

## ToxFAQs: CABS™/Chemical Agent Briefing Sheet

# Dioxins

March 2006

What are dioxins and what are dioxin-like compounds?

Term	Overview
<b>Dioxins</b>	Dioxins, or chlorinated dibenzo- <i>p</i> -dioxins (CDDs), are a class of structurally similar chlorinated hydrocarbons. The basic structure is comprised of two benzene rings joined via two oxygen bridges at adjacent carbons on each of the benzene rings. There are eight homologues of CDDs, monochlorinated through octachlorinated. Each homologous group contains one or more isomers or congeners.
<b>Dioxin</b>	A term used interchangeably with 2,3,7,8-tetrachlorodibenzo- <i>p</i> -dioxin (2,3,7,8-TCDD or TCDD). This is the most toxic form of dioxins.
<b>Dioxin-like compounds</b>	These compounds are from a group of halogenated aromatic hydrocarbons that have molecules shaped like TCDD. They produce similar toxic effects as dioxin. They include certain chlorinated dibenzofurans (CDFs), polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs), brominated dibenzo- <i>p</i> -dioxins (BDDs), and brominated dibenzofurans (BDFs).

Not all dioxins have the same toxicity or ability to cause illness and adverse health effects. The most toxic chemical in the group is TCDD. It is the standard to which other dioxins are compared. The levels of other dioxins measured in the environment are converted to a TCDD-equivalent concentration on the basis of how toxic they are compared to TCDD. These converted dioxin levels are then added together to determine the total equivalent (TEQ) concentration of the dioxins in a sample.

What are the characteristics of dioxin-like compounds?

The halogenated dioxins and furans are a diverse set of chemicals.

- Dioxin consists of two benzene molecules joined with two oxygen bridges.
- Furans consist of two benzene molecules fused to a central furan ring.
- There are 75 dioxin isomers and 135 furan isomers.
- Not all the isomers are biologically active and they differ in toxicity.
- Seven of the dioxins commonly found in tissue samples possess dioxin-like toxicity;
- Ten of the furans commonly found in tissue samples possess dioxin-like toxicity.

## What are the common uses of dioxins?

Dioxins are not intentionally produced and have no known use. They are the by-products of various industrial processes (i.e., bleaching paper pulp, and chemical and pesticide manufacture) and combustion activities (i.e., burning household trash, forest fires, and waste incineration). The defoliant Agent Orange, used during the Vietnam War, contained dioxins. Dioxins are found at low levels throughout the world in air, soil, water, sediment (the bottom of rivers, streams, and lakes), and in foods such as meats, dairy, fish, and shellfish. The highest levels of dioxins are usually found in soil, sediment, and in the fatty tissues of animals. Much lower levels are found in air and water.

CDDs are not manufactured commercially in the United States except on a small scale for use in chemical and toxicological research. They are unique among the large number of organochlorine compounds of environmental interest in that they were never produced intentionally as desired commercial products.

## What are the sources and routes of exposure for dioxins?

Dioxins are produced as by-products of incomplete combustion and some chemical processes, including natural ones.

### General sources of exposure

Dioxins enter the physical environment by release during

- Combustion
- Metal smelting and refining
- Manufacturing of chlorinated chemicals
- Paper bleaching
- Natural biological and photochemical processes
- Mobilization from environmental reservoirs (e.g., stirred sediments)

The chart below lists specific sources and routes of exposure.

