

Health Consultation

Dioxin Contamination on Residential Property
in the Tittabawassee River Floodplain
Saginaw County, Michigan

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**Prepared by the
Michigan Department of Community Health**

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Agency for Toxic Substances and Disease Registry
Division of Health Assessment and Consultation
Atlanta, Georgia 30333

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Acronyms and Abbreviations

2,4-D	2,4-dichloro-phenoxyacetic acid
2,4,5-T	2,4,5-trichloropheoxyacetic acid
AhR	aryl hydrocarbon receptor
ATSDR	Agency for Toxic Substances and Disease Registry
COPC	Contaminants of Potential Concern Committee of the World Trade Center
	Indoor Air Task Force Working Group
DHHS	United States Department of Health and Human Services
DLC	dioxin-like compound
EMEG	environmental media evaluation guide
EPA	United States Environmental Protection Agency
EU	exposure unit
FDA	United States Food and Drug Administration
IARC	International Agency for Research on Cancer
kg	kilogram
LD ₅₀	lethal dose to 50 percent of test animals
MDCH	Michigan Department of Community Health
MDEQ	Michigan Department of Environmental Quality
mg/day	milligram per day
MRL	minimum risk level
NAS	National Academy of Sciences
NHANES	National Health and Nutrition Examination Surveys
NTP	National Toxicology Program
PCBs	polychlorinated biphenyls
PEI	Pilot Exposure Investigation: Dioxin Exposure in Adults Living in the Tittabawassee River Floodplain Saginaw County, Michigan
PCB	polychlorinated biphenyl
pg/g	picograms per gram
pg/kg-month	picogram per kilogram-month
pg/w	picograms per wipe
ppt	parts per trillion
PTMI	provisional tolerable monthly intake
RDCC	residential direct contact criterion
TCDD	2,3,7,8-tetrachlorodibenzo-p-dioxin
TDS	Total Dietary Study
TEF	toxic equivalency factor
TEQ	toxic equivalent
TMI	tolerable monthly intake
UCL	upper confidence limit
UMDES	University of Michigan Dioxin Exposure Study
USDA	United States Department of Agriculture
WHO	World Health Organization

Summary

The Michigan Department of Community Health (MDCH) assisted the United States Environmental Protection Agency (EPA) and the Michigan Department of Environmental Quality (MDEQ) in evaluating dioxin-like compound (DLC) contamination in soil and dust in a residential area in the floodplain of the Tittabawassee River in the city of Saginaw, Michigan.

MDCH has reached three conclusions in this health consultation report:

1. *MDCH concluded that people living in a residential area of the city of Saginaw, Michigan breathed, touched, and accidentally ate DLCs in soil and dust for a year or longer, and this may have harmed their health.* MDCH calculated that adults and children living on affected properties took in DLCs at a higher rate than considered safe by the World Health Organization (WHO). The results of indoor dust sampling confirmed that outdoor DLC contamination is also found inside their homes. This was a past public health hazard.

Next Steps: No additional steps are needed by public health agencies to address this conclusion.

2. *MDCH concluded that the cleanup conducted under oversight of the EPA effectively removed DLCs from the top two feet of soil and from inside the homes and other residential buildings in the area.* Contaminated soil was removed to a depth of two feet below ground surface in residential areas and one foot below ground surface in non-residential areas. Clean fill, topsoil, sod and landscaping were added to restore the properties and to stop people from contacting deeper soil contamination that was not removed. Driveways and the shared dirt road were paved to prevent fugitive dust emissions from vehicle traffic. Indoor cleanup activities were conducted to remove contamination present in residents' homes. There is no apparent current public health hazard.

Next Steps: No additional steps are needed at this time to address this conclusion.

3. *MDCH concluded that future flooding of the Tittabawassee River could redeposit contaminants onto resident's yards.* DLC contaminated sediments are likely to be deposited onto residential properties during future Tittabawassee River flood events and people may be exposed to the renewed contamination. This is a potential future public health hazard.

