDD. The EPA recommended additional sampling in the future to monitor levels of dioxins in the community. In 1996, the MDEQ took additional soil samples from public properties such as parks and school yards and found total dioxins (TEQ) at concentrations exceeding the Michigan residential cleanup criterion for soil. The Dow plant site, it's northeastern perimeter, and a community road-way leading from the Dow plant to a landfill were also sampled. Concentrations at the plant perimeter and on the road-way exceeded 1 ppb. In 1998, as a follow-up alternative to additional community sampling, the Dow Company and the DEQ agreed to sample the Dow Corporate Center property as a surrogate for the community. Levels of TEQs detected at the Corporate Center ranged from 77-583 parts per trillion (ppt).

No public health assessment has been conducted by either the MDCH or the ATSDR.

D. **Public Health Issue(s)**

Table 1. Levels of total dioxins detected in soil in the city of Midland.

Soil Samples Location	Range of TEQ detected in ppt	DEQ Cleanup Criterion in ppt	ATSDR Chronic Soil EMEMG for a Child in ppt	ATSDR Chronic Soil EMEMG for an Adult in ppt	ATSDR Action Level for TCDD
Northeast Plant Perimeter	6 - 1068	90	50	700	1000
Road-Way (Haul Route)	10 - 2663	90	50	700	1000
Dow Corporate Center	77 - 583	90	50	700	1000
Northeast Quadrant of Midland	22 - 598	90	50	700	1000

Table 2. Levels of total dioxins (TEQ) detected in fish in the Tittabawassee River downstream of Midland.

Date	Range of 2,3,7,8-TCDD in ppt	Range of TEQ in ppt	MDCH Advisory Trigger in ppt
1976 - 1980	3 - 695	NA	10
1983 - 1989	1.1 - 530	1.11 - 10.91	10
1990 - 1999	1 - 209	4.56 - 73.90	10
2000 -	Data pending	Data pending	10

Demographics

The city of Midland is the county seat of Midland County, Michigan and encompasses an area approximately 28 square miles. The population of Midland was approximately 38,090 in 1990. Twenty five percent of the population in 1990 were children under the age of 17 years.

Previous Health Studies

At the request of the MDEQ Air Quality Division (AQD) and in support of the AQD review of an application made by the Dow Company for an air quality permit for a new incinerator, the MDCH performed a statistical analysis of cancer incidence for zip codes 48640 and 48642, Midland County, and Bay County. This analysis showed that the 1994 through 1998 age-adjusted incidence rate for all cancers combined in zip code 48640, which includes the Dow plant site, was significantly higher than the corresponding rates for all white residents in Midland County, Bay County, and the State of Michigan. Incident rates were also elevated in this zip code for lung and prostate cancer. No elevations in cancer rates were indicated for zip code 48642. (see attachment)

E. **Exposure Pathways**

Pathway	Source of Contaminant	Contaminant and Level	Environmental Media	Exposure Point	Exposure Route	Exposed Population	Time Frame
Direct Contact with Soil	Incinerator Emissions	Dioxins and Furans 6 - 2663 ppt	Soil	Soil in the city of Midland	Incidental Ingestion Dermal Contact Particulate Inhalation	Residents of Midland	Past Presen Future
Fish Consumption	Release to Surface Water	Dioxins and Furans	Fish 1.1 - 73.9 ppt	Tittabawassee River	Ingestion	Anglers and their families	Past Presen Future

Level of Community Interest (*Difficult to gauge at this time. The Michigan Environmental Council, a well-organized environmental group is one of the petitioners. However, Midland is a corporate town and support for the company is high)*

___X___ High — Large numbers of inquiries about the site/release; well attended meetings about a site/release; the involvement of national, state, and local environmental activist groups, and community groups that are well-organized; extensive environmental, health and/or political interest and extensive national, state and local media coverage.

___X___ Medium — Involvement of the petitioner and community groups without the involvement of national, and state environmental activist groups; some national or state environmental, health and/or political interest; only local media coverage.

_____ Low — Involvement of the petitioner; no community, environmental, health, or political interest; no media coverage.

F. **Decision Criteria**

2.1 Are the location, concentration, and toxicity of the hazardous substances related to the petition, site, or release possibly of public health concern?

Yes, levels of dioxins detected in soil in the city of Midland and in fish in the Tittabawassee River downstream of Midland exceed health-based comparison values. Dioxin and related compounds are believed to cause both carcinogenic and noncarcinogenic human health effects at extremely low levels of exposure.

2.2 Is there an exposed or potentially exposed population as indicated in the petition and as determined by evaluating the human exposure pathways for the hazardous substance release(s)?

Yes, dioxins are present in soil throughout the city of Midland. More than 38,000 people live in the city, 25% of which are children under the age of 17. The Tittabawassee River is a valuable State of Michigan fishery resource and is heavily utilized both by the residents of Midland and by other communities down river.

2.3 Is there a plausible relationship between possible human exposure to a release of hazardous substances and community health concerns or adverse health outcomes?*

Yes, the U.S. EPA, the International Agency for Research on Cancer, and the National Toxicology Program have determined that exposure to dioxins is associated with elevated rates of all cancers combined as well as several particular cancers including lung and soft tissue sarcoma. Elevated incidence rates of all cancers combined, lung and prostate cancer have been detected in the city of Midland. Additional information is needed to determine if exposure to dioxins is related to other health effects in the population of Midland and the surrounding communities.

G. **Recommendation:**

The scoping team recommends:

____	No further action	__X__	Further characterization
__X__	Public Health Consultation/SRU	__X__	Public Health Assessment
__X__	Health Education	__X__	Exposure Investigation

____ *Refer as a Public Health Consultation to a toxicologist, epidemiologist or physician for determination of plausible relationship between possible human exposure to a release of hazardous substances and community health concerns or adverse health outcomes, if relationships are not readily available utilizing the tox. profiles.

____ Referral to:

Attachment C

ATSDR Letter to Petitioners for Dow Midland site dated November 2, 2001

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Agency for Toxic Substances
and Disease Registry
Atlanta GA 30333

November 2, 2001

In May 2001, you wrote to the Agency for Toxic Substances and Disease Registry (ATSDR), about the Dow Chemical Company, Midland, Michigan and dioxin contamination. ATSDR acknowledged your letter to be a petition for a public health assessment. The following outlines ATSDR's response to your petition.

