Dioxin

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December 2001

Note: The information presented in this paper is based on the current public review draft of the Dioxin Reassessment (i.e., United States Environmental Protection Agency [USEPA] 1994 Dioxin Reassessment) (USEPA, 1994a). However, in June of 2000 the USEPA released a revised preliminary-draft of the Dioxin Reassessment in which the USEPA is proposing to classify 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) as a known human carcinogen (TCDD is currently considered by the USEPA to be a probable human carcinogen) (USEPA, 2000). In addition, the revised assessment indicates that TCDD is approximately 10 times more potent a carcinogen than previously thought (USEPA, 2000). See http://www.epa.gov/ncea/pdfs/dioxin/dioxreass.htm for more information. It is important that Navy Remedial Project Managers (RPMs) are aware of this information and understand that it may change substantially before being finalized. Furthermore, the USEPA states,

> *NOTICE: THESE DOCUMENTS ARE PRELIMINARY DRAFTS. They have not been formally released by the U.S. Environmental Protection Agency and should not at this stage be construed to represent Agency policy or factual conclusions. These documents are being provided now for external scientific review and will also be submitted to EPA's Science Advisory Board. They should not be cited or referred to as EPA's final assessment of dioxin risks (http://www.epa.gov/ncea/dioxin.htm).*

Executive Summary

Polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) (i.e., dioxins) are, as a class, the most potent carcinogens ever evaluated by the USEPA. This group of chemicals has caused great concern to the general public, as well as intense interest in the scientific community. The following issues should be considered when dealing with sites impacted by dioxins:

1. Sites where dioxins are of concern are likely to undergo much more scrutiny and public discussion than typical hazardous waste sites. Because of the widespread concern over dioxins, it is important to develop an effective risk communication strategy to address stakeholders concerns throughout the investigation and remediation processes.

2. Dioxins are persistent in the environment and readily bioaccumulate up the food chain. Consequently, dioxins are of particular concern at sites where indirect exposure pathways (e.g., ingestion of fruits/vegetables, meat, dairy products, and breast milk) are of concern.

3. Analytical methods for determining dioxin concentration in environmental samples should be selected in consultation with a risk assessor to ensure that the detection limits are below risk-based screening concentrations because some analytical methods cannot detect dioxins at levels low enough to support risk assessment evaluations.

4. Historically, the USEPA has used a soil screening criterion of 1 part per billion (ppb) 2,3,7,8-Tetrachloro-p-dibenzodioxin (TCDD) Toxicity Equivalents (TEQs) for residential settings and 5 to 20 ppb TEQ for commercial and industrial settings (USEPA, 1999). These concentrations are higher than risk-based screening levels and project managers should be aware of these benchmarks when evaluating remedial alternatives at a site.

Key Issues and Concepts

- ☑ Dioxins are a high profile family of chemicals that have generated considerable concern among the general public because they are among some of the most toxic chemicals ever evaluated for toxicity in animals.

- ☑ Dioxins are ubiquitous in the environment at low levels. It is believed that the majority of exposure to dioxins is through consumption of food products such as beef and milk.

- ☑ 2,3,7,8-TCDD is the most toxic of the dioxin compounds. The toxicity of all other dioxins are expressed relative to 2,3,7,8-TCDD via Toxic Equivalence Factors (TEFs). 2,3,7,8-TCDD Toxic Equivalents (TEQs) are determined by multiplying the compound concentrations by their respective TEF and summing them.

- ☑ 2,3,7,8-TCDD, and related compounds, have the ability to produce a wide spectrum of responses in animals (e.g., cancer, reproductive/developmental, and immunotoxic effects) and presumably, in humans.

- ☑ It is unclear how toxic dioxins are to humans because the deleterious effects observed in animals have not been convincingly demonstrated in humans.

- ☑ The background concentration of dioxins in U.S. soil is approximately 8 parts per trillion TEQ (USEPA, 1994b).

- ☑ Dioxins rapidly decompose in sunlight; therefore, soil sampling depth intervals should be evaluated to determine if they are representative of plausible exposures (USEPA, 1994c).

- ☑ Dioxins are unwanted byproducts of combustion and chemical manufacturing. As such, wind direction is often an important factor in determining deposition of dioxins. Therefore, where appropriate, a historic wind rose pattern should be used to focus sampling in areas that are predominantly downwind of a source.