Next Steps: A post-removal plan will be developed to prevent people from contacting DLC contamination that may result from flooding events in the Tittabawassee River floodplain. MDCH will remain available to assist the MDEQ and the EPA at high priority areas in the Tittabawassee River floodplain.

Purpose and Health Issues

On May 1, 2001, a Midland resident and two Michigan-based environmental organizations petitioned the federal Agency for Toxic Substances and Disease Registry (ATSDR) to conduct a public health assessment of DLC contamination in communities adjacent to Midland, Michigan. ATSDR and the MDCH have a cooperative agreement for conducting assessments and consultations for potential health hazards at sites of environmental contamination within the state of Michigan. MDCH has agreed to prepare public health consultations in response to the 2001 petition. ATSDR will review MDCH's work and provide technical support as needed.

The present consultation addresses DLC contamination found in soil and indoor dust samples collected from residential properties located in the Tittabawassee River floodplain. Additional consultations that address other contaminated media may be developed in the future with the ultimate goal of providing a full understanding of the related public health issues.

Background

On June 12, 2003, the MDEQ issued a Hazardous Waste Management Facility Operating License to the Dow Chemical Company (Dow) for its Midland, Michigan plant site. The Dow plant encompasses approximately 1,900 acres on the southern perimeter of the city of Midland. The Tittabawassee River flows through the plant site and then southeast to the confluence with the Saginaw River, which continues northeast to the Saginaw Bay of Lake Huron.

Under the 2003 operating license, Dow is required to investigate and address off-site releases of DLCs and other contaminants of concern. As part of the ongoing investigation, consultants for Dow collected soil and sediment samples from the Tittabawassee River and along transects laid across the floodplain on either side of the river. Dow submitted partial analytical results from these sampling efforts to the MDEQ in the fall of 2007.

Beginning in early 2008, the MDCH met with the MDEQ, the EPA, and the EPA's consultant to identify several areas where higher DLC levels were identified by the Dow 2007 sampling event. Residential or other high use areas where higher DLC levels were found were designated as "Exposure Units" (EU) and were given a numerical designation (e.g., EU001, EU002). MDCH and MDEQ recommended that a residential area immediately adjacent to the Tittabawassee River be given first priority and this area was designated as EU001.

EU001 is located in Saginaw County, within the city of Saginaw on the north shore of the Tittabawassee River near the confluence with the Shiawassee and Saginaw Rivers (Figure 1). The Tittabawassee River frequently floods the EU001 area, sometimes more than once per year depending on weather events. When the area floods, DLC contaminated soil and sediment from upstream locations is carried onto residential properties where residents can make contact with the contamination and track it into their homes. As the flood water recedes, DLC contamination may also be transported to other downstream locations (EPA 2008). Soil, indoor dust, and chicken egg samples were collected by the MDEQ and MDCH between 2000 and 2002. The results submitted by Dow in 2007, as well as these previous sampling efforts indicated the potential for widespread DLC soil contamination. Analysis of four eggs from chickens kept on property in the area had elevated levels of DLC contamination, consistent with the observed soil contamination.

A private dirt road runs through the area, which is approximately 1,000-feet long by 150-feet wide. The area is divided into 26 parcels of property that include 11 private residences as well as open lots that residents use for a variety of activities (EPA 2008). Each property was identified in sampling plans and other project documents as Property A, Property B and so forth. The EPA tasked the Weston Solutions, Inc. (Weston) Superfund Technical Assessment and Response Team (START) with environmental sampling at EU001.

Discussion

The ATSDR has developed a soil Environmental Media Evaluation Guide (EMEG) screening level for DLCs of 50 parts per trillion (ppt) expressed as total dioxin toxic equivalent (TEQ) to assess the need for further evaluation of DLC contamination in soil (ATSDR 2008). The EMEG was developed from the ATSDR minimum risk level (MRL) based on neurodevelopmental effects observed in the offspring of female rhesus monkeys exposed during pregnancy (ATSDR 1998).