After reviewing the public health issues and community concerns about potential dioxin contamination and the Dow Midland facility, ATSDR has found a reasonable basis to prepare public health consultations to address the concerns associated with the Dow facility. The public health consultations will review and summarize the existing environmental and health data for dioxin concentrations in soils in the Midland community and in fish found in community streams. The consultations will evaluate possible ways that people could be exposed to harmful substances, document and evaluate community health concerns, state health-based conclusions, and make recommendations. We believe that the health consultations will provide timely, appropriate responses to the concerns.

ATSDR maintains a cooperative agreement with the Michigan Department of Community Health (MDCH), under which MDCH conducts public health assessments and other environmental health activities in Michigan. ATSDR has requested that MDCH complete the public health consultations and release them for public review in fiscal year 2002, which began October 1, 2001. MDCH has a talented staff with a good track record for successfully conducting public health evaluations, and they understand the needs of Michigan communities. ATSDR will review MDCH's work and provide technical support as needed. We have enclosed a fact sheet about public health consultations.

Thank you for referring your concerns to ATSDR. We welcome your comments about this response and the planned public health consultations. If you have questions about our proposed plan of action, please contact Dr. Mark Johnson, ATSDR Senior Regional Representative, at telephone (312) 886-0840, or Alan Yarbrough, ATSDR Technical Project Officer, at telephone (404) 498-0427. Dr. Linda Larsen, MDOH, may be contacted at (517-335-8566). Community members may also contact ATSDR by calling our toll-free telephone number, 1-888-42-ATSDR (1-888-422-8737).

Sincerely yours,

Robert C. Williams, P.E., DEE
Assistant Surgeon General
Director, Division of Health Assessment and Consultation

Enclosure

cc:
Linda D. Larsen, Ph.D.
Michigan Department of Community Health

Attachment D

Dioxin and Dioxin-Like Compounds in Soil,
Part 1: ATSDR Interim Policy Guideline

Toxicology and Industrial Health, Vol. 13, No. 6, 1997 759

DIOXIN AND DIOXIN-LIKE COMPOUNDS IN SOIL, PART I: ATSDR INTERIM POLICY GUIDELINE

CHRISTOPHER T. DE ROSA, DAVID BROWN,* ROSALINE DHARA, WOODROW GARRETT, HUGH HANSEN, JAMES HOLLER, DENNIS JONES, DENISE JORDAN-IZAGUIRRE, RALPH O'CONNOR, HANA POHL, AND CHARLES XINTARAS

Agency for Toxic Substances and Disease Registry
U.S. Department of Health and Human Services
Atlanta, Georgia

PURPOSE

The Agency for Toxic Substances and Disease Registry (ATSDR) has adopted this interim policy guideline to assess the public health implications of dioxin and dioxin-like compounds in residential soils near or on hazardous waste sites. These compounds include

- 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD)
- Related chlorinated dibenzo-*p*-dioxins (CDDs)
- Chlorinated dibenzofurans (CDFs)
- Other structurally related groups of chemicals from the family of halogenated aromatic hydrocarbons.

These substances are defined under the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA), as amended, commonly known as Superfund. This interim policy guideline will provide a clear and consistent understanding of ATSDR's current approaches and judgments regarding hazards posed by the presence of TCDD and its less toxic dioxin-like congeners, the CDDs and CDFs, in residential soils. Likely users of this interim policy guideline include:

- ATSDR and state-based health assessors
- ATSDR partners including relevant federal, state, and local health and environmental entities
- Concerned community groups.

1. Address all correspondence to: Christopher T. De Rosa, Ph.D., Director, Division of Toxicology, Agency for Toxic Substances and Disease Registry, Mailstop E-29, 1600 Clifton Road, NE, Atlanta, GA 30333. Tel.:(404)639-6300. Fax:(404)639-6315. E-mail:cyd0@cdc.gov.

2. Abbreviations: ATSDR, Agency for Toxic Substances and Disease Registry; CDDs, chlorinated dibenzo-*p*-dioxins; CDFs, chlorinated dibenzofurans; CERCLA, Comprehensive Environmental Response, Compensation, and Liability Act of 1980; EMEG, environmental media evaluation guide; FDA, U.S. Food and Drug Administration; MRL, minimal risk level; TCDD, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin; TEF, toxicity equivalency factor; TEQs, toxicity equivalents.

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

4. Note: *65 Bulkley Avenue North, Westport, CT 06880.

5. Reprinted from the *Journal of Clean Technology, Environmental Toxicology and Occupational Medicine*, Vol. 6, No. 2, 1997.

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INTERIM POLICY GUIDELINE

This interim policy guideline is based on a current understanding of the toxicology and epidemiology associated with TCDD and its congeners (see "Background" section) and on exposure potential when soil is the primary medium of interest.

This guidance is consistent with the Dioxin and Dioxin-Like Compounds in Soil, Part II: Technical Support Document for ATSDR Interim Policy Guideline (De Rosa et al., 1997) and with the ATSDR Public Health Assessment Guidance Manual (ATSDR, 1992). They explain how to use comparison values to select contaminants for further evaluation and then draw conclusions about the public health implications of the contaminants. Assessments of public health implications are based on considerations of site-specific factors affecting the extent and characteristics of exposure and on the toxicology and epidemiology of the compounds selected for evaluation.

This guidance for dioxin and dioxin-like compounds is unique because of the potency of TCDD itself, and the need to consider the total potency of all dioxin and dioxin-like compounds detected in soil. The toxicity of a dioxin-like compound is commonly referred to in terms of its dioxin toxicity equivalency factor (TEF). See "Background" section for further information.

These guidelines and procedures apply to human exposure for direct ingestion of soils contaminated with dioxin and dioxin-like compounds in residential areas and may not be appropriate for other exposure scenarios. The guidance will be evaluated in view of new data that may become available. The science basis for the guidance is outlined in the "Background" discussion.

Step 1. Screening for contaminants of concern

Review soil sampling data and compare levels against dioxin comparison values (environmental media evaluation guide or EMEG for children) that are not site-specific. If one or more soil sampling values exceed the screening value of 50 parts per trillion (ppt) of toxicity equivalents (TEQs), further site-specific evaluations are needed as described next and in Table 1.

If samples exceed this screening value, then ATSDR generally assumes that further evaluation is required. However, even if samples are below these values, ATSDR policy states that it may still be necessary to conduct a more detailed site-specific evaluation under the following conditions:

- community health concerns
- health assessor's concerns about other combinations of contaminants.

