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EPA Seeks Public Input on Interim Guidance for Dioxins in Soil Cleanup Goals

WASHINGTON - The U.S. Environmental Protection Agency (EPA) announced today it is seeking public comment on draft interim preliminary remediation goals (PRGs) for cleanup of dioxins in soil. Today's announcement fulfills a commitment by EPA Administrator Lisa P. Jackson to announce interim cleanup goals by the end of 2009. Dioxins are contaminants that are very widespread in the environment that have been of concern to EPA and the public health community for decades. This action would strengthen EPA's preliminary remediation goals at dioxin contaminated sites.

"While EPA works to complete the dioxin reassessment, this interim guidance will help us make better informed decisions on cleanup alternatives at contaminated sites," said Mathy Stanislaus, assistant administrator for EPA's Office of Solid Waste and Emergency Response. "We are following through on our commitment to use the best available science to help protect human health and the environment."

Dioxins may cause a large number of different health effects, like cancer and reproductive effects. Dioxins are of concern because they are the result of combustion, and are absorbed from the air into the food chain where they can stay for many years.

Currently, EPA's recommended dioxin PRGs are 1,000 part per trillion (ppt) for dioxin in residential soil and a level within the range of 5,000-20,000 ppt in commercial/industrial soil. The draft interim PRGs proposed today are 72 ppt for residential land uses and 950 ppt for commercial/industrial land uses, thus lowering the amount of dioxins levels for residential land uses and commercial/industrial land uses.

In addition, the draft interim PRGs differ from the current dioxin PRGs in that they include consideration of the potential absorption of dioxin through skin exposure. This will provide a tool for site evaluation that was not available when EPA last recommended PRGs for dioxins in soil in 1998.

In 1991, in light of significant new data on the potential human health effects of dioxins, EPA began the development of a comprehensive evaluation of exposure and human health effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), the most toxic of the group of chemicals known as dioxins, and other dioxin-like compounds. This draft dioxins assessment has been through several independent external peer reviews, the latest a 2004 review by a scientific panel convened by the National Academy of Sciences. When the EPA dioxin risk assessment is complete, it will be the agency's scientific foundation for future decision-making about dioxins in the environment.

EPA will be taking public comment on the draft interim PRGs for 50 days following publication in the Federal Register, and anticipates issuing the final interim PRGs in June 2010. Upon

completion of the dioxins reassessment, currently expected by the end of 2010, EPA will consider the need to update the interim PRGs.

More information on the draft recommended interim PRGs and how to comment:
http://www.epa.gov/superfund/policy/remedy/sfremedy/remedies/dioxinsoil.html

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OSWER 9200.3-56

PUBLIC REVIEW DRAFT

DRAFT RECOMMENDED INTERIM PRELIMINARY REMEDIATION GOALS FOR DIOXIN IN SOIL AT CERCLA AND RCRA SITES

Prepared by:

U.S. Environmental Protection Agency
Office of Superfund Remediation and Technology Innovation
Washington, D.C.

December 30, 2009

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LIST OF ACRONYMS AND ABBREVIATIONS

ARAR	Applicable or Relevant and Appropriate Requirement
ATSDR	Agency for Toxic Substances and Disease Registry
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CSF	Cancer Slope Factor
ECEH	European Centre for Environmental Health
EPA	U.S. Environmental Protection Agency
HAD	Health Assessment Document
HEAST	Health Effects Assessment Summary Table
HI	Hazard Index
HQ	Hazard Quotient
IPCS	International Programme on Chemical Safety
IRIS	Integrated Risk Information System
LOAEL	Lowest-Observed-Adverse-Effect-Level
MCL	Maximum Contaminant Level
MRL	Minimal Risk Level
NAS	National Academy of Sciences
NCEA	National Center for Environmental Assessment
NCP	National Contingency Plan
NOAEL	No-Observed-Adverse-Effect-Level
NPL	National Priority List
NTP	National Toxicology Program
ODW	Office of Drinking Water
OEM	Office of Emergency Management
ORD	Office of Research and Development
OSRTI	Office of Superfund Remediation and Technology Innovation
OSWER	Office of Solid Waste and Emergency Response
OW	Office of Water
PCB	Polychlorinated biphenyl
PCDD	Polychlorinated dibenzodioxin
PCDF	Polychlorinated dibenzofuran
pg	Picogram (10^{-12} grams)
PM2.5	Particulate material less than 2.5 um
PM10	Particulate material less than 10 um
POCD	Program Operations and Coordination Division
ppb	Parts per billion
PPRTV	Provisional Peer Reviewed Toxicity Value
ppt	Parts per trillion
PRG	Preliminary Remediation Goal

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LIST OF ACRONYMS AND ABBREVIATIONS - continued

PTMI	Provisional Tolerable Monthly Intake
PWG	Pathology Working Group
RAGS	Risk Assessment Guidance for Superfund
RBA	Relative Bioavailability
RCRA	Resource Conservation and Recovery Act
RfD	Reference Dose
ROD	Records of Decision
RSC	Relative Source Contribution
STSC	Superfund Technical Health Risk Support Center
TCDD	2,3,7,8-Tetrachlorodibenzo-p-dioxin
TDI	Tolerable Daily Intake
TEF	Toxicity Equivalency Factors
TEQ	TCDD Toxic Equivalent
WHO	World Health Organization

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PUBLIC REVIEW DRAFT

DRAFT RECOMMENDED INTERIM PRELIMINARY REMEDIATION GOALS FOR DIOXIN IN SOIL AT CERCLA AND RCRA SITES

OVERVIEW

In May 2009, the U.S. Environmental Protection Agency's (EPA) Administrator Lisa P. Jackson decided that EPA needs to accelerate work underway to reassess the human health risks from exposures to dioxin. EPA's *Science Plan for Activities Related to Dioxins in the Environment* (EPA 2009a) details a plan, with interim milestones, for completion of the Agency's dioxin reassessment and other efforts related to dioxins in the environment. In a letter dated May 26, 2009, to the community of the Tittabawassee River/Saginaw River and Bay Contamination Site in Michigan, the Administrator stated:

> "As we move forward to develop remediation strategies at this site, the science on dioxin's health and ecological effects will obviously play an important role in our decisions. Although EPA scientists, supported by external peer review bodies, have invested considerable time and effort in evaluating the scientific literature on dioxin, we need to be sure that EPA's assessment of dioxin's risks to people and the environment is brought to bear at this and other dioxin-contaminated sites in a timely manner. Accordingly, I am, in parallel with this letter, announcing a commitment to accelerate our scientific work on dioxin. Our goal is to issue a final dioxin assessment by the end of 2010. In addition, our Office of Research and Development and Office of Solid Waste and Emergency Response will review current dioxin cleanup guidance set by the Agency and the States with the aim of recommending interim preliminary remediation goals informed by the latest science and the work of state agencies. We will announce these interim PRGs by the end of the year."

EPA's Office of Research and Development (ORD) expects to complete the dioxin reassessment by the end of 2010, subject to further consideration of the science and the scope and complexity of the revisions that will need to be made. ORD will be responding to all National Academy of Sciences (NAS) comments received on EPA's draft 2003 dioxin reassessment.

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EPA's Office of Solid Waste and Emergency Response (OSWER) has developed draft recommended interim Preliminary Remediation Goals (PRGs) for dioxin in soil, informed by the best available science and work of state agencies at this time. On October 13, 2009, EPA posted a proposed plan for developing the interim PRGs, (available at: www.epa.gov/superfund/policy/remedy/sfremedy/remedies/dioxininterimplan.html) and requested comments on the proposed plan. EPA has taken these comments into account, establishing a docket (available at: http://www.regulations.gov and go to Docket No. EPA-HQ-SFUND-2009-1002) where comments received to date can be found. EPA has considered these comments in formulating the draft recommended interim PRGs (available at: http://www.regulations.gov and go to Docket No. EPA-HQ-SFUND-2009-0907).

EPA expects to finalize these draft recommended interim PRGs for soil in June 2010 after receipt and evaluation of public comments on all aspects of this draft interim guidance. Until these draft recommended interim PRGs are finalized, EPA will continue to use the 1998 recommended interim PRGs (EPA 1998). The finalized recommended PRGs are intended for interim use until EPA issues its final dioxin reassessment (hereafter "recommended interim PRGs" refers to PRGs that once finalized are to be used in the interim until EPA issues its final dioxin reassessment). At that time, EPA intends to issue updated recommended PRGs based on the final dioxin reassessment. Also at that time, EPA intends to re-evaluate cleanup decisions at Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) and Resource Conservation and Recovery Act (RCRA) sites that were based on the 2010 recommended PRGs to ensure that cleanups remain protective for human health.