Dioxin Toxic Equivalencies
Dioxin toxic equivalents (TEQs) are calculated by multiplying the level of a dioxin-like compound by its toxicity equivalency factor (see page 9 for additional information). The resulting TEQs are then added together to determine the total dioxin TEQ concentrations in a soil sample.

Additionally, the MDEQ has promulgated a Residential Direct Contact Criterion (RDCC) for soil of 90 ppt TEQ for DLCs under the Natural Resources and Environmental Protection Act, Part 201, Environmental Remediation, 1994 PA 451, as amended (MDEQ 2004). The residential RDCC for DLCs identifies a soil concentration that is protective against the adverse health effect of cancer as a result of long-term dermal exposure to and incidental ingestion of contaminated soil (MDEQ 2001). The ATSDR EMEG and the MDEQ RDCC will be used here to screen levels of DLCs found in soil samples at EU001 for further evaluation.

Environmental Contamination

Surface Soil

Table 1 presents the concentrations of DLCs detected in surface soil samples collected from 0-12 inches below ground surface by Weston in April 2008. The 0-12 inches depth is consistent with agreed-upon interim response activities conducted at properties in the floodplain (ATS 2008). Typically, MDCH uses sample depths of 0-3 inches to evaluate the potential for direct contact with contaminated surface soils. However, because frequent flood events transport DLCs onto upland properties, the 0-12 inch samples taken at EU001 are representative of concentrations to which residents are exposed. Sampling data provided in 2006 by a Dow contractor following a flood event supports this assumption. The contractor collected samples of flood-deposited sediments from “turf mats¹” positioned at 48 locations along the Tittabawassee River floodplain, several of which were located immediately downstream of EU001. Concentrations of DLCs ranged from 599 to 1671 ppt (dry weight) in three sediment samples collected from the floodplain elevation most consistent with the residences at EU001 (ATS 2006). These data demonstrate that flood events continuously renew DLC concentrations at the soil surface and support the use of the 0-12 inch samples as representative of soil direct contact exposures.

¹ Turf mats were 20-inch squares of synthetic carpet (i.e., Astroturf) that were secured to the ground with metal stakes (Limno-Tech, Inc. 2006)

Figure 1. Site Location Map EU001, Saginaw, Michigan



Weston 2008

Table 1. Dioxin-Like Compounds in Soil (0-12 inches), EU001, Saginaw, Michigan, 2008

	Range (ppt)	Median (ppt)	Mean (ppt)	95%UCL (ppt)	EMEG (ppt)	RDCC (ppt)
All Properties	1.3 – 23,000	1,500	2,110	2,331	50	90
Property A	NA	NA	NA	NA	50	90
Property B	1,400 – 6,200	2,650	3,430	4,603	50	90
Property C	120 – 6,800	2,050	2,413	3,589	50	90
Property D	12 – 2,600	980	1,035	1,394	50	90
Property E	11 – 7,600	1,600	1,789	2,421	50	90
Property F	1.3 – 500	110	159	257	50	90
Property G	120 – 6,900	3,300	3,009	4,808	50	90
Property H	1,100 – 10,000	4,300	4,447	5,282	50	90
Property I	980 – 15,000	2,200	3,345	5,401	50	90
Property J	120 – 9,300	1,700	2,187	3,521	50	90
Property K	270 – 4,000	1,000	1,361	1,794	50	90
Property L	NA	NA	NA	NA	50	90
Property M	2,400 – 5,000	3,700	3,700	4,143	50	90
Property N	NA	NA	NA	NA	50	90
Property O	150 – 6,000	3,550	3,346	4,210	50	90
Property P	150 – 23,000	2,050	2,890	4,283	50	90
Property Q	380 – 5,800	1,900	2,054	2,668	50	90
Property R	28 – 5,000	550	1,116	1,625	50	90
Property S	160 – 660	320	341	460	50	90
Property T	670 – 1,700	NC	NC	NC	50	90
Property U	40 – 11,891	2,300	2,578	3,386	50	90
Property V	10 – 3,800	129	585	851	50	90
Property W	8.5 – 3,100	475	690	926	50	90
Property X	680 – 8,600	4,000	4,103	4,919	50	90

ppt: parts per trillion toxic equivalent (TEQ)

(Weston 2008)

95% UCL: 95 percent upper confidence limit on the arithmetic mean.