Step 2. Evaluating potential exposure pathways

Further evaluation includes the most critical aspect of health hazard evaluations, that is, the determination of likelihood, extent, and duration of exposure of populations. Thus, the health assessor uses the following to determine the existence of a potential or completed exposure pathway—past, present, or future:

- site visits and observations
- detailed review of data packages for land use scenarios, contaminant locations, and site locations
- evaluation of receptor populations and potential points of contact.

If a completed or potentially completed exposure pathway is identified, then the extent of exposure and public health implications are further evaluated.

Site-specific exposure scenarios based on site-specific factors are evaluated in conjunction with relevant toxicologic, epidemiologic, and medical information. This involves assessing site-specific information about the likelihood, frequency, routes, and levels of exposure to contaminants, and the populations that are likely to be exposed.

Where estimated levels of exposure in soil fall in the range of greater than 50 ppt to less than 1 part per billion (ppb) TEQs (Table 1), a weight-of-evidence approach is recommended to evaluate the exposure and the public health implications of the exposure.

Health assessors must ask the following questions:

- How extensive is the contamination?
- Is the contamination isolated or widespread?
- Is the contamination in surface soils or areas easily accessible to children or adults? Is it in areas with no vegetation or in any other areas?
- At this site, how often (daily, weekly, monthly) and for what length of time (months, years, lifetimes) would exposures be likely to occur?

Many of these estimates depend on professional judgment and experience regarding the likelihood of exposures from soils in different kinds of sites. For further information on the evaluation process see ATSDR (1992).

Interpretation of Health Guidance Values

The policy incorporates information on exposure potential from residential soils and residential exposure scenarios. It should be noted that the levels (in TEQs) $\leq$ 50 ppt (0.05 ppb), $>$ 0.05 ppb but $<$ 1 ppb, and $\geq$ 1 ppb in residential soils are guidance values and should not be construed to indicate that actual health effects will occur. The policy provides a protective framework for evaluating the health implications of exposures to dioxin and dioxin-like compounds in residential soils on a site-specific basis.

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 ≤ 50 ppt (0.05 ppb) TEQs	EVALUATION LEVELS > 0.05 ppb but < 1 ppb TEQs	ACTION LEVEL** ≥ 1 ppb TEQs
• 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: • Bioavailability • Ingestion rates • Pathway analysis • Soil cover • Climate • Other contaminants • Community concerns • Demographics • Background Exposures	Potential public health actions considered, such as: • 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.

Step 3. Defining public health implications/actions

Where exposures to concentrations in residential soils exceeding 1 ppb TEQs are significant, ATSDR health assessors should consider judging the site a public health hazard and consider site-specific public health recommendations/actions to prevent or interdict exposures (Table 1).

BACKGROUND FOR INTERIM POLICY GUIDELINE

Dioxin and Dioxin-Like Compounds

Dioxin and dioxin-like compounds are structurally related groups of chemicals from the family of halogenated aromatic hydrocarbons. Depending on the number of chlorine-substituted positions, there are several congeners in each group. The most toxic and the most studied congener is TCDD.

TEFs were developed to compare the relative toxicity of individual dioxin-like compounds to that of TCDD (Tables 2 and 3). This comparison is based on the assumption that dioxin and dioxin-like compounds act through the same mechanism of action. The TEF for TCDD is defined as one, whereas TEF values for all other dioxin-like compounds are less than one. TEQs are used to assess the risk of exposure to a mixture of dioxin-like compounds. A 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 TEF_i for that compound. The total TEQs is the sum of the TEQs for each of the congeners in a given mixture:

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

Adverse Health Effects

Studies in animals demonstrated a wide range of effects associated with dioxin exposure including death, cancer, and wasting, as well as hepatic, immunologic, neurologic, reproductive, and developmental effects. In contrast to laboratory results, direct exposure information is not available in human studies; therefore, body burden is used as a surrogate. Body burdens in some animal studies were in the same range as those associated with adverse health effects in human studies. For more information, see Technical Support Document for ATSDR Interim Policy Guideline: Dioxin and Dioxin-Like Compounds in Soil (ATSDR, 1997). These results underscore the need for research to elucidate the toxicity at low doses to human populations and to evaluate exposures in at-risk populations (see Appendix 1) in view of total body burdens of dioxin and dioxin-like compounds.

TABLE 2. 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

[a]Any isomer that contains chlorine in the 2,3,7,8-positions

CDDs = chlorinated dibenzo-*p*-dioxins; CDFs = chlorinated dibenzofurnas; TCDD = tetrachlorodibenzo-*p*-dioxins.

Source: derived from EPA (1989).

TABLE 3. Recommended Toxicity Equivalency Factors (TEFs) for Dioxin-Like PCBs

PCB	WHO proposed interim values[a]	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		

[a]Interim 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).

Screening Level for Dioxin and Dioxin-Like Compounds in Soil

While identifying levels of potential concern to human health, ATSDR considers a spectrum of contaminant concentrations. In general, ***screening levels*** are concentrations used to select contaminants of concern at hazardous waste sites that are taken forward in the health assessment process for further evaluation (screening levels are also called comparison values; see Appendix 1 - Glossary).

A minimal risk level (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 over a specified duration and route of exposure. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors and others to identify contaminants and potential health effects that may be of concern at hazardous waste sites. The intermediate-duration oral MRL of 1 picogram/kilogram/day or pg/kg/day for TCDD (ATSDR, 1989) was based on reproductive effects in rats. The intermediate-duration oral MRL was also adopted as a chronic oral MRL. Based on this value, an EMEG of 50 ppt (0.05 ppb) TCDD, which is equivalent to 50 ppt (0.05 ppb) TEQs, was derived for exposure from contaminated soil. Uncertainty factors of 1000 (total) were used in the calculations of the MRL (for further details, see Appendix 3 of the Technical Support Document). Based on a review of more recent literature, ATSDR scientists conclude that the MRL of 1 pg/kg/day is approximately two orders of magnitude below the noncancer health effect levels observed in recent studies. This is also true for cancer effect levels.

Evaluation Levels for Dioxin and Dioxin-Like Compounds in Soil

Evaluation levels are concentrations > 50 ppt (0.05 ppb) but < 1 ppb TEQs at which site-specific factors, including, but not limited to, bioavailability, ingestion rates, pathway analysis, soil cover, climate, other contaminants, community concerns, demographics, and background exposure, are considered in a deliberative process to assess the nature and extent of contamination and its impact on the community. Such an evaluation process may prompt further assessment at the next level where actions are considered. The evaluation levels are to be used as a framework to guide procedures for that judgment process. Thus, judgments in the evaluative phase are linked to actions where consideration is given to interventions from a public health perspective.