PURPOSE

The purpose of this guidance is two-fold:

1. To recommend the use of PRGs to protect against cancer and non-cancer effects associated with human exposure to dioxin in soil at CERCLA and RCRA sites, and,

2. To discuss the interim use of these recommended PRGs for soil at CERCLA and RCRA sites

These draft recommended interim PRGs are intended for use in evaluating dioxin (2,3,7,8-tetrachlorodibenzo-p-dioxin, TCDD) and other dioxin-like compounds in soil. Dioxin-like compounds, including other polychlorinated dibenzodioxins (PCDDs), dibenzofurans (PCDFs) and biphenyls (PCBs) may collectively be evaluated using the

recommended PRGs for dioxin after adjustment to account for relative toxicity using toxicity equivalency factors (TEFs) to calculate dioxin toxicity equivalent (TEQ) concentrations. EPA recommends the use of the TEFs developed by the World Health Organization (WHO) (van den Berg et al. 1998, 2006) based on review of the toxicological literature. For example, if a soil contained 10 ppt of dioxin (i.e, TCDD) and also contained 20 ppt of some other dioxin-like chemical that was 1/10 as toxic as dioxin, the toxicity equivalent concentration for the other dioxin-like compound would be 2 ppt, and the total TEQ concentration for the soil would be 10 + 2 = 12 ppt dioxin TEQ. The total dioxin TEQ concentration would then be compared to the recommended PRG. EPA acknowledges that there is uncertainty associated with risk estimates based on TEQs. Therefore, risk assessors should identify the fraction of the TEQ attributable to dioxin and to each chemical class of dioxin-like compounds (i.e., PCDDs, PCDFs, and PCBs).

For CERCLA and RCRA sites, Regions generally should consider using the recommended interim PRGs in this guidance as a starting point for residential and commercial/industrial soil cleanup levels. EPA encourages State and Tribal programs that do not use PRGs to consider the recommended interim PRGs as starting point concentrations to develop cleanup levels.

This guidance supersedes OSWER's previous PRG guidance for dioxin in soil (EPA 1998). These draft recommended interim soil PRGs are national levels protective for cancer and non-cancer effects from human exposure by ingestion and dermal contact with surface soils. Inhalation exposure is not included for the draft recommended interim PRGs, because at present, there is no available inhalation unit risk value for dioxin that has been derived in accordance with current guidance for inhalation risk assessment (EPA 2009d). However, inhalation exposure to dioxin (particulates and vapor) is expected to be low (< 2.4%) compared to oral exposure in most cases (see Attachment 1). Therefore, risks due to inhalation of particulates and vapors are expected to be minimal. Regions should continue to develop PRGs on a site-specific basis for other media (e.g., sediments, which involve biotransfer and bioaccumulation through indirect pathways) and for ecological assessments.

This guidance is consistent with OSWER's guidance (EPA 2003a) on using a hierarchy of existing chemical toxicity value sources; it does not represent a new or independent review of dioxin toxicity, which ORD is currently conducting as part of the final dioxin reassessment. As a result, there is uncertainty associated with these draft recommended interim PRGs because they do not take into account peer review comments on the new science that was reviewed by the NAS, and new science that was released since the NAS review. A final dioxin reassessment is still under development.

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This draft guidance presents current OSWER technical and policy recommendations regarding PRGs for soil contaminated with dioxin. While OSWER developed this draft guidance for facility response actions under CERCLA and RCRA corrective action, other regulators, including the States, may find it useful in their programs, although they may choose to use alternative assessments consistent with their own programs and policies. In addition, EPA may use and accept other technically sound approaches after appropriate review, either at its own initiative or at the suggestion of other interested parties. This draft guidance does not impose any requirements or obligations on EPA, the States, other Federal agencies, or the regulated community. It is important to understand that this document does not substitute for statutes that EPA administers or their implementing regulations, nor is it a regulation itself. Thus, this document does not impose legally binding requirements on EPA, the States, or the regulated community, and may not apply to a particular situation based upon the specific circumstances. Rather, the document suggests approaches that may be used at particular sites as appropriate, given site-specific circumstances.

BACKGROUND

Description of PRGs

Consistent with CERCLA and the National Contingency Plan (NCP), protection of human health and the environment is a requirement for selected remedies (see 40 CFR §300.430(f)(1)(i)(A)). In the CERCLA remedy selection process, PRGs typically are used when developing cleanup levels. At CERCLA sites, PRGs typically are "specific statements of desired endpoint concentrations of risk levels (55 FR 8713, March 8, 1990) that are conservative, default endpoint concentrations used in screening and initial development of remedial alternatives before consideration of information from site-specific risk assessments". In accordance with the NCP (see 40 CFR §300.430(e)(2)(i)(A)), PRGs are generally at the low end of the risk range and typically are used in screening and initial development of remedial alternatives before consideration of more detailed information from the site-specific risk assessment.

The NCP (40 CFR §300.430(e)(2)(i)(A)) states:

> "Remediation goals shall establish acceptable exposure levels that are protective of human health and the environment and shall be developed by considering the following:

(A) Applicable or relevant and appropriate requirements (ARARs) under federal environmental or state environmental or facility siting laws, if available, and the following factors:

(*1*) For systemic toxicants, acceptable exposure levels shall represent concentration levels to which the human population, including sensitive subgroups, may be exposed without adverse effect during a lifetime or part of a lifetime, incorporating an adequate margin of safety;

(*2*) For known or suspected carcinogens, acceptable exposure levels are generally concentration levels that represent an excess upper bound lifetime cancer risk to an individual of between 10^{-4} and 10^{-6} using information on the relationship between dose and response. The 10^{-6} risk level shall be used as the point of departure for determining remediation goals for alternatives when ARARs are not available or are not sufficiently protective because of the presence of multiple contaminants at a site or multiple pathways of exposure;

(*3*) Factors related to technical limitations such as detection/quantification limits for contaminants;

(*4*) Factors related to uncertainty; and

(*5*) Other pertinent information."

<u>1998 OSWER Guidance on PRGs for Dioxin in Soil</u>

This draft interim guidance, when finalized, will supersede the 1998 OSWER directive entitled *"Approach for Addressing Dioxin in Soil at CERCLA and RCRA Sites"* (EPA 1998). The 1998 OSWER directive recommended that a soil concentration of 1 part per billion (ppb), which is equivalent to 1,000 parts per trillion (ppt) of dioxin (as TEQ) be generally used as a starting point for developing cleanup levels for CERCLA removal sites and as a PRG for CERCLA remedial sites for dioxin TEQ in surface soil involving a residential exposure scenario. For commercial/industrial exposure scenarios, a soil concentration within the range of 5 ppb (5,000 ppt) to 20 ppb (20,000 ppt) dioxin TEQ was recommended as a starting point for developing cleanup levels for CERCLA sites. A range in soil concentrations was recommended for commercial/ industrial soils due to the greater variability in exposures associated with the commercial/industrial scenarios. The PRGs were also generally recommended as a starting point for actions taken at RCRA corrective action sites. These levels were recommended unless extenuating site-specific circumstances warranted a different level.

Based on the oral cancer slope factor (CSF) developed by EPA (1985), EPA (1998) estimated that the lifetime excess cancer risks to residents from oral exposure to dioxin in soil at a PRG of 1,000 ppt dioxin TEQ was about 2.5E-04, and that lifetime excess cancer

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risks to workers at a PRG of 5,000 ppt dioxin TEQ corresponds to a risk of about 1.3E-04. Dermal exposure was not considered for either residential or commercial/industrial land use. EPA (1998) noted that these risks were at the higher end of the range of excess cancer risks.

Need to Update the 1998 OSWER PRGs

In developing this guidance, the Agency has evaluated several attributes of the current PRGs for dioxin in soil that are not consistent with the best available science on dioxin. These inconsistencies include the following:

- The derivation procedure did not consider potential non-cancer effects of dioxin
- The value for residents considered oral exposure only, and did not include dermal exposure
- The value for workers is based on an indoor worker (oral exposure only), while the most exposed worker is usually an outdoor worker with both oral and dermal exposure

Based on a consideration of a number of factors, the Administrator has determined that it is important to develop updated interim PRGs to be used until the release of the final dioxin reassessment. The following sections describe the approach used by EPA to provide and select new recommended interim PRGs for dioxin.

RECOMMENDATIONS

Recommended Toxicity Values

The most common health effect in people exposed to large amounts of dioxin is chloracne. Chloracne cases have typically been the result of accidents or significant contamination events. Chloracne is a severe skin disease with acne-like lesions that occur mainly on the face and upper body. Other effects of exposure to large amounts of dioxin include skin rashes, skin discoloration, excessive body hair, and possibly mild liver damage.

One of the main concerns over health effects from dioxins is the risk of cancer in adults. Several studies suggest that workers exposed to high levels of dioxins at their workplace over many years have an increased risk of cancer. Animal studies have also shown an increased risk of cancer from long-term exposure to dioxins.

Finally, based on data from animal studies, there is some concern that exposure to low levels of dioxins over long periods (or high level exposures at sensitive times) might

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result in reproductive or developmental effects (FDA, 2008). Consequently, both a cancer slope factor and a non-cancer toxicity value are used to derive PRGs for cancer and non-cancer effects.