EMEG: Environmental Media Evaluation Guide

RDCC: Residential Direct Contact Criterion

NA: soil data Not Available for this property.

NC: statistics Not Calculated because of insufficient sample size.

All soil and dust samples were analyzed for the 17 dioxin and furans for which TEFs are available. All DLC concentrations are presented in ppt (Weston 2008). Detected levels of DLCs in surface soils exceeded the ATSDR screening level EMEG in 387 of 426 samples, and the MDEQ RDCC in 376 of 426 samples (Weston 2008). The range of detected concentrations varied widely between properties and sometimes on individual properties as well. Lower concentrations were found on properties where fill material had been brought in to increase the elevation and thus discourage flooding.

Subsurface Soil

In addition to surface soil, Weston collected soil samples from two lower intervals: 18-24 and 30-36 inches below ground surface. Subsurface soil samples were held in archives at the

analytical laboratory until surface soil sampling results were evaluated. Twenty subsurface samples were ultimately analyzed; 10 at the 18-24 inch depth and 10 at the 30-36 inch depth. Table 2 presents the results of subsurface sample analysis for all EU001 properties.

Table 2. Dioxin-Like Compounds in Subsurface Soil, EU001, Saginaw, Michigan, 2008.

	Depth (inches)	Range (ppt)	EMEG (ppt)	No. Exceedances EMEG	RDCC (ppt)	No. Exceedances RDCC
All Properties	18 – 24	1 – 33,000	50	8/10	90	8/10
	30 – 36	2 – 9,200	50	8/10	90	6/10

ppt: parts per trillion toxic equivalent (TEQ)

EMEG: Environmental Media Evaluation Guide

RDCC: Residential Direct Contact Criterion

Weston 2008

Of the 20 subsurface samples analyzed, 16 exceeded the ATSDR screening level EMEG and 14 exceeded the MDEQ RDCC, confirming that DLC contamination was present in deeper soils (Weston 2008). No summary statistics (e.g., median, mean or UCL) are presented here because the density of subsurface sampling does not support such calculations. While the EMEG value generally applies to surface soil only, the MDEQ RDCC is intended to be applied to the entire soil profile to be protective of residential exposures should subsurface soils be excavated and brought to the surface where people may be exposed in the future.

Dust and Wipe Sampling

Bulk dust and dust wipe samples were also collected at EU001 to determine if outdoor soil contamination had migrated into resident's homes via track-in or blowing dust from the dirt road. Wipe samples were also collected from outdoor hard surfaces (paved concrete) where bulk soil samples could not be obtained. Table 3 presents the results of the analysis of dust and wipe samples collected from EU001 properties.

Table 3. Dioxin-Like Compounds in Dust and Wipe Samples, EU001, Saginaw, Michigan, 2008.

	Type of Sample	Range	Screening Value	No. Exceedances
All Properties	Bulk Indoor Dust	55 – 3,100 pg/g	0.6 pg/g	9/9
	Indoor Wipe	6 – 210 pg/m ²	0.4 pg/m ²	1/5
	Outdoor Wipe	240 – 990 pg/m ²	NA	NA

pg/g: picograms per gram, or ppt toxic equivalent (TEQ)

pg/m²: picograms TEQ per square meter of wipe

NA = not available

Weston 2008

The *Contaminants of Potential Concern (COPC) Committee of the World Trade Center Indoor Air Task Force Working Group* developed screening values for DLCs in indoor dust to be used in buildings affected by the destruction of the World Trade Center (COPC 2003). The COPC calculated a bulk dust screening level of 60 picograms per gram (pg/g or ppt) TEQ based on a target cancer risk of 1 additional cancer in 10,000 people. At the state of Michigan target cancer risk of one additional cancer in 100,000 people the screening value for bulk indoor dust samples is 0.6 pg/g. Dioxin TEQ concentrations in bulk indoor dust samples collected from homes in EU001 exceeded the COPC screening value in all nine samples.