Specific sources and routes of exposure	
<b>Exposure through diet</b>	The major sources of human exposure (96%) are <ul style="list-style-type: none"><li>• Animal fats found in meats</li><li>• Full fat dairy products</li><li>• Fatty fish (herring, mackerel, salmon, sardines, trout, tuna)</li></ul>
<b>Exposure through air</b>	<ul style="list-style-type: none"><li>• Breathing incineration gases released from medical, municipal, and hazardous waste incinerators.</li><li>• Breathing gases released by industrial processes from paper mills, cement kilns, and metal smelters.</li></ul>

Specific sources and routes of exposure	
<b>Exposure through occupation</b>	<p>People who perform the following types of work can be exposed to dioxins:</p> <ul style="list-style-type: none"> <li>• Production and handling of certain chlorinated phenols (such as 2,4,5-trichlorophenol or pentachlorophenol [PCP])</li> <li>• Production or handling of chlorinated pesticides, such as 2-4-dichlorophenoxyacetic acid (2,4-D) and other herbicides</li> <li>• Chlorinated pesticide application</li> <li>• Pressure treatment of wood with PCP and handling of PCP-treated wood</li> <li>• Production of chlorinated paper at pulp and paper mills</li> <li>• Operation of municipal solid waste or hazardous waste incinerators</li> <li>• Hazardous waste clean-up operations</li> </ul>
<b>Accidental exposure</b>	Rare cases of high level exposures through industrial accidents such as occurred in Seveso, Italy.
<b>Exposure from waste sites</b>	Potential chronic low level exposure by living next to a hazardous waste site containing dioxins. Currently, in the United States, there are 126 Superfund sites (with a completed exposure pathway) contaminated with dioxins.

What are the possible toxic effects of dioxins?

Toxic effects of dioxin exposure	
<b>Biochemical effects</b>	<p>Dioxin is believed to exert its toxicity by acting on</p> <ul style="list-style-type: none"> <li>• Detoxification enzymes such as cytochrome P450 enzymes CYP1A1, CYP1A2, and CYP1B1</li> <li>• Estrogen receptors</li> <li>• Cytokines (tumor necrosis factor) and interleukins (1 and 6)</li> <li>• Generation of oxidative species leading to cellular oxidative stress</li> <li>• Growth factors (transforming growth factor [TGF], epidermal growth factor [EGF], and glucocorticoid receptors)</li> </ul>
<b>Cellular effects</b>	Dioxins are believed to affect the growth regulation of cells. They can induce or block programmed cell death (apoptosis). Thus, dioxins can induce either cell proliferation or differentiation. This may lead to tissue underdevelopment (hypoplasia), overgrowth (hyperplasia), transformation (metaplasia), or tumor formation (neoplasia).

Toxic effects of dioxin exposure	
<b>Carcinogenicity</b>	<p>TCDD carcinogenicity in animals is well established. All cancer bioassays have been positive. They show that dioxin is a complete carcinogen that does not require another chemical exposure for full action.</p> <ul style="list-style-type: none"> <li>• TCDD appears to be a potent tumor promoter. However, the specific carcinogenic mechanism for TCDD has not been fully elucidated.</li> <li>• TCDD produces cancer at all sites in animals. Epidemiological data support that TCDD increases cancer incidence in all sites for humans.</li> <li>• World Health Organization (WHO), National Institute for Occupational Safety and Health (NIOSH), and the U.S. Environmental Protection Agency (EPA) concluded that dioxin increases the risk for all cancers.</li> <li>• Dioxin also increases the risk for several individual cancers, including soft-tissue malignant tumor (sarcoma), lung cancer, cancer of the lymphatic tissue (non-Hodgkin's lymphoma), and malignant enlargement of the lymph nodes, spleen, and liver (Hodgkin's disease).</li> </ul>
<b>Confirmed human health effects (noncancers)</b>	<p>Dioxins can cause several health effects:</p> <ul style="list-style-type: none"> <li>• A skin disorder known as chloracne</li> <li>• Transient mild liver damage (hepatotoxicity)</li> <li>• Peripheral nerve damage (neuropathy)</li> </ul>
<b>Suspected health effects</b>	<p>Suspected health effects of dioxins include the following:</p> <ul style="list-style-type: none"> <li>• Respiratory cancers</li> <li>• Prostate cancer</li> <li>• Multiple myeloma (malignant tumor of the bone marrow)</li> <li>• Porphyria cutanea tarda (liver dysfunction and photosensitive skin lesions)</li> <li>• Type 2 diabetes</li> <li>• Neurobehavioral development effects in infants</li> <li>• Men in highly exposed populations are less likely to father boys.</li> </ul>