Hierarchy for Selecting Interim Toxicity Values

OSWER has developed a recommended hierarchy (EPA 2003a) for the selection of toxicity values, including those used in developing PRGs. As discussed in EPA (2003a), the first tier of toxicological information is found in EPA's Integrated Risk Information System (IRIS), and is developed by EPA's ORD National Center for Environmental Assessment (NCEA). Generally, any values in IRIS are considered to be Tier 1. If no data are available in IRIS, the next preference (Tier 2) is Provisional Peer Reviewed Toxicity Values (PPRTVs) developed by EPA NCEA's Superfund Technical Health Risk Support Center (STSC). If toxicity values are not available from either Tier 1 or 2, other high quality sources of toxicity information can be used. These are considered Tier 3 values in this hierarchy.

As discussed in EPA (2003a), toxicity values generally are not appropriate for use as Tier 3 values until they have been through peer review, the peer review comments have been addressed, and the analysis is made publicly available. Also, toxicity values should be based on similar methods and procedures as those used for Tier 1 and Tier 2, and the methods and processes used to develop the values should be transparent. It should be noted that these procedures are specific to CERCLA/RCRA cleanup programs and are not necessarily the approach taken by other EPA programs.

At present, EPA has not derived any Tier 1 or Tier 2 toxicity values for dioxin, either for cancer or non-cancer effects. Consequently, for the purposes of providing these recommended interim PRGs for dioxin, EPA reviewed available toxicity values to identify the most appropriate Tier 3 values (EPA 2009b, 2009c). The recommended interim Tier 3 toxicity values that are discussed in this guidance may be appropriate for the Regions to use to assess human health risks until toxicity values for dioxin are available in EPA's IRIS database or until further scientific analysis indicates that alternate values should be used. When a new IRIS toxicity assessment is finalized, EPA intends to review cleanup level decisions to ensure that sites addressed using these interim toxicity values remain protective, given the revised toxicity values. If important new scientific information becomes available before a new IRIS toxicity assessment is finalized, EPA may issue additional guidance addressing the recommended interim toxicity values discussed in this guidance.

Recommended Cancer Slope Factor

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Because EPA does not have a Tier 1 or Tier 2 cancer toxicity value for dioxin, EPA reviewed available cancer slope factors for dioxin (EPA 2009b) to determine whether they would meet EPA's Tier 3 criteria. Five primary candidate values were identified, as follows:

- EPA's Office of Health and Environmental Assessment (EPA 1985) developed an oral cancer slope factor of 1.56E-04 $(pg\text{-}kg\text{-}day)^{-1}$. This was based on the combined incidence of lung, palate, and nasal carcinomas, and liver hyperplastic nodules or carcinomas in female rats in the study by Kociba et al. (1978).
- EPA (1997a) (EPA's Health Effects Assessment Summary Table, or HEAST) included an oral CSF of 1.5E-04 $(pg\text{-}kg\text{-}day)^{-1}$. The citation for the CSF in HEAST lists EPA (1985) as one of the sources for the HEAST value.
- California (CalEPA) (1986, 2002) developed an oral cancer slope factor of 1.3E-04 $(pg/kg\text{-}day)^{-1}$. This is based on the occurrence of hepatocellular adenomas and carcinomas in male mice in a study by the National Toxicology Program (NTP 1982).
- Michigan (MDEQ 1998) utilizes an oral cancer slope factor of 7.5E-05 $(pg/kg\text{-}day)^{-1}$, which is based on a re-analysis of the histological slides of livers from female rats from the Kociba et al. (1978) study using the liver tumor classification scheme proposed by NTP in 1986 (Maronpot et al. 1986, EPA 1990).
- Minnesota (MNDOH 2003) uses an oral cancer slope factor of 1.4E-03 $(pg/kg\text{-}day)^{-1}$, which is based on the draft re-evaluation of the exposure-response data for liver cancer in female rats reported in the draft EPA (2003b) dioxin reassessment.

More detailed descriptions of these five alternative slope factors are presented in Attachment 2.

The slope factor identified by Minnesota is not considered appropriate because it is based on the 2003 EPA draft dioxin reassessment (EPA 2003b), which has not been finalized. The slope factor identified by Michigan is based on an updated and peer-reviewed evaluation of the Kociba et al. (1978) data using the updated NTP tumor classification system. However, documentation of the slope factor of 75,000 $(mg/kg\text{-}day)^{-1}$, including its derivation, peer review and supporting information, is very brief and the information that is publicly available is limited or not completely transparent. The slope factor listed in HEAST of 1.5E-04 $(pg/kg\text{-}day)^{-1}$ is slightly different from the slope factor listed in the source document (EPA 1985) of 1.56E-04 $(pg/kg\text{-}day)^{-1}$. Because of this, the HEAST was not considered to be transparent as to the derivation of the CSF and how the value came to be changed slightly from that listed in the source document. Of the two remaining slope factors (EPA 1985, CalEPA 1986), both are publicly available,

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transparent as to their derivation, and were adequately peer-reviewed. However, the slope factor of 1.56E-04 $(pg/kg\text{-}day)^{-1}$ derived by EPA (1985) is preferred because it is based on the incidence of all significant tumors combined, rather than the incidence of liver tumors alone.

Recommended Non-Cancer Toxicity Factor

As noted above, EPA has not yet derived a Tier 1 or Tier 2 non-cancer toxicity value (Reference Dose, or RfD) for dioxin. Therefore, EPA reviewed non-cancer toxicity values developed by States, foreign countries, or other health agencies (EPA 2009b, 2009c). Based on a review of available documents, the following candidate values were identified:

- A chronic oral Minimal Risk Level (MRL) value of 1 pg/kg-day developed by the Agency for Toxic Substances and Disease Registry (ATSDR). This value is based on behavioral effects in the offspring of female monkeys exposed to dioxin in the diet for 16 months, including the period of gestation and lactation (ATSDR 1998).
- A chronic oral RfD value of 1 pg/kg-day developed by the EPA's Office of Drinking Water (ODW) (EPA 1987) to support derivation of a lifetime health advisory for TCDD. This value is based on the occurrence of reproductive effects in animals.
- A range of Tolerable Daily Intake (TDI) values, ranging from about 1 pg/kg-day to 4 pg-kg-day, developed by the WHO (WHO 1991, 1998; JECFA 2002). These values are derived by identifying a no-effect tissue burden in exposed animals for a range of non-cancer effects, and computing the average daily intake level that would yield the no-effect tissue burden in humans.

Each of these approaches is described in greater detail in Attachment 2.

Of these values, OSWER recommends the chronic oral MRL value of 1 pg/kg-day developed by ATSDR (1998) generally as the most appropriate value for use in the development of non-cancer PRGs. This value is well documented and peer reviewed, and qualifies as an OSWER Tier 3 toxicity value. This toxicity value is consistent with the RfD of 1 pg/kg-day developed by EPA's ODW (EPA 1987), and is also consistent with the low end of the range of TDI values developed by WHO (1991, 1998; JECFA

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2002). Note that ATSDR (2008) has used the 1 pg/kg-day value to derive a soil screening concentration of 50 ppt[1] dioxin TEQ.

Recommended Exposure Pathways and Parameters

EPA provides guidance on the calculation of PRGs in two main documents, including *Risk Assessment Guidance for Superfund (RAGS) Volume I, Part B (Development of Risk-Based Preliminary Remediation Goals)* (EPA 1991) and *Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites* (EPA 2002a). For the purposes of this effort, EPA has utilized default exposure equations and exposure parameters discussed in the more recent EPA guidance (2002a) along with the RAGS dermal guidance (EPA 2004). For workers, RAGS B recommends evaluating only indoor workers, while EPA (2002a) recommends evaluating both indoor and outdoor workers. Also, EPA (2002a) recommends evaluating non-cancer risk to a resident based on the soil intake rate of a child, which is considered more protective of children than the approach used in RAGS B (that uses a time-weighted average intake rate across childhood and adulthood). Soil PRGs calculated using EPA 2002a equations are generally appropriate provided that conditions at the site are the same as the conditions assumed in the calculations. Site managers wishing to use PRGs developed with these protective equations should consider whether it may be appropriate to modify any of the assumptions in deriving site-specific PRGs.

The equations and exposure assumptions recommended by EPA (2002a, 2004) for oral and dermal exposure of residents and workers (both indoor and outdoor workers) to soil are provided in Tables 1 to 4. In brief, some of the key exposure assumptions for these populations are as follows:

- Residents and outdoor workers are assumed to be exposed by both oral and dermal exposure

[1] ATSDR's soil screening levels are calculated in accordance with ATSDR's Public Health Assessment Guidance Manual (ATSDR 2005). The dioxin soil screening level is based on ATSDR's chronic oral MRL value of 1 pg/kg-day, assuming a soil intake rate of 0.2 g/day by a 10-kg child. Dermal exposure is not included. The assumption of a body weight of 10 kg is consistent with previous exposure factor recommendations from EPA, while EPA currently recommends a body weight of 15 kg for a child. Moreover, the 50 ppt screening level is not intended for use as a PRG, or to serve as a remedial goal. Rather, ATSDR uses the soil screening concentration as an initial comparison value for health assessments and to make public health recommendations, such as community health education or site access limitations..