Action Level for Dioxin and Dioxin-Like Compounds in Soil

Action levels are concentrations of chemicals at which consideration of action to interdict exposure occurs; 1 ppb TCDD in residential soil was identified by Kimbrough et al. (1984) as a "level of concern," and recommended as "a reasonable level to begin consideration of action to limit exposure." 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). With the advancement of knowledge about dioxin-like chemicals and their assumed common mechanism of toxicity, the TEQs were introduced into the risk assessment process. Since then, 1 ppb of total dioxins (expressed as TEQs) in soil has been used as an action level by ATSDR.

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 a typical default value of 70 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. This value is marginally lower, but from a risk assessment perspective, it is essentially equivalent to the ATSDR media-specific screening level/comparison value (EMEG) of 50 ppt.

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 health 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. 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 to be protective of human health. The EMEG of 50 ppt (0.05 ppb) is at the low end of the range reflecting currently recognized areas of scientific uncertainty; this range is 50–50 000 ppt (or 0.05–50 ppb), which is based on the 1000-fold uncertainty factor used to derive the MRL.

CONCLUSIONS

ATSDR concludes that the action level of 1 ppb (TEQ) for dioxin and dioxin-like compounds, when coupled to a site-specific context of evaluation for the range > 50 ppt (0.05 ppb) to < 1 ppb TEQs in residential soil, is protective of public health and continues to represent a level at which consideration of health action to interdict exposure, including cleanup, should occur. This conclusion is based on ATSDR's review and evaluation of

- more recent experimental and epidemiologic research findings
- ATSDR's historical use of the term "action level"
- the range of health guidance values developed by ATSDR including the MRL and EMEG
- the limitations and uncertainties of ATSDR's health guidance values and the scientific data on which these values are based.

ATSDR considers this action level to be both reasonable and protective for the following reasons:

- ATSDR's MRL is approximately two orders of magnitude below effect levels in experimental and epidemiologic studies.
- Cancer risk-specific doses and screening values for end points other than cancer are essentially equivalent from a risk assessment perspective.

WHERE TO FIND MORE INFORMATION

For more information on the historical and scientific background of dioxin in soil values, their proper use, and data on limitations associated with these numbers, please refer to Dioxin and Dioxin-Like Compounds in Soil, Part II: Technical Support Document for ATSDR Interim Policy Guideline (De Rosa et al., 1997).

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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-*p*-dioxins
BDFs	Brominated dibenzofurans
CDDs	Chlorinated dibenzo-*p*-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-*p*-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-*p*-dioxins (CDDs) and certain chlorinated dibenzofurans (CDFs), polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs), brominated dibenzo-*p*-dioxins (BDDs), and brominated dibenzofurans (BDFs).
Dioxins	A term used interchangeably with chlorinated dibenzo-*p*-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-*p*-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:

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

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

CHRISTOPHER T. DE ROSA, DAVID BROWN,* ROSALINE DHARA, WOODROW GARRETT, HUGH HANSEN, JAMES HOLLER, DENNIS JONES, DENISE JORDAN-IZAGUIRRE, RALPH O'CONNOR, HANA POHL, AND CHARLES XINTARAS

Agency for Toxic Substances and Disease Registry
U.S. Department of Health and Human Services
Atlanta, Georgia

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1. Address all correspondence to: Christopher T. De Rosa, Ph.D., Director, Division of Toxicology, Agency for Toxic Substances and Disease Registry, Mailstop E-29, 1600 Clifton Road, NE, Atlanta, GA 30333. Tel.:(404)639-6300. Fax:(404)639-6315. E-mail:cyd0@cdc.gov.

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 dibenzofurnas; 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, polybrominted 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.

4. Note: *65 Bulkley Avenue North, Westport, CT 06880.

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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
• The EMEG for TCDD is 50 ppt	Evaluation of site-specific factors, such as:	Potential public health actions considered, such as:
• This is based on an MRL of 1 pg/kg/day for TCDD (ATSDR, 1989).	• Bioavailability • Ingestion rates • Pathway analysis	• Surveillance • Research • Health studies
• For screening purposes 50 ppt TCDD is assumed to be equivalent to 50 ppt TEQs	• Soil cover • Climate • Other contaminants • Community concerns • Demographics • Background Exposures	• 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 (Birnbaum, 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:

- 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).

- 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.

- 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

- 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

- 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

- That ATSDR and EPA continue their efforts to assure earlier consultation at sites

- 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

- 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-*p*-dioxins
BDFs	Brominated dibenzofurans
CDDs	Chlorinated dibenzo-*p*-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-*p*-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-*p*-dioxins (CDDs) and certain chlorinated dibenzofurans (CDFs), polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs), brominated dibenzo-*p*-dioxins (BDDs), and brominated dibenzofurans (BDFs).
Dioxins	A term used interchangeably with chlorinated dibenzo-*p*-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-*p*-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:

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

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

[a]Any 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		

[a]Interim 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).

APPENDIX 3 - MRLs AND EMEGs FOR TCDD

CURRENT MRLs

ATSDR published the *Toxicological Profile for TCDD* (ATSDR, 1989). Minimal risk levels (MRLs) listed in the profile were for acute, intermediate-duration, and chronic oral exposures (see Table 3-1).

Acute Oral MRL

The acute oral MRL of 100 pg/kg/day was based on hepatotoxic effects in guinea pigs that were observed following administration of a single gavage dose of 0.1 µg/kg TCDD (Turner and Collins, 1983).

An uncertainty factor of 10 was used for extrapolation from animals to humans, a factor of 10 for human variability, and a factor of 10 for the use of a lowest-observed-adverse-effect level (LOAEL).

Intermediate Oral MRL

The LOAEL of 0.001 µg/kg/day was considered for derivation of the intermediate-duration oral MRL of 1 pg/kg/day. At this exposure level, dilated pelvises and changes in gestational index were observed in rats (Murray et al., 1979) and abortions were reported in monkeys (Allen et al., 1979).

An uncertainty factor of 10 was used for extrapolation from animals to humans, a factor of 10 for human variability, and a factor of 10 for the use of a LOAEL.

Chronic Oral MRL

The intermediate-duration oral MRL of 1 pg/kg/day was also adopted as the chronic oral MRL.

PROPOSED MRLs

The *Toxicological Profile for CDDs* was in a draft stage in 1993/1994. The internal MRL workgroup proposed oral MRLs for TCDD (see Table 3-1).