- ☑ Some polychlorinated biphenyls (PCBs) are thought to also exhibit dioxin-like toxicity. When PCB congener concentrations are available, the usual PCB slope factor approach can be supplemented by analysis of dioxin TEQs to evaluate dioxin-like toxicity.

1.0 Introduction

Dioxins are a group of chemicals that are colorless, odorless, and contain carbon, hydrogen, oxygen, and chlorine. There are 75 individual compounds comprising the PCDDs, differentiated by the positioning of the chlorine(s), and 135 different PCDFs. These are called individual congeners. The most widely studied of these compounds is 2,3,7,8-TCDD. This compound is considered the most toxic of the group and represents the reference compound for this class of compounds (USEPA, 1994a).

Dioxins have caused great concern in the general public as well as intense interest in the scientific community. There have been several events where people have been exposed to dioxins including an industrial accident in which dioxins were released to the environment in a residential area in Seveso, Italy; the spraying of waste oil that contained dioxins on roads in Times Beach, Missouri; and the spraying of Agent Orange in Vietnam which contained dioxins as contaminants (USEPA, 1994c). Much of the public concern revolves around the characterization of these compounds as among the most potent toxicants ever studied. Indeed, based on traditional toxicology studies, these compounds are extremely potent in producing a variety of effects in experimental animals at levels hundreds or thousands of times lower than most chemicals of environmental interest (USEPA, 1994c).

2.0 Dioxin in the Environment

Dioxins are unwanted byproducts of combustion (e.g., incinerators, coal combustion) and chemical manufacturing (e.g., weed killers, wood preservatives). They decompose rapidly in sunlight but tend to be persistent for up to ten years in soil layers not exposed to sunlight. In soil, sediment, and water dioxins are primarily associated with particulate and organic matter (USEPA, 1994c).

Dioxins have been detected all over the earth. They are found in small amounts in the soil, air, sediment, and water worldwide. They are also found in most plants, animals, and people. Combustion sources emit dioxins into the air where it exists bound to particulates or in vapor form. While in the air, dioxins can be breathed in by people and animals. The dioxins attached to particulates deposit on land, oceans, lakes, and rivers where they may be absorbed by plants (primarily via root uptake) or ingested by animals.

Dioxins have a high affinity for lipids and bioaccumulate to a greater extent in organisms with a high fat content. It is generally thought that dietary intake is the primary pathway of human exposure to dioxins. It has been suggested that greater than 90 percent of human exposure to dioxin occurs through the diet, with foods from animal origins being the predominant pathway (USEPA, 1994c).

3.0 Dioxin Toxicity

3.1 Toxicity Summary

Note: The information presented in this section is based on the current revision of the Dioxin Reassessment (i.e., USEPA 1994 Dioxin Reassessment) (USEPA, 1994a) and does not incorporate information presented in the March 2000 revised preliminary-draft of the USEPA Dioxin Reassessment (http://www.epa.gov/ncea/pdfs/dioxin/dioxreass.htm) (USEPA, 2000). In the March 2000 preliminary draft Dioxin Reassessment the USEPA is proposing to classify TCDD as a known human carcinogen and indicates that TCDD is approximately 10 times more potent a carcinogen than previously thought (USEPA, 2000). Navy RPMs should be are aware of this information and understand that it may change substantially before being finalized. Consequently, the information presented below may or may not be outdated when the draft USEPA Dioxin Reassessment is finalized.

The USEPA reassessment of dioxins began in 1991, when USEPA announced that it would conduct a scientific reevaluation of the health risks resulting from exposure to dioxins. The main motivation for the reassessment was new mechanistic information concerning dose/response. In September 1994, the USEPA released the first draft of the Health Assessment Document for 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) and Related Compounds (USEPA, 1994c). Some key findings of the reassessment are as follows:

- **Human Studies** – Exposure to TCDD and related compounds is associated with chloracne and with subtle biochemical and biological changes whose clinical significance is as yet unknown. It is very difficult to determine a dose/response for other serious health effects because relatively few chronic effects related to exposure to dioxin-like compounds have been observed in humans.

- **Carcinogenicity** – There is adequate evidence of carcinogenicity in animals based on long-term bioassays. It has also produced cancer in rats and mice that were fed high levels of the chemical over a long period of time (USEPA, 1999). Epidemiological evidence for carcinogenicity in humans remains controversial. The USEPA states that "there is sufficient evidence to conclude that the compound is a probable human carcinogen." The International Agency for Research on Cancer currently identifies 2,3,7,8-TCDD as a being carcinogenic to humans (ATSDR, 1998).