The COPC also developed settled dust screening values based on exposure to dust on indoor surfaces. To calculate the settled dust screening level used at the World Trade Center (WTC), the committee assumed a single contaminant release and dissipation (break down) over time to calculate a value of 1,700 pg/m² based on a target cancer risk of 1 additional cancer in 10,000 people (COPC 2003). Because the source of dioxins in indoor dust at EU001 is the outdoor soil contamination, which is frequently renewed by river flooding, the WTC screening value is not appropriate for this site. Instead, Table 3 presents the indoor dust screening value of 0.4 pg/m² that results if the dissipation factor is removed from the calculation and the target cancer risk is adjusted to 1 additional cancer in 100,000 people. Dioxin TEQ concentrations in one of five settled indoor dust samples collected from homes in EU001 exceeded this screening value. No screening value is available for dust on outdoor surfaces.

Exposure Pathways Analysis

To determine whether people are, have been, or are likely to be exposed to contaminants, MDCH evaluates the environmental and human components that could lead to human exposure. An exposure pathway contains five elements:

1. **Source** - Is there a likely source of the contamination or release?
2. **Environmental Transport and Media** – How are contaminants moving through environmental media such as soil, water or air?
3. **Exposure Point** – Where might people come into contact with contamination?
4. **Exposure Route** – Are people eating, breathing, or touching the contamination?
5. **Exposed Population** – What group of people might be exposed to the contamination?

In addition, MDCH considers the **Time Frame** because the elements of an exposure pathway can change with time. Exposure to contamination may have happened in the past, may be current, or could happen in the future. All five elements of an exposure pathway must be present within a time frame for a pathway to be complete. If one or more elements are missing, the exposure pathway is incomplete. The exposure pathway elements for Tittabawassee River sediments, outdoor soil, and indoor dust at EU001 are shown in Table 4. The last column in Table 4 called **Status**, shows whether or not a pathway is complete.

Table 4. Exposures Pathways for Dioxin-Like Compounds, EU001, Saginaw, Michigan.

Source	Environmental Transport and Media	Chemicals of Concern	Exposure Point	Exposure Route	Exposed Population	Time Frame	Status
The Dow Chemical Company, Midland	Deposition of Tittabawassee River sediments onto EU001 during flood events.	Dioxin-Like Compounds	Outdoor soil and Sediment.	Eating, Breathing, Touching	People who frequently visit or live in EU001	Past	Complete
						Current	Incomplete
						Future	Potential
The Dow Chemical Company, Midland	Tracking/blowing of outdoor contaminants into EU001 homes.	Dioxin-Like Compounds	Indoor dust.	Eating, Breathing, Touching	People who frequently visit or live in EU001	Past	Complete
						Current	Incomplete
						Future	Potential

It is likely that people were exposed to the DLC contamination at EU001 in the past. However, because the contaminated surface soils have been removed, the dirt road has been paved, and the inside of residents' homes has been cleaned it's not likely that people are currently exposed to the contamination.

DLC contaminated sediments are likely to be deposited onto residential properties during future Tittabawassee River flood events at EU001. Because people may be exposed to this contamination in the future time frame, this pathway is potentially complete for both exposure pathways.