### How are dioxins distributed in the human body?

Distribution Methods	
<b>Accumulation in body fat</b>	<p>After being absorbed, dioxin distributes to organs according to lipid (fat) content and readily accumulates in body fat. The 2000–2001 National Health and Nutrition Examination Survey (NHANES) survey found dioxin in serum at the range of 6.4 to 7.4 picogram/grams (serum lipid adjusted) in certain U.S. populations (5.8 pg/g lipid is the detection limit).</p>

Distribution Methods	
<b>Elimination</b>	<p>Levels of dioxin and dioxins in the environment have been declining since the 1980s.</p> <ul style="list-style-type: none"> <li>• Dioxins are stored in fatty tissue and excreted through bile into the feces. Nursing females also expel TCDD through their milk.</li> <li>• In animals, the major route of TCDD elimination is through bile into feces.</li> <li>• TCDD taken orally by animals is metabolized relatively slowly. Metabolism occurs mainly in the liver through detoxification. Once metabolites are formed, they are rapidly excreted in the bile and urine.</li> <li>• Major metabolites consist of hydroxylated or methoxylated dioxin derivatives. These are excreted as glucuronide and sulfate conjugates.</li> <li>• Unabsorbed TCDD is excreted through direct elimination in the feces.</li> <li>• The half-life of TCDD in the human body ranges from 7 to 12 years.</li> </ul>

Is there a test to see if my child or I have been exposed to dioxins?

Medical Tests	
<b>Blood and fatty tissue tests for TCDD levels</b>	<p>Fatty tissue and blood serum can be analyzed for the presence of TCDD by gas chromatography-mass spectrometry (GC-MS). This method can quantify TCDD to 100 parts per quadrillion. Serum levels have been correlated with fatty tissue levels in persons with long-term exposure. However, analyses of serum or fat TCDD levels by GC-MS are expensive and time-consuming. The testing <b>is not</b> done routinely, unless there is a valid concern regarding acute high dose or significantly increased exposure.</p>

What are the government/organizational guidelines for exposure to dioxins?

Agency	Guidelines
<b>WHO</b>	Total Daily Intake 1–4 picograms per kilogram per day (pg/kg/day)
<b>EPA</b>	No established reference concentrations (RfC) or reference doses (RfD)

## What are the minimal risk levels for exposure to dioxins?

ATSDR MINIMAL RISK LEVELS (MRLs)			
Name	Route	Duration	MRL
Dioxins	Oral	Acute	200 pg/kg/day
		Intermediate	20 pg/kg/day
		Chronic	1 pg/kg/day

## What are the most important or common mediating factors?

Factors that determine how severe the health effects are from dioxin exposure include

- dose
- age of the person exposed (children and fetuses are the most susceptible)
- duration of exposure
- health of the person exposed
- diet (consumption of meat, full fat dairy products, and fatty fish)

## Future Research Needs:

To close gaps in scientific knowledge of the health effects of dioxins, a *long-term* research program is needed that would focus on the following information needs:

<b>Physical and chemical properties</b>	Information on physical and chemical properties of certain congeners (particularly 1,2,3,7,8,-pentachlorodibenzo- <i>p</i> -dioxin and 1,2,3,6,7,8-hexachlorodibenzo- <i>p</i> -dioxin) would help clarify the different fate and transport pathways of the homologous groups
<b>Production, import/export, use, and release and disposal</b>	CDD releases are not required to be reported to EPA, so there are no Toxics Release Inventory data for CDDs.
<b>Environmental fate</b>	A better understanding of how CDDs behave in the environment will help answer such questions as <ul style="list-style-type: none"> <li>• What is the importance of vapor-phase versus particulate transport?</li> <li>• Why does the environmental behavior of congeners differ?</li> <li>• What is significance of processes that reintroduce CDDs into the atmosphere after deposition?</li> </ul>