- **Reproductive and Developmental** – Dioxins' ability to cause reproductive and developmental toxicity in animals (fish, birds, mammals) is well known. In lab animals, dioxins have been

responsible for skin and hair abnormalities, cleft palates, kidney abnormalities in offspring, increased numbers of miscarriages and even death. The USEPA suggests that developmental/reproductive effects may be the most sensitive human endpoints.

- **Immunotoxicity** – There is limited evidence of immunotoxicity in humans. Exposure to dioxins resulted in immunotoxic effects in animals.

- **Noncarcinogenic Reference Dose (RfD)** – There is currently no USEPA recommended RfD for dioxins. An RfD for dioxins, calculated based on animal data and standard uncertainty factors to account for species differences and sensitive subpopulations, would likely result in reference intake levels on the order of 10 to 100 times below the current estimates of "background" daily intake in the general population (USEPA, 1994a). Therefore, there is no noncarcinogenic RfD for dioxins.

- **Cancer Slope Factor** - The cancer slope factor decreased from 150,000 to 100,000 (kg-day/mg) based on the USEPA reassessment which attempted to bring more data into the evaluation of cancer potency. The latter value has not been added to the Integrated Risk Information System (IRIS) profile (i.e., there is not agency consensus that the new slope factor should be used).

Because many of the health effects described above can also be caused by other chemicals and certain natural diseases, it is difficult to link an illness to dioxins without a documented history of high exposure.

3.2 Toxic Equivalent Factors (TEF) and Toxic Equivalents (TEQ)

Only 7 of the 75 congeners of PCDDs are thought to have dioxin-like toxicity; these have chlorine substitutions in, at least, the 2, 3, 7, and 8 positions. Only 10 of the 135 possible congeners of PCDFs are thought to have dioxin-like toxicity; these also have substitutions in the 2, 3, 7, and 8 positions (USEPA, 1994a). The toxicity of other 2,3,7,8-substituted congeners are expressed relative to 2,3,7,8-TCDD, the most toxic of the group, using TEFs.

TEFs were developed to compare the relative toxicity of individual dioxin-like compounds to that of TCDD. This comparison is based on the assumption that TCDD and TCDD-like compounds act through the same mechanisms of action. The TEF for TCDD is defined as one, whereas TEF values for all other TCDD-like compounds are less than one. Toxicity equivalents (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 toxicity equivalency factor (TEF_i) for that compound. The total TEQ is the sum of the TEQs for each of the congeners in a given mixture. The following equation summarizes this approach:

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

The toxic equivalency factors currently recommended by the USEPA are presented in Table 1 (Van Leeuwen, 1997).

Some PCBs are thought to also exhibit dioxin like toxicity even though they are distinctly different compounds. When PCB congener concentrations are available, the usual PCB slope-factor approach can be supplemented by analysis of dioxin TEQs to evaluate dioxin-like toxicity. Risks from the dioxin-like congeners are evaluated using TEFs would be added to risks from the rest of the mixture (USEPA, 1996).

Table 1
Toxicity Equivalency Factors (TEFs) for Dioxins (Van Leeuwen, 1997)

Constituent	TEF*
Chlorinated Dibenzodioxins	
Mono-, Di-, and Tri-CDDs	0
2,3,7,8-TCDD	1
Other TCDDs	0
2,3,7,8-PeCDD	1
Other PeCDDs	0
2,3,7,8-HxCDD	0.1
Other HxCDDs	0
2,3,7,8-HpCDD	0.01
Other HpCDDs	0
OCDD	0.0001
Chlorinated Dibenzofurans	
Mono-, Di-, and Tri-CDFs	0
2,3,7,8-TCDF	0.1
Other TCDFs	0
1,2,3,7,8-PeCDF	0.05
2,3,4,7,8-PeCDF	0.5
Other PeCDFs	0
2,3,7,8-HxCDF	0.1
Other HxCDFs	0
2,3,7,8-HpCDF	0.01
Other HpCDFs	0
OCDF	0.0001

*–The TEFs presented above are based on the weighting system proposed by the World Health Organization in 1998 (Van Leeuwen, 1997).