Toxicological Evaluation

Dioxins and dioxin-like compounds are a group of chlorinated chemicals with similar structures and chemical properties that includes polychlorinated dioxins, furans, and some polychlorinated biphenyls (PCBs). They are often referred to collectively as "dioxins" or "dioxin-like compounds" or DLCs, as they are found in the environment as a mixture of several of these chemicals. Dioxins and furans are not intentionally produced and have no known use. Not all DLCs have the same toxicity or ability to cause illness and adverse health effects. However, it is likely that all DLCs cause adverse health effects through a similar biologic mechanism of action. The available science indicates that the health effects resulting from exposure to multiple DLCs are additive.

The most toxic chemical in the group is 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). The World Health Organization (WHO) developed toxic equivalency factors (TEF) to compare the relative toxicity of other DLCs to that of TCDD. The levels of other DLCs measured in the environmental or biologic samples are multiplied by a TEF to produce a TCDD toxic equivalent or TEQ concentration. The resulting TEQs for all DLCs measured in a sample are then added together to determine the total dioxin TEQ concentration for that sample.

In 2005, the WHO International Programme on Chemical Safety expert panel reevaluated the TEFs for dioxins, furans, and some PCBs. Previously, TEFs were based on an arithmetic scale and assigned increments of 0.01, 0.05, 0.1, etc. However, the WHO expert panel decided to use a logarithmic scale for the 2005 reevaluation and assigned TEFs of 0.03, 0.1, 0.3 and so on based on an assessment of the available literature, which included information that had become available since the 1998 TEFs were established (Van den Berg et al. 2006).

The National Research Council of the National Academies of Science (NAS) reviewed the TEF approach as part of its Evaluation of the EPA reassessment of the health risks from dioxins and related compounds (Dioxin Reassessment). The NAS committee concluded that "the toxic equivalency factor methodology provides a reasonable, scientifically justifiable, and widely accepted method to estimate the relative potency of DLCs" (NAS 2006).

There is a wealth of scientific information concerning the potential health effects of exposure to DLCs, much of which has already been summarized by the ATSDR in the *Toxicological profile for Chlorinated Dibenzo-p-dioxins (CDDs)* (ATSDR 1998) or by the EPA in the draft Dioxin Reassessment. Appendix A provides a brief review of additional information that has become

available since these documents were completed. Health effects of DLCs observed in human studies include cancer, chloracne, diabetes, disruption of the endocrine, immune and reproductive systems, and developmental effects in children.

Background Exposures

When evaluating the potential for noncancer health effects resulting from exposure to DLCs, it is important to consider the level of exposure already occurring due to levels of DLCs in the national food supply. The United States Food and Drug Administration (FDA) Center for Food Safety and Applied Nutrition has estimated the exposure levels that would result from consumption of foods sampled in their Total Dietary Studies (TDS) conducted in 2001 and 2002. DLC concentration data were linked to consumption amounts for each food sampled in the TDS to provide an estimate of dietary exposure to DLCs by age group (FDA 2004). For children ages 1-6 years, the FDA TDS indicates an average TEQ intake from dietary sources of 24.1 picogram per kilogram-month (pg/kg-month). For adults, the FDA provides a TEQ intake from background dietary sources of 9.9 pg/kg-month. These intake levels can be compared to the WHO Tolerable Monthly Intake (TMI) of 70 pg/kg-month that is protective of both cancer and noncancer health effects (WHO 2001).

Bioavailability of DLCs in Tittabawassee River Floodplain Soil

Site-specific bioavailability pilot studies were conducted by a Dow contractor in 2005 and 2006 to determine if DLCs in Tittabawassee floodplain soils would be absorbed through the intestines and distributed to body tissues. Floodplain soil with a TEQ concentration of about 850 ppt was mixed into the feed of rats and immature swine for 30 days. The level of DLCs was then measured in the liver and adipose (fat) tissues of the animals and compared to levels in referent animals that had been given similar levels of DLCs in feed and corn oil spiked to contain the same level of contaminants. While a full study using multiple soil samples was never completed, the results of the pilot study indicate that relative bioavailability of DLCs ranged from 52 to 89 percent in rats (depending on the particular congener measured) and from 23 to 37 percent in immature swine (Exponent 2005). These results confirm that DLCs in floodplain soil can be absorbed through the intestines and into the body.