	Information regarding the degradation of other congeners, specifically octachlorodibenzo- <i>p</i> -dioxin (OCDD), and their degradation products in water, sediment, and soil would be useful in evaluating the various pathways of human exposure.
<b>Bioavailability from environmental media</b>	More information is needed about oral and skin exposures to determine the bioavailability of CDDs from food, water, and soil. More information is needed to examine the discrepancy in the mass balance from CDDs ingested from foods and eliminated in feces. For inhalation exposure, information on the bioavailability from fly ash and sediments would be useful. Information is also needed on the selective uptake of the 2,3,7,8-substituted CDD congeners.
<b>Food chain bioaccumulation</b>	Information is needed from a larger number of species on their retention of 2,3,7,8-substituted CDD congeners. General information on retention and distribution of other CDDs would be useful in better understanding aquatic and terrestrial food chains.
<b>Exposure levels in environmental media</b>	Reliable monitoring data for the levels so that the information obtained on levels known body burdens of CDDs to assess the vicinity of hazardous waste sites.
<b>Exposure levels in humans</b>	Additional biological monitoring data are needed for those U.S. populations surrounding hazardous waste sites or municipal, medical, or industrial incinerators. Comparisons are needed for urban versus rural exposures. Data are also needed for other potentially exposed populations such as subsistence fishers and hunters. Information on tissue levels in the general population worldwide is mostly deficient. As they are identified, exposed populations should be evaluated to characterize exposure levels and health effects. This information may show a need to conduct health studies on these populations.

For more information

<b>ATSDR online resources</b>	<ul style="list-style-type: none"> <li>• <b>Interaction Profile for Persistent Chemicals Found In Breast Milk</b> <a href="http://www.atsdr.cdc.gov/interactionprofiles/ip03.html">http://www.atsdr.cdc.gov/interactionprofiles/ip03.html</a></li> <li>• <b>Minimal Risk Levels (MRLs) for 2,3,7,8-tetrachlorodibenzo-<i>p</i>-dioxin (TCDD), polychlorinated biphenyls (PCBs) and 2,3,4,7,8 pentachlorodibenzofuran</b> <a href="http://www.atsdr.cdc.gov/mrls.html">http://www.atsdr.cdc.gov/mrls.html</a></li> <li>• <b>National Exposure Registry</b> <a href="http://www.atsdr.cdc.gov/NER/dxn.html">http://www.atsdr.cdc.gov/NER/dxn.html</a></li> <li>• <b>Public Health Statement for Chlorinated Dibenzo-<i>p</i>-dioxins (CDDs)</b> <a href="http://www.atsdr.cdc.gov/toxprofiles/phs104.html">http://www.atsdr.cdc.gov/toxprofiles/phs104.html</a></li> <li>• <b>Public Health Statement for Chlorodibenzofurans (CDFs)</b> <a href="http://www.atsdr.cdc.gov/toxprofiles/phs32.html">http://www.atsdr.cdc.gov/toxprofiles/phs32.html</a></li> </ul>
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- **ToxFAQs™ for Chlorinated Dibenzo-*p*-dioxins(CDDs)**  
<http://www.atsdr.cdc.gov/tfacts104.html>
- **ToxFAQs™ for Chlorodibenzofurans (CDFs)**  
<http://www.atsdr.cdc.gov/tfacts32.html>
- **Toxicological Profile for Chlorinated Dibenzo-*p*-dioxins (CDDs)**  
<http://www.atsdr.cdc.gov/toxprofiles/tp104.html>
- **Toxicological Profile for Chlorodibenzofurans (CDFs)**  
<http://www.atsdr.cdc.gov/toxprofiles/tp32.html>

**For more information, contact:**

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