Acute Oral MRL

The acute oral MRL of 20 pg/kg/day was based on the LOAEL of 0.01 µg/kg/day TCDD that induced suppressed serum complement activity in B6C3F1 mice exposed to 14 daily doses administered by gavage-in-oil vehicle (White et al., 1986).

An uncertainty factor of 10 was used for extrapolation from animals to humans, a factor of 10 for human variability, and a factor of 10 for the use of a LOAEL. Furthermore, a modifying factor of 0.5 was applied to adjust for the difference in higher bioavailability of TCDD from gavage-in-oil vehicle than from food or soil.

Intermediate Oral MRL

The **intermediate-duration oral MRL** of 7 pg/kg/day was based on a no-observed-adverse-effect level (NOAEL) of 0.0007 µg/kg/day TCDD for decreased thymus weight in guinea pigs exposed for 90 days in their feed (DeCaprio et al., 1986). The LOAEL in the study was 0.005 µg/kg/day.

An uncertainty factor of 10 was used for interspecies extrapolation and a factor of 10 for human variability. The NOAEL for deriving an intermediate-duration exposure MRL is also supported by the same level NOAEL for liver effects in the DeCaprio et al. study. The liver effects reported at higher levels consisted of hepatocellular inclusions and hypertriglyceridemia.

Chronic Oral MRL

A **chronic oral MRL** of 0.7 pg/kg/day was based on a LOAEL of 0.0002 µg/kg/day TCDD in the feed of monkeys that resulted in mild learning and behavioral impairment in their offspring (Bowman et al., 1989).

An uncertainty factor of 3 was used for the use of a minimal LOAEL, a factor of 10 was used for interspecies extrapolation, and a factor of 10 for human variability.

Environmental media evaluation guides (EMEGs) are media-specific comparison values that are used to select contaminants of concern at hazardous waste sites.

EMEGs are derived for air, water, and soil environmental media. They are based on inhalation and oral MRLs for air and water/soil exposures, respectively. The methodology and formula for derivation of EMEGs are described in ATSDR's Public Health Assessment Guidance Manual (ATSDR, 1992).

EMEGs are estimates of external dose. They do not provide data on how much of the dose is actually absorbed. No EMEGs are available for the dermal exposure route.

EMEGs based on these MRLs are presented in Tables 3-2a and 3-2b.

TABLE 3-1. MRLs* for TCDD

Year	Exposure duration	MRL* in pg/kg /day	UF LOAEL /NOAEL	UF inter-species	UF sensitivity	MF**	End point	Study
1989	acute	100	10	10	10		LOAEL for hepatotoxicity guinea pigs	Turner and Collins, 1983
1989	inter-mediate	1	10	10	10		LOAEL for abortions and other reproductive, developmental effects rats, monkeys	Murray et al., 1979 Allen et al., 1979
1989	chronic	1	10	10	10		LOAEL for abortions and other reproductive, developmental effects rats, monkeys	Murray et al., 1979 Allen et al., 1979
1994	acute	20	10	10	10	0.5	LOAEL for suppressed serum complement activity mice	White et al., 1986
1994	inter-mediate	7		10	10		NOAEL for decreased thymus weight; liver toxicity guinea pigs	DeCaprio et al., 1986
1994	chronic	0.7	3	10	10		LOAEL for mild learning and behavioral impairment monkey offspring	Bowman et al., 1989

*The MRL is calculated as MRL = (NOAEL or LOAEL)/(UF x MF), where MRL = minimal risk level (mg/kg/day), NOAEL = no-observed-adverse-effect level (mg/kg/day), LOAEL = lowest-observed-adverse-effect level (mg/kg/day), UF = uncertainty factor (unitless), MF = modifying factor (unitless)
**MF for bioavailability was used in the derivation of an acute MRL (1994)

TABLE 3-2a. EMEGs (in ppb) Based on 1989 TCDD MRLs

Exposure duration	Child	Adult
acute	5	70
intermediate	0.05	0.7
chronic	0.05	0.7

TABLE 3-2b. EMEGs (in ppb) Based on 1994 TCDD MRLs

Exposure duration	Child	Adult
acute	1	14
intermediate	5	5
chronic	0.04	0.5

*The EMEG is calculated as EMEG = (MRL)(BW)/IR, where EMEG = environmental media evaluation guide (mg/kg), BW = body weight in kg (adult = 70 kg; child = 10 kg), IR = soil ingestion rate (mg/day) (adult = 100 mg/day; child = 200 mg/day)

APPENDIX 4 - RECENT HEALTH EFFECTS STUDIES

Introduction

A significant number of toxicological studies have been conducted since the development of the 1 ppb action level for dioxin and dioxin-like compounds in residential soil. Many of these studies have examined human health effects after known or suspected exposure. In addition, in these intervening years, analytical techniques have been perfected to permit determination of very low levels of dioxin and dioxin-like compounds in environmental and biologic media. Significant advances have also been made in assessing possible health effects associated with exposure. This appendix is a synopsis of this more recent information.

Mechanism of Action

Recent studies have indicated that dioxin and dioxin-like compounds act through the same mechanism of action mediated by the Ah receptor, and that responses to their toxicity have been shown to be similar in several species (Birnbaum, 1994; DeVito et al., 1995).

Human Studies

Direct exposure information is generally not available in human studies, and so body burden is used as a surrogate. In this approach, the exposure is estimated from measured body burden, the elimination rate for humans, and the time since the exposure incident. Positive correlations have been observed between dioxin exposure and cancer (Fingerhut et al., 1991; Zober et al., 1990; Manz et al., 1991). More recent studies on cohorts investigated previously confirmed the association between dioxin exposure and higher cancer mortality (Flesch-Janys et al., 1995; Becher et al., 1996; Ott and Zober, 1996). The correlation was dose-dependent and increased with the latency period. IARC (1997) classified TCDD as a Group 1 carcinogen (carcinogenic to humans).

For health end points other than cancer, epidemiologic studies suggest a positive correlation between exposure to TCDD and development of chloracne (Mocarelli et al., 1986; Pazderova-Vejlupkova et al., 1981; Reggiani, 1980; Zober et al., 1990), dermal hyperpigmentation and hirsutism (Poland et al., 1971; Jirasek et al., 1974), elevated hepatic enzyme levels, mainly γ-glutamyl transferase (Mocarelli et al., 1986; May, 1982), and increased risk of diabetes (Sweeney et al., 1992; Table 4-1).