The bioavailability of DLCs in floodplain soil is also confirmed by the analysis of eggs from chickens that were kept on contaminated soil at EU001. Concerned about potential food chain exposure to DLCs in floodplain soil, the MDEQ collected four chicken eggs and a soil sample from the chicken coop area at an EU001 residence. The soil sample contained 780 ppt TEQ. DLCs were detected in the eggs at concentrations ranging from 16 to 48 ppt TEQ (MDEQ 2002). The egg analysis revealed a pattern of dioxin and furan congeners similar to the pattern in the soil sample, which was also consistent with the general pattern seen in most floodplain soils where furans are the dominant contaminant.

In order to evaluate the significance of the egg results, MDEQ reviewed an investigation carried out in 1997 by the FDA and the U.S. Department of Agriculture (USDA) when high levels of dioxin were discovered in animal feed. As part of this investigation, the FDA determined that the level of dioxin in exposed animals and animal products should be less than one ppt and the USDA issued an advisory to poultry and egg producers indicating the need to have exposed animal products tested before marketing and to destroy animals that had been fed the adulterated

feed (USDA 1997). Based on the USDA advisory, MDCH recommended that the home owner immediately stop eating the eggs from chickens kept in the floodplain.

Dose Reconstruction

DLCs are persistent compounds that build up in the body, and remain stored in fat and other tissues for long periods of time. The level of DLCs in the body is expressed by a “body burden” measure in units of DLCs per unit of body weight or per unit of body fat. Animals eliminate these compounds from their bodies much faster than people, so the daily dose needed to reach a given body burden level is much lower in people than that needed to reach the same dose in animals.

In 2001, the WHO Expert Committee on Food Additives developed a provisional tolerable monthly intake (PTMI) for DLCs of 70 pg/kg-month by applying a scaling formula to body burden measurements from animal studies to produce a daily dose that would result in a similar body burden level in people (WHO 2001). The PTMI is based on observed developmental affects in male offspring exposed before birth and through weaning. Because male offspring are believed to be most sensitive to the effects of DLCs, the PTMI is likely protective of other potential health effects.

Using the equation shown below, MDCH estimated the dose of DLCs that people living at EU001 could have received in the past through incidental ingestion (accidental eating) of contaminated soil and compared the estimated dose to the PTMI.

$$Intake = \frac{CS \times IR \times Abs \times CF}{BW} \times 30_{days / month}$$

where

Intake	pg/kg-month
CS	= 95% UCL concentration in soil from Table 1 (converted to pg/kg)
IR	= soil intake rate
	100 milligram per day (mg/day) for adults
	200 mg/day for children ages one to six years
Abs	= 50 percent absorption of DLCs (0.5)
CF	= conversion factor 10^{-6} kg/mg
BW	= body weight
	70 kilograms (kg) for adults
	15 kg for children ages one to six years.

For adults, the estimated dose of DLCs from incidental ingestion of soil in the past added to the intake rate from background dietary sources exceeds the PTMI at most of the properties in EU001. For children the estimated dose of DLCs from incidental ingestion of soil in the past added to the intake rate from background dietary sources is from one to 16 times the WHO PTMI. People who live at EU001 would have additional exposure to DLCs if they eat locally caught fish, and meat, eggs, or dairy products produced in the flood plain of the Tittabawassee River.

Human Health Effects in the Tittabawassee River Floodplain

The MDCH conducted an exposure investigation of dioxin blood levels as reported in “A Pilot Exposure Investigation (PEI): Dioxin Exposure in Adults Living in the Tittabawassee River Floodplain Saginaw County, Michigan.” Dioxin blood levels of people living in the Tittabawassee River floodplain were also examined in the University of Michigan Dioxin Exposure Study (UMDES 2009). However, the number of people living in EU001 is very small. If any of these people participated in either the MDCH PEI or in the UMDES, it would be a breach of confidentiality agreements and contrary to the Michigan Public Health Code to discuss their blood test results in this consultation or in any other public forum without their individual and explicit consent.