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- Indoor workers are assumed to be exposed by oral exposure only, as no significant dermal exposure is expected.
- Inhalation exposure is not included for any population because at present, there is no available inhalation unit risk value for dioxin that has been derived in accordance with current guidance for inhalation risk assessment (EPA 2009d).
- Inhalation exposure to dioxin (particulates and vapor) is expected to be low (< 2.4%) compared to oral exposure in most cases (see Attachment 1).
- For evaluation of cancer PRGs, residential exposure is assumed to begin at birth and extend for 30 years. This includes exposure for 6 years as a child and 24 years as an adult. Worker exposures are assumed to occur for 25 years, but only as an adult.
- For non-cancer PRGs, exposure as a resident is assumed to occur only as a child. This assumption is thought to be generally conservative (EPA 2002), since exposure to soil is higher for a child than for an adult resident. For workers, exposure is assumed to occur only as an adult.

The equations shown in Tables 1 to 4 include two additional terms not explicitly included in the equations recommended by EPA (2002a):

- RBA. Relative bioavailability (RBA), for purposes of this guidance, is the ratio of the absorption of dioxin from soil compared to the absorption that occurred in the study used to derive the oral cancer slope factor or the oral reference dose for dioxin. For the calculations included in this document, the value of RBA is assumed to be 1.0 (i.e., dioxin absorption is the same as that occurring in the study.) This is an appropriate assumption for establishing a default PRG because use of a RBA factor of 1.0 will ensure protectiveness. However, this assumption may need to be revisited when performing site-specific assessments.

- RSC. The Relative Source Contribution (RSC) is the amount of a daily safe intake for non-cancer effects that is "allocated" to soil. RSCs should be applied only for effects that have a non-zero threshold, and are used mainly by EPA in developing water standards (EPA 2000). In cases where other sources (e.g., the diet) contribute a substantial fraction of the ingestion exposure, then the RSC term may be set to some lower value. The national average dioxin contribution from diet is estimated to be more than 90% (from beef, pork, poultry, other meats, dairy, eggs, milk, and fish). If we accounted for this 90% contribution from food, then the RSC would be 0.1 and the PRG would be one-tenth of the non-cancer PRG value that we are currently recommending. However, an RSC adjustment for soil is not often used at Superfund sites, where soil is an exposure source for the following reasons. The available dietary data are for adults, but the PRGs are

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developed for children who are exposed to lower concentration levels in the current food supply. In addition, EPA's responsibilities are to evaluate and manage only contaminant sources related to the site. For those individuals near Superfund sites, the contribution of soil derived dioxin exposures relative to food derived exposures is expected to be much greater than the national average. Therefore, for all PRG calculations performed in this document, the value of RSC is set to 1.0.

Draft Interim Recommended PRGs for Dioxin in Soil

Cancer PRGs

Based on the recommended oral cancer slope factor of 1.56E-04 $(pg/kg\text{-}day)^{-1}$ discussed above, recommended interim soil PRGs for protection against cancer effects at the 1E-06 risk level may be computed in accordance with current EPA equations and default exposure assumptions shown in Table 1 and Table 2. The results are shown below:

Potential Soil PRGs for Dioxin Based on Cancer (1E-06 Risk Level)

Land Use	Receptor	PRG (ppt TEQ)
Residential	Resident	3.7
Commercial/ Industrial	Indoor Worker	37
	Outdoor Worker	17

All PRGs are shown to two significant figures

Non-Cancer PRGs

Based on the recommended oral non-cancer interim toxicity value of 1 pg/kg-day selected above, recommended interim non-cancer PRGs for residential and commercial/industrial land use that correspond to a Hazard Quotient (HQ) of 1 may be calculated in accordance with current EPA equations and default exposure assumptions shown in Table 3 and Table 4. These results are shown below:

Potential Soil PRGs for Dioxin Based on Non-Cancer Effects (HQ of 1)

Land Use	Receptor	PRG (ppt TEQ)
Residential	Resident	72
Commercial/ Industrial	Indoor Worker	2,000
	Outdoor Worker	950

All PRGs are shown to two significant figures

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Draft Recommended Interim PRGs

Based on consideration of oral and dermal exposures to dioxin and other dioxin-like compounds in soil, EPA recommends the interim PRGs for dioxin in soil calculated based on non-cancer effects: 72 ppt dioxin TEQ in residential soil and 950 ppt dioxin TEQ in commercial/industrial soil. EPA believes that these recommended interim PRGs generally provide adequate protection against non-cancer effects. In addition, they generally are protective for cancer effects at approximately the 1E-05 risk level, which is within EPA's protective risk range of 1E-04 to 1E-06 (see 40 CFR §300.430(e)(2)(i)(A)). It should be noted that because these recommended interim PRGs correspond to a HQ of 1, they limit the upper bound cancer risk level to 1E-05 rather than the typical upper limit of 1E-04. These recommended interim PRGs are set at a more protective cancer risk level than the 1998 PRGs, which reflect a cancer risk level of 2E-04. These draft recommended interim PRGs are expected to be higher than typical background levels for residential and most commercial/industrial soils, respectively (ATSDR 1998).

Land Use	PRG (ppt TEQ)
Residential	72
Commercial/Industrial	950

All recommended PRGs are shown to two significant figures

EPA believes the draft recommended PRGs described above if finalized would be appropriate for use on an interim basis until EPA releases its final dioxin reassessment.

However, EPA is also considering an alternative concentration of 3.7 ppt dioxin TEQ in residential soil and 17 ppt dioxin TEQ in commercial/industrial soil as the point of departure for determining PRGs. These alternative draft PRGs are at the 1E-06 risk level and therefore are also consistent with the NCP provision for PRGs (see 40 CFR §300.430(e)(2)(i)(A)(2)), which states 1E-06 is the point of departure for determining remediation goals. These alternative values are protective for non-cancer as well as cancer effects. EPA notes that PRGs based on a 1E-06 cancer risk level would likely be within or possibly below background concentrations of dioxins in U.S. soils. A recent EPA report found mean rural soil concentrations ranging from 0.2 to 11.4 ppt dioxin TEQ (EPA 2007). Generally, it is OSWER policy to not set site specific cleanup levels at concentrations below site specific natural background levels (EPA 2002b). Thus, if EPA were to finalize these alternative values, soil background levels would need to be identified at CERCLA sites in order to develop appropriate cleanup levels. While EPA is

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taking comments on all aspects of this draft guidance, EPA is particularly interested in comments on the utility of these alternative values.

IMPLEMENTATION

This guidance does not affect or replace statutory or regulatory requirements (e.g., CERCLA Section 121 provisions on meeting or waiving ARARs) under CERCLA or RCRA. For example, the maximum contaminant level (MCL) for dioxin in drinking water is 30 pg/L, and this should continue to be considered as an ARAR for the cleanup under CERCLA of ground water that may be used as drinking water (unless a more stringent state ARAR requires a lower concentration).

These draft recommended interim PRGs are informed by the best available toxicity values as evaluated using OSWER's toxicity hierarchy (EPA 2003a) and calculated using current EPA exposure assumptions, which have been updated since the 1998 PRG guidance (EPA 1998) was issued. Once finalized, regions may consider using these recommended interim PRGs at both CERCLA and RCRA sites where the Agency is determining dioxin soil cleanup levels. When EPA's ORD finalizes its dioxin reassessment, OSWER will evaluate the impact of the dioxin reassessment and will update these PRGs as appropriate.

These draft recommended interim soil PRGs are national levels protective for cancer and non-cancer effects from ingestion and dermal contact with surface soils in residential and commercial/industrial exposure scenarios. Inhalation exposure is not included for the draft recommended interim PRGs, because at present, there is no available inhalation unit risk value for dioxin that has been derived in accordance with current guidance for inhalation risk assessment (EPA 2009d). However, inhalation exposure to dioxin (particulates and vapor) is expected to be low (< 2.4%) compared to oral exposure in most cases (see Attachment 1). Therefore, risks due to inhalation of particulates and vapors are expected to be minimal. Once finalized, the interim guidance will supersede OSWER's previous PRG guidance for dioxin in soil (EPA 1998). These draft recommended interim soil PRGs are national levels protective for cancer and non-cancer effects from human contact (ingestion, dermal contact, and inhalation exposure (this is minimal for dioxin particulates and vapors)) with surface soils in residential and commercial/industrial exposure scenarios. Exposure to dioxin by the inhalation route is not expected to be significant compared to oral exposure (see Attachment 1). Regions should continue to develop PRGs on a site-specific basis for other media, like sediments, that involve biotransfer and bioaccumulation up the aquatic food chain to fish consumed by humans and for ecological assessments where the receptors are terrestrial biota, such as plants and animals, not humans.