4.0 Background Dioxin Concentrations

There has been a significant amount of study attempting to characterize background concentrations of dioxins throughout the world. In the United States, the ambient background concentration of dioxins in soils is approximately 8 parts per trillion TEQ (USEPA, 1994b). Background concentrations of dioxins have also been determined for a variety of food crops. Depending on the type of site and issues involved it may be prudent to determine "area background" dioxin concentrations. Alternatively, the background data determined by the USEPA could be used in some cases to provide context to site-specific dioxin concentrations.

5.0 Analytical and Data Issues

5.1 Analytical Methods

The analytical costs of evaluating soil samples for dioxin congeners are high relative to other methods. For risk assessment purposes it is necessary to quantitate the different 2,3,7,8-dioxin congeners in order

to determine the 2,3,7,8-TCDD TEQ for each sample. This means that samples that are analyzed for total dioxins are of little use for risk assessment purposes because there is no way to apply the congener-specific TEFs to the mixture. In addition, when considering different analytical methods it is important to evaluate the sample quantitation limits and compare them to risk-based screening concentrations to ensure that the method that is selected is adequate for risk assessment. USEPA Method 8280a is unable to provide data for levels less than 1 ppb TEQ (USEPA, 1995). USEPA Method 8290 can provide analytical data in the range of 50 part per trillion (ppt) to 1 ppb TEQ and has a detection limit of 1 – 5 ppt TEQ (USEPA, 1994d). A Risk Assessor should be consulted to determine which analytical method, or combination thereof, is appropriate for a site.

5.2 Importance of Non-Detected Data

A key risk assessment issue related to dioxins is how to deal with non-detected data. Use of one-half of the detection limit for non-detects is a reasonable but conservative approach to estimate concentrations in samples. However, if one-half of the detection limit is used for all non-detected data to calculate a TEQ, then the resulting concentration may result in a cancer risk greater than 1E-06. This reinforces the need for selecting sensitive analytical methods to avoid the case where non-detected results "drive" the overall risks.

The USEPA recommends that in general, "eliminate those chemicals that have not been detected in any samples of a particular medium (USEPA, 1989)." This principle should be applied to all chemicals (including dioxins); if an individual congener is not detected in any sample then it should be excluded from further consideration in the risk assessment.

6.0 Exposure Scenarios

It is estimated that 90% of human exposure to dioxins occurs via the diet with foods from animals (e.g., beef, dairy, eggs) being the predominant source (ATSDR, 1998). Based on this, and the fact that dioxins are persistent and readily bioaccumulate, risk assessors should pay special attention to indirect exposure pathways at sites where dioxins are a concern. Food consumption pathways should be critically evaluated during the development of the Conceptual Site Model. Both current and plausible future land use considerations should be assessed to determine if food consumption pathways should be evaluated at a site. Including indirect exposure pathways will significantly increase (i.e., potentially by orders of magnitude) the risks at a site.

7.0 Risk Management Considerations

7.1 Stakeholder Concern and Risk Communication

At sites where dioxins are an issue there is likely to be a great deal of regulatory focus. In addition, there may also be a great deal of public concern and scrutiny. Therefore, it is important to consider the stakeholders at each site, identify their concerns, and develop an effective risk communication strategy before an investigation is undertaken.

7.2 Historical Risk Management Precedents

The USEPA has typically used the following concentrations as benchmarks of concern (i.e., values that are used to assist in making risk management decisions) when making risk management decisions:

- USEPA presently considers values above 1 part per billion TEQ in neighborhood soils (i.e., a child residential scenario) to be an amount that needs further study or may need to be cleaned up (USEPA, 1999).

- USEPA considers values above 5 to 20 parts per billion TEQ in commercial soils (i.e., a worker occupational scenario) to be an amount that needs further study or may need to be cleaned up (USEPA, 1999).

These concentrations are higher than risk-based screening concentrations and project managers should be aware of these benchmarks when evaluating remedial alternatives at a site.

Sources of Additional Information

Agency for Toxic Substances and Disease Registry – Toxicological Profile for Chlorinated Dibenzo-p-Dioxins. 1998. U.S. Dept. of Health and Human Services. http://www.atsdr.cdc.gov/toxprofiles/tp104.html.

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USEPA. 1995. Method 8280a: Polychlorinated Dibenzodioxins (PCDDs) and Polychlorinated Dibenzofurans (PCDFs) by High-Resolution Gas Chromatography/Low-Resolution Mass Spectrometry (HRGC/LRMS).

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