Other studies showed an association between development of subtle health effects (e.g., lower vitamin K levels, mild changes in liver enzymes, decreased neurologic optimality, and subtle changes in hormonal levels) in infants and their exposure to dioxin and dioxin-like chemicals from maternal milk (Pluim et al., 1992, 1994a, 1994b; Huisman et al., 1995; Koopman-Esseboom et al., 1994; Table 4-2). It is important to note that in reviewing the issues surrounding breastfeeding, the World Health Organization has concluded that the risks to infants do not outweigh the positive biologic and psychologic aspects of breastfeeding (Johnson, 1992a).

It has been suggested that dioxin and dioxin-like chemicals have the ability to disrupt endocrine function at low levels of exposure. A recent study of the cohort of people exposed during the Seveso accident indicated an alteration of the human sex ratio in their offspring (Mocarelli et al., 1996). In the 7-year period following the exposure, 26 males versus 48 females were born, but the study was limited by not providing information on sex-related spontaneous abortions in the cohort. A study of occupationally exposed workers reported altered reproductive hormone levels (Egeland et al., 1992). Other studies indicate low-exposure contamination of maternal milk with dioxin and dioxin-like compounds may have an impact on the hypothalamic-pituitary-thyroid regulatory system in newborns (Pluim et al., 1992; Koopman-Esseboom et al., 1994).

Animal Studies

Studies in animals demonstrated a wide range of effects associated with CDDs exposure including mortality, cancer, wasting, and hepatic, immunologic, neurologic, reproductive, and developmental effects (ATSDR, 1989). In support of the findings that showed endocrine system disruption in humans, studies in animals reported that TCDD affects the adrenal (DiBartolomeis et al., 1987; Gorski et al., 1988a, 1988b) and thyroid glands (Hermansky et al., 1988; Hong et al., 1987; Lu et al., 1986; Henry and Gasiewicz, 1987; Rozman et al., 1985) and also alters estradiol (Umbreit et al., 1987), testosterone, and dihydrotestosterone levels (Mebus et al., 1987; Moore et al., 1985).TCDD decreased responsiveness of the ventral prostate to testosterone in male offspring of exposed female rats and inhibited sexual differentiation in the central nervous system without altering sexual dimorphism in estrogen-receptor concentrations (Bjerke et al., 1994; Bjerke and Peterson, 1994). In animal studies, effects have been seen with the lowest doses evaluated, with the most sensitive end point being neurobehavioral changes in the offspring of dioxin-exposed monkeys (Schantz et al., 1992). A summary of critical study results and observed effect levels is presented in Table 4-3.

Body Burdens and Associated Health Effects

Health effects reported from human studies and associated body burdens of TCDD are listed in Table 4-1; these body burdens range from concentrations of 18 to 2,357 ng/kg. As can be seen from a comparison of animal and human studies shown in Table 4-3, body burden concentrations calculated for effect dosage rates in animal studies are in the same range as body burden concentrations associated with health effects in human studies. These results underscore the need for research to elucidate the toxicity of dioxin at low doses to human populations (CCEHRP, 1992) and to evaluate exposures in at-risk populations in view of total body burdens of dioxin and dioxin-like compounds.

Based on this review of more recent data, ATSDR has determined that its MRL of 1 pg/kg/day for TCDD is approximately two orders of magnitude below the health effect levels observed in recent studies. This is also true of cancer effect levels (Kociba et al., 1978). Independently, the Health Council of the Netherlands (1996) reassessed the risk associated with dioxin and dioxin-like compounds based on recent studies and recommended a health-based exposure limit equal to 1 pg/kg/day total TEQs.

ATSDR concludes that the chronic oral MRL of 1 pg/kg/day TCDD is protective of public health based on the fact that the MRL is approximately two orders of magnitude below the effect levels demonstrated experimentally and in epidemiologic studies.

TABLE 4-1. **Health Effects Associated with Exposure to TCDD and Body Burdens in Humans**

Duration of exposure	System	Effect	Body burdens ng/kg body weight	Reference
< 1 year	Dermal	Chloracne in children	2357[a]	Mocarelli et al., 1991
< 1 year	Reproductive	No increased risk of spontaneous abortion	> 24[b]	Wolfe et al., 1995
≥ 15 years	Gastrointestinal	No increased risk of clinical gastrointestinal disease	418[c]	Calvert et al., 1992
≥ 15 years	Hepatic	No increased risk of clinical hepatic disease	418[c]	Calvert et al., 1992
Not specified	Dermal	Chloracne in 5/7 subjects	80.5[d] 18[e]	Schecter et al., 1993
11 years	Dermal	Chloracne	646[f]	Jansing and Korff, 1994
6.5 years	Immunologic	Immunosuppression	156–176[g]	Tonn et al., 1996
≥ 15 years	Neurologic	No increased risk for peripheral neuropathy	418[c]	Sweeney et al., 1993
≥ 15 years	Reproductive	Increased prevalence of high luteinizing hormone and low testosterone levels	31[h]	Egeland et al., 1994
Not specified	Genotoxicity	No chromosome aberrations or sister chromatid exchanges	63-833[i]	Zober et al., 1993
≥ 1 year	Cancer	Increased cancer mortality risk	124–459[j]	Fingerhut et al., 1991
≥ 20 years	Cancer	Increased cancer mortality rate	69–461[k]	Manz et al., 1991

TABLE 4-1. **Health Effects Associated with Exposure to TCDD and Body Burdens in Humans (cont'd)**

[a]Calculated using serum TCDD levels measured shortly after exposure. Body burdens were calculated using body weights of 13 kg for 1–3 year olds, 20 kg for 4–6 year olds, 28 kg for 7–10 year olds, 45 kg for 11-year-old males, and 55 kg for 16-year-old females and body fat percentages of 15% for 0–10 year olds, 15% for 11-year-old males, and 20% for 16-year-old females (ICRP, 1981).

[b]Calculated using the reported mean half-life adjusted serum TCDD level of > 110 ppt and assuming the average worker weighed 70 kg with 22% body fat (DeVito et al., 1995). The authors calculated the half-life adjusted serum TCDD level using a half-life of 7.1 years.

[c]Calculated using the reported mean half-life adjusted serum TCDD level of 1900 pg/g lipid and assuming the average worker weighed 70 kg with 22% body fat (DeVito et al., 1995).

[d]Calculated by averaging the reported individual body burdens divided by the reference body weight of 75 kg for males and 65 kg for females. The authors calculated half-life adjusted serum TCDD levels using the assumption of 75 kg and 65 kg body weights for male and female workers, respectively, and a half-life of 5 years.