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At CERCLA National Priority List (NPL) sites, including, where appropriate, other Federal agency-lead and state-lead sites, Regions should consult with the Office of Superfund Remediation and Technology Innovation (OSRTI) Site Assessment and Remedy Decisions Branch on all proposed dioxin cleanups that are conducted under Superfund. Consultation should be initiated at the risk assessment stage, and continue through the process.

For removal actions, Regions should contact Headquarters for concurrence on non-NPL removal actions where dioxin is a principal contaminant of concern (EPA 1989). For non-time critical removal actions involving dioxin, consultation may involve both OEM and OSRTI. The use of removal authority is determined on a site-specific basis, and trigger levels for initiating a removal action are sometimes higher than the levels used as either PRGs (or starting points) or final cleanup levels.

For sites where another Federal agency is the lead agency, OSRTI will notify the Federal Facilities Restoration Reuse Office of ongoing consultations regarding dioxin soil cleanup levels. The Office of Site Remediation Enforcement will provide support if enforcement issues are identified. For consultation procedures, refer to OSWER Directive 9200.4-19 (EPA 1996) and OSWER Directive 9200.1-18FS (EPA 1997b).

Once finalized, Regions performing five-year-reviews of CERCLA remedial sites where soils contaminated with dioxin or other dioxin-like compounds have been left in place should consider this guidance on recommended interim PRGs when evaluating whether the original remedies in the Records of Decision (ROD) remain protective for the contaminated areas. Consistent with existing five-year-review guidance (EPA 2001), OSWER recommends that the five-year-reviews include an evaluation of existing site data, identification of the need for additional site data, and identification of areas potentially needing cleanup based on the review of this existing data. This information can be used to evaluate whether additional data collection and/or site cleanup is appropriate. Once the final dioxin reassessment has been released, OSWER may issue additional guidance on implementation of the PRGs.

In the case of EPA-lead RCRA corrective action sites, Regions should provide the Program Implementation and Information Division within the Office of Resource Conservation and Recovery (ORCR) with proposed dioxin soil cleanup levels (i.e., prior to notice and comment) in order to ensure appropriate implementation of the recommended interim PRGs, once they are finalized. For State-lead RCRA corrective action sites, we would also encourage States to use the dioxin levels recommended by this guidance as starting points in developing soil cleanup levels, unless they have developed their own standards or guidance. Because States are the primary implementers

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of the RCRA Corrective Action program, this guidance does not recommend specific procedures for implementation under RCRA. States are encouraged to share their approaches with the Regions in a manner consistent with established procedures for EPA support and oversight of state RCRA Corrective Action programs.

Point of Contact

If you have any questions, please contact Marlene Berg by phone at 703-603-8701 or by e-mail at berg.marlene@epa.gov.

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TABLE 1
RECOMMENDED EQUATION FOR COMPUTING CANCER PRGS FOR EXPOSURE OF RESIDENTS TO DIOXIN IN SOIL

$$PRG\ (pg/g) = \frac{TR \cdot AT \cdot 365\ \text{days/yr}}{EF \cdot [SF_o \cdot IF_{soil/adj} + (SF_o / ABS_{GI}) \cdot SFS \cdot ABS_d \cdot EV] \cdot RBA}$$

Parameter (description)	Units	Default Value
TR (target cancer risk)	dimensionless	1E-04 to 1E-06
AT (averaging time)	years	70
EF (exposure frequency)	days/yr	350
SF_o (oral slope factor)	$(\text{pg-kg-day})^{-1}$	1.56E-04 (a)
$IF_{soil/adj}$ (age-adjusted soil ingestion factor)	g-yr/(kg-d)	0.114
ABS_{GI} (gastrointestinal absorption fraction)	pg absorbed/pg ingested	1.0
SFS (age adjusted dermal factor)	g-yr/kg-event	0.360
ABS_d (dermal absorption fraction)	pg absorbed/pg on skin	0.03 (b)
EV (dermal exposure frequency)	events/day	1
RBA (relative bioavailability)	--	1

Source: EPA 2002 Equation 3-1
Includes oral and dermal exposure.
(a) Based on EPA (1985)
(b) Based on EPA (2004)

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TABLE 2
RECOMMENDED EQUATION FOR COMPUTING CANCER PRGS FOR EXPOSURE OF WORKERS TO DIOXIN IN SOIL

$$PRG\ (pg/g) = \frac{TR \cdot BW \cdot AT \cdot 365\ \text{days/yr}}{(EF \cdot ED)[\cdot IR \cdot oSF + (SF_o / ABS_{GI}) \cdot AF \cdot ABS_d \cdot EV \cdot SA] \cdot RBA}$$

Parameter (description)	Units	Default Value	
		Indoor Worker	Outdoor Worker
TR (target cancer risk)	Dimensionless	1E-04 to 1E-06	1E-04 to 1E-06
BW (body weight)	Kg	70	70
AT (averaging time)	Years	70	70
EF (exposure frequency)	days/yr	250	225
ED (exposure duration)	Years	25	25
SF_o (oral slope factor)	$(pg\text{-}kg\text{-}day)^{-1}$	1.56E-04 (a)	1.56E-04 (a)
IR (soil ingestion rate)	g/day	0.05	0.10
ABS_{GI} (gastrointestinal absorption fraction)	pg absorbed/pg ingested	1.0	1.0
ABS_d (dermal absorption fraction)	pg absorbed/pg on skin	--	0.03 (b)
EV (dermal exposure frequency)	events/day	--	1
AF (dermal adherence factor)	g/cm^2	--	2E-04
SA (dermal surface area)	cm^2	--	3300
RBA (relative bioavailability)	--	1	1

Source: EPA 2002 Equation 4-1
Includes oral and dermal exposure for outside workers. Dermal exposure not quantified for an indoor worker.

(a) Based on EPA (1985)
(b) Based on EPA (2004)

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TABLE 3
RECOMMENDED EQUATION FOR COMPUTING NON-CANCER PRGS FOR EXPOSURE OF RESIDENTS TO DIOXIN IN SOIL

$$PRG\ (pg/g) = \frac{THQ \cdot BW \cdot AT \cdot 365\ \text{days/yr} \cdot RSC}{EF \cdot ED \cdot [IR_{soil}\ /\ RfD_o + (AF \cdot ABS_d \cdot EV \cdot SA)\ /\ (RfD_o \cdot ABS_{GI})] \cdot RBA}$$

Parameter (description)	Units	Default Value
THQ (target hazard quotient)	dimensionless	1
BW (body weight - child)	kg	15
AT (averaging time)	years	6
EF (exposure frequency)	days/yr	350
ED (exposure duration)	years	6
RfD_o (oral reference dose)	pg/kg-day	1.0 (a)
IR_{soil} (soil ingestion rate)	g/day	0.20
ABS_{GI} (gastrointestinal absorption fraction)	pg absorbed/pg ingested	1.0
AF (dermal adherence factor)	g/cm^2	2E-04
ABS_d (dermal absorption fraction)	pg absorbed/pg on skin	0.03 (b)
EV (dermal exposure frequency)	events/day	1
SA (dermal surface area exposed - child)	cm^2	2,800
RBA (relative bioavailability)	--	1
RSC (relative source contribution)	--	1

Source: EPA 2002 Equation 3-2
Includes oral and dermal exposure.
(a) Based on ATSDR (1998) chronic oral MRL
(b) Based on EPA (2004)

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TABLE 4
RECOMMENDED EQUATION FOR COMPUTING NON-CANCER PRGS FOR EXPOSURE OF WORKERS TO DIOXIN IN SOIL

$$PRG\ (pg/g) = \frac{THQ \cdot BW \cdot AT \cdot 365\ \text{days/yr} \cdot RSC}{EF \cdot ED \cdot [IR_{soil} / RfD_o + (AF \cdot ABS_d \cdot EV \cdot SA) / (RfD_o \cdot ABS_{GI})] \cdot RBA}$$

Parameter (description)	Units	Default Value	
		Indoor Worker	Outdoor Worker
THQ (target hazard quotient)	Dimensionless	1	1
BW (body weight)	Kg	70	70
AT (averaging time)	Years	70	70
EF (exposure frequency)	days/yr	250	225
ED (exposure duration)	Years	25	25
RfD_o (oral reference dose)	pg/kg-day	1.0 (a)	1.0 (a)
IR (soil ingestion rate)	g/day	0.05	0.10
ABS_{GI} (gastrointestinal absorption fraction)	pg absorbed/pg ingested	--	1.0
ABS_d (dermal absorption fraction)	pg absorbed/pg on skin	--	0.03 (b)
EV (dermal exposure frequency)	events/day	--	1
AF (dermal adherence factor)	g/cm^2	--	2E-04
SA (dermal surface area)	cm^2	--	3,300
RBA (relative bioavailability)	--	1	1
RSC (relative source contribution)	--	1	1

Source: EPA 2002 Equation 4-2
Includes oral and dermal exposure for outdoor workers. Dermal exposure not quantified for an indoor worker.
(a) Based on ATSDR (1998) chronic oral MRL
(b) Based on EPA (2004)

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ATTACHMENT 1

EVALUATION OF RELATIVE DIOXIN INTAKE FROM INHALATION AND INGESTION EXPOSURE

Exposure to a contaminant in soil may occur by a number of pathways, including direct ingestion of soil, dermal contact with soil, inhalation of soil particulates in air, and inhalation of vapors of the chemical released from soil to air. This Attachment compares the relative magnitude of human exposure to dioxin in soil by the inhalation route (including both inhalation of dioxin on airborne particulates and inhalation of dioxin vapor) compared to intake by the oral route using EPA's default residential and commercial/industrial land exposure parameters. The dermal pathway is not included in the comparison because dermal exposure is expressed in terms of absorbed dose, while the oral and inhalation pathways are expressed in terms of administered dose. However, based on default exposure assumptions, the dermal pathway is relatively minor compared to oral. This Attachment does not compare risks associated with oral and inhalation pathways because there is no available inhalation unit risk value for dioxin that has been derived in accordance with current guidance for inhalation risk assessment (EPA 2009d).

Relative Contribution from Inhalation of Particulates

The ratio of the amount of dioxin inhaled on respirable soil particles (e.g., PM10s or PM2.5s) compared to the amount of dioxin ingested with soil can be calculated as described below.

$$\text{Dose Inhaled (mg/day)} = C_{soil} \cdot C_{PM10} \cdot BR$$
$$\text{Dose Ingested (mg/day)} = C_{soil} \cdot IR$$

where:

C_{soil} = concentration of dioxin in soil
C_{PM10} = concentration of soil particles less than 10 μm in size in air (mg/m^3)
BR = breathing rate (m^3/day)
IR = soil ingestion rate (mg/day)

The concentration of PM10 particles in air is given by:

$$C_{PM10}\ (\text{mg/m}^3) = (1\text{E-06 mg/kg}) / PEF$$

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where PEF = particulate emission factor (m^3/kg).

The ratio of the daily intakes of dioxin by these two routes is then:

$$\text{Ratio(inhal/ingest)} = BR / (IR \cdot PEF)$$

EPA (1991) provides recommended default values for breathing rate and soil ingestion rate for residents and workers, and EPA (2002) provides a recommended default PEF for residential and industrial land use. Based on these inputs, the resulting ratio of daily intakes (inhalation compared to oral) are as follows:

Parameter	Parameter Value		
	Child	Adult	Worker
BR (m^3/day)	10	20	10
IR (kg/day)	2E-04	1E-04	1E-04
PEF (m^3/kg)	1.36E+09	1.36E+09	1.36E+09
Ratio (inhalation of dioxin on particulates vs. oral intake from soil)	**0.00004**	**0.00015**	**0.00007**

As indicated, based on recommended default exposure parameters, the amount of dioxin inhaled as respirable particulates is likely to be small (<< 1%) compared to the amount ingested with soil.

Relative Contribution from Inhalation of Volatiles

Similarly, the ratio of the daily intake of a chemical due to inhalation of the volatilized chemical in air to the chemical ingested on soil:

$$\text{Ratio(inhal/ingest)} = BR / (IR \cdot VF)$$

where VF = volatilization factor (m^3/kg).

The value of the VF term may be calculated using Equation 4-8 in EPA (2002). Recommended default inputs and chemical-specific terms are shown in Table A1-1. Based on these parameters, the value of VF is estimated to be 8.4E+06 m^3/kg. Based on this, the ratios of dioxin intake from vapor inhalation compared to soil ingestion are as follows:

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Parameter	Parameter Value		
	Child	Adult	Worker
BR (m^3/day)	10	20	10
IR (kg/day)	2E-04	1E-04	1E-04
VF (m^3/kg)	8.4E+06	8.4E+06	8.4E+06
Ratio (inhalation of vapors vs. oral intake)	**0.006**	**0.024**	**0.012**

As seen, exposure by inhalation of dioxin released to air from soil is likely to be small (< 2.4%) compared to the amount of dioxin ingested in soil.

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TABLE A1-1
RECOMMENDED DEFAULT INPUTS AND CHEMICAL-SPECIFIC VALUES USED IN VOLATILIZATION FACTOR CALCULATION

Parameter (description)	Units	Value	Source
Q/Cvol (inverse of the ratio of geometric mean air concentration to volatilization flux at a center of a square source)	g/m^2-s per kg/m^3	68.18	[a]
T (exposure interval)	s	9.5E+08	[a]
P_b (dry soil bulk density)	g/cm^3	1.5	[a]
Θ_a (air-filled soil porosity)	L_{air}/L_{soil}	n- Θ_w	[a]
n (total soil porosity)	L_{pore}/L_{soil}	1-(P_b/ P_s)	[a]
Θ_w (water-filled soil porosity)	L_{air}/L_{soil}	0.15	[a]
P_s (soil particle density)	g/cm^3	2.65	[a]
f_{oc} (fraction organic carbon in soil)	g/g	0.006	[a]
D_i (diffusivity in air)	cm^2/s	4.7E-02	[b]
H' (Henry's law constant)	dimensionless	2.04E-03	[c,d]
D_w (diffusivity in water)	cm^2/s	8E-06	[b]
K_d (soil-water partition coefficient)	cm^3/g	K_{oc} A f_{oc}	[a]
K_{oc} (soil-organic carbon partition coefficient)	cm^3/g	3.98E+06	[e]

Chemical-specific values are shaded in grey.

[a] EPA (2002)
[b] GSI Chemical Database: http://www.gsi-net.com/en/publications/gsi-chemical-database/single/240.html
[c] SRC PHYSPROP Database: http://www.syrres.com/what-we-do/product.aspx?id=133
[d] Converted to dimensionless using EPA's On-line Tools for Site Assessment Calculation http://www.epa.gov/athens/learn2model/part-two/onsite/henryslaw.html
[e] SRC CHEMFATE Database: http://www.srcinc.com/what-we-do/databaseforms.aspx?id=381

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ATTACHMENT 2

DESCRIPTION OF CANDIDATE CANCER AND NON-CANCER TOXICITY VALUES FOR DIOXIN

A. DERIVATION OF CANCER SLOPE FACTORS

The first step in computing recommended cancer-based Preliminary Remediation Goals (PRGs) for dioxin is to select the cancer slope factor. A review of the approaches used by U.S. states, territories (EPA 2009b) and other U.S. health agencies has identified five potential values, as discussed below.

EPA (1985)

EPA's Office of Health and Environmental Assessment reviewed the toxicity data for dioxin and prepared a Health Assessment Document (HAD) in September 1985 (EPA 1985). The HAD evaluated the cancer dose-response data from each of two published studies in animals:

- A two-year oral feeding study in male and female rats (Kociba et al. 1978). The HAD evaluation considered two alternative pathological analyses of the slides from the study, including the findings of the original pathologist (Kociba) and also an independent reviewer (Squire) employed by EPA's Cancer Assessment Group.

- A two-year oral gavage study in male and female rats and mice performed by the National Toxicology Program (NTP) of the National Cancer Institute (NTP 1982).

The HAD fit a number of alternative cancer dose response data sets from each of these studies to the linearized multistage model to derive a series of alternative estimates of an oral cancer slope factor. These results are summarized in Table A2-1. The HAD found that the highest slope factor was obtained using the data from Kociba et al. (1978), using the combined incidence of carcinomas in lung, carcinoma and hyperplastic nodules in liver, and carcinoma in nasal turbinates and hard palate in female rats. Based on the histopathological analysis of Kociba, the slope factor was 1.51E-04 $(pg/kg\text{-}day)^{-1}$, while based on the histological analysis by Squire, the slope factor was 1.61E-04 $(pg/kg\text{-}day)^{-1}$. The HAD identified the geometric mean of these two values (1.56E-04 $(pg/kg\text{-}day)^{-1}$) as

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the recommended slope factor. This approach was peer-reviewed by an expert panel assembled for a peer review workshop in Cincinnati in 1983, and by the Environmental Effects, Fate and Transport committee of EPA's Science Advisory Board.

EPA (1997)

EPA's Health Effects Assessment Summary Table (HEAST) (EPA 1997a) identifies an oral cancer slope factor of 1.5E-04 $(pg/kg\text{-}day)^{-1}$. HEAST tables are described in EPA (1997) as containing "provisional risk assessment information" that "have not had enough review to be recognized as high quality, Agency-wide consensus information." The primary source of the oral slope factor value for dioxin is the EPA (1985) HAD, but the reason that the value listed is 1.5E-04 $(pg/kg\text{-}day)^{-1}$ rather than 1.56E-04 $(pg/kg\text{-}day)^{-1}$ is not clear. The value was indicated as being provisional, and was qualified as being under further evaluation. Although the HAD (EPA 1985) is peer-reviewed, specific information on the peer review status of the value in HEAST has not been found.