[e]Same as footnoted, but using a half-life of 10 years.

[f]Calculated using the reported mean half-life adjusted serum TCDD level of 2935 pg/g blood fat and assuming the average worker weighed 70 kg with 22% body fat (DeVito et al., 1995). The authors calculated the half-life adjusted serum TCDD level using a half-life of 7 years.

[g]Calculated using the reported mean current serum TCDD level of 329.5 pg/g blood lipid. Half-life adjusted serum TCDD level was calculated using a half-life of 11.6 years (Wolfe et al., 1994), background TCDD concentration of 5 ng/kg lipid, and 13–15 years elapsed time. Body burdens were calculated assuming the average worker weighed 70 kg with 22% body fat (DeVito et al., 1995).

[h]Calculated using the reported mean current serum TCDD level of 15 ppt. Half-life adjusted serum TCDD levels were calculated using a half-life of 11.6 years (Wolfe et al., 1994), background TCDD concentration of 5 ng/kg lipid, and 34 years of elapsed time. Body burdens were calculated assuming the average worker weighed 70 kg with 22% body fat (DeVito et al., 1995).

Calculated using the reported mean of current serum TCDD levels of 340–472 ppt (based on lipid content of blood). Half-life adjusted serum TCDD levels were calculated using a half-life of 11.6 years (Wolfe et al., 1994), background TCDD concentration of 5 ng/kg lipid, and 35 years of elapsed time. Body burdens were calculated assuming the average worker weighed 70 kg with 22% body fat (DeVito et al., 1995).

[j]Calculated using the reported mean current serum TCDD level of 233 pg/g lipid. Half-life adjusted serum TCDD levels were calculated using a half-life of 11.6 years (Wolfe et al., 1994), background TCDD concentration of 5 ng/kg lipid, and 35 years of elapsed time. Body burdens were calculated assuming the average worker weighed 70 kg with 22% body fat (DeVito et al., 1995).

[k]Calculated using the reported mean current adipose tissue TCDD level of 296 ng/kg. Half-life adjusted adipose TCDD levels were calculated using a half-life of 11.6 years (Wolfe et al., 1994), background TCDD concentration of 5 ng/kg lipid, and 1–33 years of elapsed time.

TABLE 4-2. **Breast Milk Levels of Total TEQs Associated with Health Effects in Human Infants**

Number of Children	Breast milk levels (mean levels in pg of TEQs per g of milk fat)	Health Effects	References
17	(29.85–92.88)	Late-type hemorrhagic disease of newborns correlated with increased TCDD levels in maternal milk	Koppe et al., 1991
32	29.4 (13.7–62.6)	Decreased vitamin K_1 and decarboxylated prothrombin levels in infants correlated with increased 2,3,7,8-tetraCDF and 1,2,3,6,7,8-hexaCDF levels, respectively, in breast milk at 11 weeks of age	Pluim et al., 1994a
78	> 30.75	Higher CDD and CDF levels in breast milk correlated with higher plasma levels of TSH in infants in 2nd week and 3rd month postnatally	Koopman-Esseboom et al., 1994
104	30.19	Higher CDD and CDF levels were related to reduced neonatal neurologic optimality	Huisman et al., 1995
48	not specified	Higher exposure to CDDs in breast milk was associated with increase in total T cells and lower monocyte and granulocyte counts	Weisglas-Kuperus et al., 1995
35	28.1 (8.7–62.7)	Cumulative intake correlated with ALT and AST plasma activities; inverse correlation was found between cumulative intake and number of platelets at 11 weeks of age	Pluim et al., 1994b
19	37.5 (29.2–62.7) high exposure group	Increased thyroxine levels and increased thyroxine/thyroid binding globulin ratios in a group with higher breast milk exposure as compared to lower exposure group	Pluim et al., 1992
19	18.6 (8.7–28.0) low exposure group	Baseline control values	Pluim et al., 1992

AST = aspartate aminotransferase; ALT = alanine aminotransferase; TEQs = toxicity equivalents; TSH = thyroid-stimulating hormone

TABLE 4-3. **Human Body Burdens and Animal Body Burdens Associated with Health Effects**

Duration of exposure	System	Effect	Body burdens ng/kg body weight	Reference
Studies in humans				
< 1 year	Dermal	Chloracne in children	2357[a]	Mocarelli et al., 1991
Not specified	Dermal	Chloracne in 5/7 subjects	80.5[b] 18[c]	Schecter et al., 1993
11 years	Dermal	Chloracne	646[d]	Jansing and Korff, 1994
6.5 years	Immunologic	Immunosuppression	156-176[e]	Tonn et al., 1996
≥ 15 years	Reproductive	Increased prevalence of high luteinizing hormone and low testosterone levels	31[f]	Egeland et al., 1994
≥ 1 year	Cancer	Increased cancer mortality risk	124-459[g]	Fingerhut et al., 1991
> 20 years	Cancer	Increased cancer mortality rate	69–461[h]	Manz et al., 1991
Studies in animals				
14 days	Immunologic	Suppressed serum complement in mice	74[i]	White et al., 1986
90 days	Reproductive	Decreased litter size in rats	26[j]	Murray et al., 1979
90 days	Immunologic	Decreased thymus weight in guinea pigs	164[k]	DeCaprio et al., 1986
16 months	Developmental	Behavioral alterations in offspring in monkeys	32[l]	Schantz et al., 1992
2 years	Cancer	Liver, lung carcinoma in rats	2976[m]	Kociba et al., 1978
2 years	Cancer	Liver carcinoma in mice	944[n]	NTP, 1972

TABLE 4-3. **Human Body Burdens and Animal Body Burdens Associated with Health Effects (cont'd)**

*Studies which serve as the basis for ATSDR's health guidance values

[a]Calculated using serum TCDD levels measured shortly after exposure. Body burdens were calculated using body weights of 13 kg for 1–3 year olds, 20 kg for 4–6 year olds, 28 kg for 7–10 year olds, 45 kg for 11-year-old males, and 55 kg for 16-year-old females and body fat percentages of 15% for 0–10 year olds, 15% for 11-year-old males, and 20% for 16-year-old females (ICRP, 1981).

[b]Calculated by averaging the reported individual body burdens divided by the reference body weight of 75 kg for males and 65 kg for females. The authors calculated half-life adjusted serum TCDD levels using the assumption of 75 kg and 65 kg body weights for male and female workers, respectively, and a half-life of 5 years.

[c]Same as footnote d but using a half-life of 10 years.