CalEPA (1986, 2002)

California (CalEPA 1986, 2002) also reviewed the cancer data from the study of Kociba et al. (1978) (including the histological analyses by both Kociba and Squire) and by NTP (1982). A number of different data sets were fit to the linearized multistage model to derive inhalation unit risk values. These unit risk values, and the equivalent oral cancer slope factors, are summarized in Table A2-2. In this analysis, the highest slope factor was found to occur using data from the NTP (1982) study on the incidence of carcinomas and adenomas in male mouse liver. This slope factor was 1.3E-04 $(pg/kg\text{-}day)^{-1}$ (CalEPA 1986). This slope factor was peer-reviewed in August 1986 by an independent nine-member Scientific Review Panel.

Michigan (MDEQ 1998)

Michigan uses a slope factor of 7.5E-05 $(pg/kg\text{-}day)^{-1}$, which is based on a re-analysis of the histological slides of livers from female rats from the Kociba et al. (1978) study using the liver tumor classification scheme proposed by NTP in 1986 (Maronpot et al. 1986). In this revised histological classification, lesions that were previously classified as "neoplastic nodules" and were counted as liver tumors are divided into "hepatocellular hyperplasia" and "hepatocellular adenoma." The term "hyperplasia" is reserved for proliferative lesions that are secondary responses to degenerative changes in the liver, and these are not considered to be liver tumors. Foci of cellular alteration, including hepatocellular adenoma and hepatocellular carcinoma, are considered to represent a

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spectrum of changes that comprise the natural history of liver neoplasia, and these are counted as liver tumors (Maronpot et al. 1986).

The pathology slides from Kociba et al. (1978) were originally reclassified by Squire (an independent pathologist serving as a consultant to EPA's Carcinogen Assessment Group), who reported that preliminary results from the re-reading indicated substantially lower liver tumor incidence (EPA 1990). Based on a request from the Maine Science Advisory Panel, the slides were subsequently re-evaluated under the new system by seven independent pathologists referred to as the Pathology Working Group (PWG) (Sauer 1990, Goodman and Sauer 1992). Table A2-3 summarizes the results for liver lesions derived using the original and the revised classification schemes. As shown, the incidence of liver tumors is substantially lower based on the new classification scheme than the original scheme. Based on total significant tumors (liver, lung, nasal turbinates and hard palate), the cancer slope factor based on the revised classification scheme is 7.5E-05 $(pg/kg\text{-}day)^{-1}$, as opposed to a value of 1.51E-04 using the original analysis (EPA 1990).

A three page document is publicly available on the Michigan Department of Environmental Quality website that summarizes the reevaluation of the Kociba data by the PWG; however, a description of the derivation of the cancer slope factor is not included nor is information about external peer review of that derivation. The findings of the PWG, however, were published in the peer reviewed literature. In short, documentation of the slope factor of 75,000 $(mg/kg\text{-}day)^{-1}$, including its derivation, peer review and supporting information, is very brief, and the information that is publicly available is limited or not completely transparent.

Minnesota (MNDOH 2003)

Minnesota uses a value of 1.4E-03 $(pg/kg\text{-}day)^{-1}$, which is based on the re-evaluation of the exposure-response data for liver cancer in female rats reported in the EPA 2003 draft dioxin reassessment (EPA 2003b). In this approach, the tumor incidence data reported by Goodman and Sauer (1992) were used, which are based on the revised liver pathology scheme developed by NTP in 1986 (Maronpot et al. 1986). However, the dose metric was changed from administered dose (ug/kg-day) to body burden (ug/g). This approach helps account for the large difference in half-life of TCDD in humans and rats (EPA 2003b). The dose corresponding to a specified body burden was estimated using the following equation:

$$\text{Intake (pg/kg-d)} = \text{Tissue Burden (pg/kg)} \cdot \ln(2) / [t_{1/2} \cdot f]$$

where:

$t_{1/2}$ = half-life of dioxin in the body (days). A value of 2593 days was assumed for humans and 25 days in rats.
f = fraction of an ingested dose that is absorbed (assumed to be 0.8)

Using the linearized multistage model and adjusting the dose metric as described, EPA (2003b) derived a cancer slope factor of 1.4E-03 $(pg/kg\text{-}day)^{-1}$. This value is 8.7 times higher than the cancer slope factor derived by EPA (1985), and reflects the combined effect of using body burden rather than ingested dose (31 times higher) and the effect of using the revised histopathology incidence data (3.6 times lower).

This approach and the resultant slope factor have not undergone final Agency approval or final peer review.

B. DERIVATION OF NON-CANCER TOXICITY VALUES

The first step in computing recommended non-cancer-based PRG concentrations for dioxin is to select a non-cancer toxicity value (RfD).[2] EPA currently does not have an Agency RfD for dioxin. Therefore, EPA reviewed non-cancer values used by states, foreign nations or other health agencies.

EPA Office of Drinking Water (1987)

In 1987, EPA's Office of Drinking Water (ODW) developed an oral RfD of 1 pg/kg-day for use in deriving a Lifetime Health Advisory value (EPA 1987). This RfD was based on a 3-generation reproductive study in rats (Murray et al. 1979). In this study, animals were exposed to TCDD in the diet at concentrations that produced average doses of 0, 0.001, 0.01, or 0.1 ug/kg-day. Significant decreases in fertility and neonatal survival of offspring were observed in animals exposed to the 0.1 ug/kg-day dose level. At the dose of 0.01 ug/kg-day, signs of toxicity included decreases in gestational survival, decreased pup size at birth, and decreased neonatal survival and growth. For the 0.001 ug/kg-day dose group, no effect on fertility, litter size, or postnatal body weight was observed in any generation, and effects on neonatal survival were inconsistent. However, a re-evaluation of these data by Nisbet and Paxton (1982), using different statistical methods indicated

[2] An RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used..

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that there was a reduction in the gestational index, decreased fetal weight, increased liver to body weight ratio, and increased incidence of dilated renal pelvis at the 0.001 ug/kg dose. From these results, EPA (1987) determined that a dose of 0.001 ug/kg-day was the lowest-observed-adverse-effect-level (LOAEL), and calculated an RfD by dividing the LOAEL by an uncertainty factor of 1,000, yielding a result of 1E-06 ug/kg-day (1 pg/kg-day). The uncertainty factor of 1,000 was chosen in accordance with National Academy of Sciences (NAS) and EPA ODW guidelines for use with a LOAEL from an animal study. This uncertainty factor accounts for uncertainty in extrapolation from animals to humans (10x), variation in sensitivity between humans (10x), and use of a LOAEL rather than a NOAEL (10x). ODW states that this value has been peer-reviewed, but documentation of the peer review was not located.

ATSDR (1998)

ATSDR has derived a chronic oral Minimal Risk Level (MRL)[3] of 1 pg/kg-day (ATSDR 1998). This value is based on a study by Schantz et al. (1992) in which female monkeys were exposed to dioxin in the diet for 16 months at 0, 5 or 25 ppt TCDD. After 7 months of exposure, the females were bred with unexposed males. Exposure of the females continued through mating, gestation and lactation. Only one monkey in the high dose group delivered a viable offspring, so this group was not studied further. When offspring from the control group and the 5 ppt group were 8.6 months of age, they were placed in peer groups of 4 monkeys (2 exposed, 2 control) and allowed to play without interference. Behavioral patterns (social interactions, vocalizations, locomotion, self-directed behavior, environment exploration) were monitored 4 days/week for 9 weeks. No overt signs of toxicity were observed in the mothers or the offspring, and birth weights were not adversely affected. However, significant alterations were observed in play behavior, displacement and self-directed behavior, with a tendency for offspring from exposed mothers to initiate more rough/-tumble play bouts, to retreat from play less often, and to engage in more self-directed behavior. Based on this, a dietary exposure level of 5 ppt was identified as a LOAEL. The estimated dose from this diet was 1.2E-04 ug/kg-day. This dose was adjusted by dividing by an overall uncertainty factor of 100 to account for use of a minimal LOAEL, inter-species extrapolation, and inter-individual variability. This yielded an MRL of 1E-06 ug/kg-day (1 pg/kg-day). All ATSDR Toxicity Profiles are peer reviewed and publicly available.

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[3] An 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 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.

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WHO (1991, 1998); JECFA (2002)

The World Health Organization (WHO) has been organizing expert consultations and workgroups for a number of years to derive toxicity values for the evaluation of dioxin toxicity. The results of their first consultation was issued in 1990. At that time, WHO (1991, 1992) concluded that TCDD was carcinogenic in animals, acting as a non-genotoxic promoter-carcinogen. Therefore, the consultation decided to establish a Tolerable Daily Intake (TDI)[4] based on general toxicological effects. Based on liver, immunological and reproductive effects in animals, the no-effect dose was estimated to be about 1,000 pg/kg-day. This value was adjusted to an equivalent human dose of 100 pg/kg-day using toxicokinetic data. After applying an uncertainty factor of 10 to account for insufficient data on reproductive effects in humans, a TDI of 10 pg/kg-day was recommended.