[d]Calculated using the reported mean half-life adjusted serum TCDD level of 2935 pg/g blood fat and assuming the average worker weighed 70 kg with 22% body fat (DeVito et al., 1995). The authors calculated the half-life adjusted serum TCDD level using a half-life of 7 years.

[e]Calculated using the reported mean current serum TCDD level of 329.5 pg/g blood lipid. Half-life adjusted serum TCDD level was calculated using a half-life of 11.6 years (Wolfe et al., 1994), background TCDD concentration of 5 ng/kg lipid, and 13–15 years elapsed time. Body burdens were calculated assuming the average worker weighed 70 kg with 22% body fat (DeVito et al., 1995).

[f]Calculated using the reported half-life adjusted serum TCDD level of > 140 pg/g blood lipid and assuming the average worker weighed 70 kg with 22% body fat (DeVito et al., 1995). The authors calculated the adjusted serum dioxin level using a dioxin half-life of 7.1 years and background dioxin level of 6.08 pg/g blood lipid.

[g]Calculated using the reported mean current serum TCDD level of 233 pg/g lipid. Half-life adjusted serum TCDD levels were calculated using a half-life of 11.6 years (Wolfe et al., 1994), background TCDD concentration of 5 ng/kg lipid, and 35 years of elapsed time. Body burdens were calculated assuming the average worker weighed 70 kg with 22% body fat (DeVito et al., 1995).

[h]Calculated using the reported mean current adipose tissue TCDD level of 296 ng/kg. Half-life adjusted adipose TCDD levels were calculated using a half-life of 11.6 years (Wolfe et al., 1994), background TCDD concentration of 5 ng/kg lipid, and 1–33 years of elapsed time. Body burdens were calculated assuming the average worker weighed 70 kg with 22% body fat (DeVito et al., 1995).

[i] Acute exposure study in mice (White et al., 1986). Assumed parameter values a: = 0.8 (Curtis et al., 1990), $t_{1/2}$ = 11 days (Birnbaum, 1986).

[j] Intermediate-duration exposure study in rats (Murray et al., 1979) Assumed parameter values a: = 0.8 (Curtis et al., 1990), $t_{1/2}$ = 24 days (Van den Berg et al., 1994).

[k] Assumed parameter values for guinea pigs in DeCaprio et al. (1986) study: a = 0.5 (Van den Berg et al., 1994), $t_{1/2}$ = 94 days (Olson, 1986).

[l]The lowest effect level in the current database for chronic-duration exposure. Assumed parameter values for monkeys in Schantz et al. (1992) study: a = 0.8 (value for rats from Van den Berg et al., 1994), $t_{1/2}$ = 391 days (Bowman et al., 1989).

[m]A cancer study in rats. Body burdens calculated in De Vito et al., 1995.

[n]A cancer study in mice. Body burdens calculated in De Vito et al., 1995.

APPENDIX 5 - CHRONOLOGY FOR DIOXIN AND DIOXIN-LIKE COMPOUNDS: HEALTH GUIDANCE VALUES AND POLICY STATEMENTS

1984

R. Kimbrough, H. Falk, and P. Stehr (1984) recommended 1 ppb of TCDD in soil as a level of concern for human health. They also concluded that "One ppb of 2,3,7,8-TCDD in soil is a reasonable level at which to begin consideration of action to limit human exposure for contaminated soil" (emphasis added) (p. 47). However, the authors cautioned not to use this level for every site, but rather to estimate the risk associated with each site according to specific circumstances at the site.

The estimated risk dose was 1.4 pg/kg/day TCDD (a 95% upper bound for a one-in-a-million risk estimate for cancer). The calculations were based on cancer studies in laboratory animals.

1985

EPA derived oral slope factor, q_1^*, of 1.56×10^5 $(mg/kg/day)^{-1}$ for TCDD (EPA, 1985) that represents the mean 95% upper-limit carcinogenic potency factor for humans. Based on this factor, a risk-specific dose of 0.006 pg/kg/day TCDD was calculated.

1989

ATSDR published the *Toxicological Profile for TCDD*. The profile describes the use of toxicity equivalents (TEQs) for assessing exposure to dioxin and dioxin-like compounds. MRLs for TCDD listed in the profile for the acute, intermediate-duration, and chronic exposures were 100 pg/kg/day, 1 pg/kg/day, and 1 pg/kg/day, respectively. Developmental and reproductive end points were the bases for intermediate and chronic duration MRLs. Based on the chronic MRL, the EMEG of 50 ppt is typically used in public health assessments for dioxin contaminated soil.

1990

The Food and Drug Administration (1990) introduced a risk-specific dose of 0.057 pg/kg/day TCDD (a 95% upper bound for a one-in-a-million risk estimate for cancer). The number was based on a linear low-dose extrapolation from the Kociba et al. (1978) cancer study in rats. The value applied to consumption of contaminated food, specifically fish.

1992

The Public Health Service Committee to Coordinate Environmental Health and Related Programs (CCEHRP) recommended, in the Interim Statement on Dioxins, to adopt the FDA risk-specific dose (0.057 pg/kg/day) as the risk-specific level for TCDD equivalents (TEQs).

1992

In a memo to ATSDR senior management, B. Johnson stated that "The Interim Statement, while mentioning FDA's tolerable daily intake of dioxin as 0.057 pg/kg/day, should not be understood to supplant ATSDR's position of 1 ppb of dioxin in residential soil as a soil action level." Consistent with the CCEHRP statement, ATSDR's practice incorporates the TEQ approach.

1993

The *Toxicological Profile for CDDs* was in a draft stage. The internal MRL workgroup met with representatives of other ATSDR divisions and proposed MRLs for TCDD for the acute, intermediate-duration, and chronic exposures as 20 pg/kg/day, 7 pg/kg/day, and 0.7 pg/kg/day, respectively. Developmental effects were the bases for derivation of the chronic MRL.

1995

Pohl et al. (1995) published the "Public health assessment for dioxins exposure from soil" paper.

This paper reviewed more recent findings on the potential health effects of dioxin. Based upon this review, Pohl et al. presented a proposed chronic MRL for TCDD of 0.7 pg/kg/day and a corresponding EMEG of 40 ppt for children.

From a health risk assessment perspective, the EMEG of 40 ppt is not substantially different from the current EMEG of 50 ppt based on the 1 pg/kg/day MRL (ATSDR, 1989). The MRL of 1 pg/kg/day is approximately two orders of magnitude below effect levels demonstrated experimentally or in epidemiologic studies.

APPENDIX 6 - REFERENCES

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