In 1998, the WHO European Centre for Environmental Health (WHO-ECEH) and International Programme on Chemical Safety (IPCS) performed a re-assessment of the available information on the toxicity of dioxin (WHO 1998), and reached the following key conclusions:

- The cancer effects of dioxin are mediated by a non-genotoxic mode of action that is mediated via a receptor binding mechanism. Consequently, cancer risk has a threshold, and exposures that do not cause non-cancer effects will not increase cancer risk.
- The most sensitive non-cancer effects caused by dioxin include developmental and reproductive effects in rats and monkeys.
- The most reliable metric of exposure for use in risk evaluation is tissue burden rather than ingested dose.

Based on these key conclusions, WHO (1998) estimated the TDI (pg/kg-day) for lifetime exposure in a series of 3 steps, as follows:

Step 1: Identify the tissue burden effect level for the most sensitive (and relevant) adverse responses. Based on studies in rats and monkeys, the WHO estimated that the LOAEL tissue burdens ranged from 28-73 ng/kg (28,000-73,000 pg/kg).

[4] A TDI is an estimate of the amount of a substance in air, food or drinking water that can be taken in daily over a lifetime without appreciable health risk. TDIs are calculated on the basis of laboratory toxicity data to which uncertainty factors are applied.

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Step 2: Given the tissue burden range, calculate the TDI that would yield this tissue burden range. The WHO computed the TDI using a simple steady-state pharmacokinetic model of the following form:

$$\text{TDI (pg/kg-d)} = \text{Tissue Burden (pg/kg)} \cdot [1-\exp(-\ln(2)/t_{1/2})] / f$$

where:

$t_{1/2}$ = half-life of dioxin in the body (days)
f = fraction of an ingested dose that is absorbed

WHO utilized a half-life of 7.5 years (2,738 days), and an assumed fractional absorption of 0.5 (50%). Based on this, the TDI was estimated to range from 14-37 pg/kg-day.

Step 3: Adjust the TDI to account for uncertainties. A factor of 10 was applied to address the following uncertainties: a) the use of a range of LOAELs instead of a no-effect level, b) the possible differences in susceptibility between humans and experimental animals, c) the potential differences in susceptibilities within the human population, and d) differences in half-lives of elimination for the compounds of a complex TEQ mixture. After application of the uncertainty factor, the TDI (rounded) was estimated to range from 1-4 pg/kg-day. The WHO (1998) consultation stressed that the upper range of the TDI of 4 pg/kg-day should be considered a maximal tolerable intake on a provisional basis and that the ultimate goal is to reduce human intake levels to below 1 pg/kg-day.

More recently, the Joint FAO/WHO Expert Committee on Food Additives (JECFA 2002) re-evaluated dioxin toxicity based on two new reproductive studies (Ohsako et al. 2001 and Faqi et al. 1998) published since the previous assessment.

Faqi et al. (1998) exposed female rats subcutaneously with TCDD at 0, 25, 60 or 300 ng/kg, followed by weekly maintenance doses of 0, 5, 12 or 60 ng/kg, beginning 2 weeks before the beginning of mating and continually through mating, gestation and lactation. Male offspring were assessed for sexual development and were bred to untreated females. Adverse effects on sperm were detected at all doses on postnatal day 170.

Ohsako et al. (2001) administered a single oral dose of 0, 12.5, 50, 200 or 800 ng/kg of TCDD to pregnant rats, and male offspring were assessed for reproductive development. Adverse effects that were noted on postnatal day 49 and/or day 120 included reduced anogenital distance (50, 200 or 800 ng/kg), reduced ventral prostate weight (200 or 800 ng/kg), reduced androgen receptor messenger ribonucleic acid (mRNA) production in

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ventral prostate (all doses) increased 5-alpha-reductase type 2 mRNA in ventral prostate (all doses), and decrease androgen receptor mRNA in the ventral prostate (all doses).

JECFA (2002) used two alternative models (linear model and power model) to estimate the relationship between fetal and maternal body burden and to calculate a Provisional Tolerable Monthly Intake (PTMI) for each of these two new studies. The resulting values are summarized in Table A2-4.

Based on these calculations, JECFA (2002) concluded that the range of PTMI values was 40-100 pg/kg-month, and chose the mid-point of this range (70 pg/kg-month) as the final PTMI. Assuming 30 days/month, this is equivalent to a TDI of 2.3 pg/kg-day.

Because all of the evaluations described above were performed by panels of expert scientists, all of the TDI values derived are considered to be adequately peer-reviewed.

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TABLE A2-1 CANCER SLOPE FACTORS DEVELOPED BY EPA (1985)

Study	Pathologist	Species	Gender	Tissue(s)	Tumor Type(s)	CSF $(pg/kg\text{-}day)^{-1}$
Kociba et al. 1978	Kociba	Rat	Male	Nasal turbinates/hard palate	Carcinoma	1.5E-05
Kociba et al. 1978	Squire	Rat	Male	Nasal turbinates/hard palate/tongue	Carcinoma	1.7E-05
Kociba et al. 1978	Kociba	Rat	Female	Lung Nasal turbinate/hard palate Liver	Carcinoma Carcinoma Hyperplastic nodules or carcinoma	1.51E-04
Kociba et al. 1978	Squire	Rat	Female	Lung Nasal turbinate/hard palate Liver	Carcinoma Carcinoma Hyperplastic nodules or carcinoma	1.61E-04
NTP 1982	NTP	Rat	Female	Liver	Carcinoma and neoplastic nodules	3.3E-05
NTP 1982	NTP	Mouse	Male	Liver	Carcinoma	7.5E-05
NTP 1982	NTP	Mouse	Female	Subcutaneous tissue Blood Liver	Fibrosarcoma Lymphoma or leukemia Carcinoma or adenoma	4.6E-05

Shaded cells indicate the slope factors recommended by EPA (1985) for use.

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TABLE A2-2 CANCER SLOPE FACTORS DEVELOPED BY CALEPA (1986)

Study	Pathologist	Species	Gender	Tissue(s)	Tumor Type(s)	iUR $(ng/m^3)^{-1} \times 10^3$	CSF (pg/kg-day)-1
Kociba et al. 1978	Kociba	Rat	Male	Nasal turbinates/hard palate	Carcinoma	4.2	1.5E-05
Kociba et al. 1978	Squire	Rat	Male	Nasal turbinates/hard palate/tongue	Carcinoma	4.9	1.7E-05
Kociba et al. 1978	Kociba	Rat	Female	Liver	Carcinoma and neoplastic nodules	27	9.5E-05
Kociba et al. 1978	Squire	Rat	Female	Liver	Carcinoma and neoplastic nodules	25	8.8E-05
NTP 1982	NTP	Rat	Female	Liver	Carcinoma and neoplastic nodules	9.4	3.3E-05
NTP 1982	NTP	Mouse	Male	Liver	Carcinoma and adenomas	38	1.3E-04
NTP 1982	NTP	Mouse	Female	Subcutaneous tissue	Fibrosarcoma	2.4	8.4E-06

Shaded cell indicates the slope factor recommended by CalEPA (1986) for use.

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TABLE A2-3
RECOMMENDED EQUATIONS FOR COMPUTING CANCER PRGS FOR EXPOSURE OF RESIDENTS TO DIOIXN IN SOIL LIVER TUMOR OCCURRENCE IN FEMALE RATS (KOCIBA ET AL. 1978) BASED ON TWO ALTERNATIVE HISTOPATHOLOGICAL CLASSIFICATION METHODS

Dose (ug/kg-day)	Original Analysis (EPA 1985)			Reanalysis (EPA 1990)		
	Hyperplastic nodules	Hepatocellular carcinomas	Total Animals with Liver Tumors	Adenoma	Hepatocellular Carcinoma	Total Animals with Liver Tumors
0	8/86	1/86	9/86	2/86	0/86	2/86
0.001	3/50	0/50	3/50	1/50	0/50	1/50
0.010	18/50	2/50	18/50	9/50	0/50	9/50
0.100	23/49	11/49	34/48	14/45	4/45	18/45

Source: EPA (1990, 2003b)

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TABLE A2-4. RECOMMENDED EQUATION FOR COMPUTING CANCER PRGS FOR EXPOSURE OF WORKERS TO DIOXIN IN SOIL TDI CALCULATIONS FROM JECFA (2002)

Parameter	Faqi et al. (1998)		Ohsako et al. (2001)	
	Linear Model	Power Model	Linear Model	Power Model
LOEL Maternal body burden (ng/kg)	25	25	7.6	7.6
Equivalent body burden with repeated dosing (ng/kg)	25	39	13	19
Body burden from feed (ng/kg)	3	3	3	3
Total body burden (ng/kg)	28	42	16	22
EHMI[a] (pg/kg per month)	423	630	237	330
Safety factor	9.6	9.6	3.2	3.2
PTMI (pg/kg per month)	44	66	74	103
TDI[b] (pg/kg-day)	1.5	2.2	2.5	3.4

[a] Equivalent human monthly intake

[b] Calculated based on 30 days per month

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