It is not known if any health effects or illnesses have occurred in people as a result of exposure to dioxins in the Tittabawassee River floodplain. No studies have been conducted that could determine if the health of people living on contaminated properties has been affected. It may not be possible to conduct reliable health studies in this area because the number of people living on highly contaminated property is relatively small. However, in the absence of evidence it cannot be presumed that the health of people living on contaminated property has not been impacted as complete exposure pathways have been determined to be present for people living in the Tittabawassee River floodplain.

Children’s Health Considerations

Children may be at greater risk than adults from certain kinds of exposure to hazardous substances at sites of environmental contamination. They engage in activities such as playing outdoors and hand-to-mouth behaviors that increase their exposure to hazardous substances. Children are shorter than adults, which means they breathe dust, soil, and vapors close to the ground. Their lower body weight and higher intake rate result in a greater dose of hazardous substance per unit of body weight. The developing body systems of children can sustain permanent damage if toxic exposures are high enough during critical growth stages. Prenatal exposures and those that occur in the first few years of life are more likely to cause permanent damage.

Limited human studies and many animal studies suggest that fetuses, infants and children may be more sensitive to adverse effects of dioxins because they are growing and developing rapidly. The human studies have shown that children exposed in the womb have experienced some adverse health effects that are associated with increased exposure to dioxins.

Conclusions

MDCH has reached three conclusions in this health consultation report:

MDCH concluded that people living in the EU001 residential area of the city of Saginaw, Michigan breathed, touched, and accidentally ate DLCs in soil and dust for a year or longer, and this may have harmed their health. The estimated dose of DLCs from accidentally eating soil added to the intake rate from background dietary sources of DLCs exceeded the WHO PTMI for adults and children living at EU001. The results of indoor dust sampling provide both

quantitative and qualitative confirmation that outdoor DLC contamination is present inside the homes at EU001. This was a past public health hazard.

MDCH concluded that the cleanup conducted by Dow with oversight from the EPA effectively removed DLCs from the top two feet of soil and from inside the homes and other buildings at EU001. Currently, levels of DLCs in surface soil are below the MDEQ Residential Direct Contact Criterion for soil of 90 ppt. At these soil concentrations, there is no apparent current public health hazard.

MDCH concluded that future flooding of the Tittabawassee River could redeposit contaminants onto resident's yards at EU001. DLC contaminated sediments are likely to be deposited onto residential properties during future Tittabawassee River flood events at EU001 and people living there may be exposed to the contamination. This is a potential future public health hazard.

Recommendations

Throughout 2008, MDCH met with the MDEQ, EPA, and EPA contractors to provide public health recommendations to address the DLC contamination at EU001. MDCH's recommendations included:

- Provide EU001 residents with information about the potential health effects of exposure to DLCs and actions they can take to avoid exposure.
- Involve EU001 residents in clean up decisions that will affect their properties and homes.
- Prevent further human exposure to contaminated soil at EU001.
- Prevent emission of contaminated dust from the dirt road that could enter residents' homes through open windows.
- Remove DLC contaminated dust from residents' homes.
- Develop a plan to monitor DLC recontamination at EU001 following subsequent flood events OR implement flood control measures to prevent recontamination.

Public Health Action Plan

- MDCH and EPA proactively met individually with EU001 residents to secure access agreements and to answer questions about health effects and clean up actions.
- MDCH participated in EPA sponsored private meetings limited to EU001 residents where clean up plans were explained and residents' concerns were addressed.
- MDCH and the MDEQ developed a series of informational brochures available at www.michigan.gov/deq to provide information concerning health effects of DLCs and how to avoid exposure. MDCH made these brochures available to EU001 residents and answered additional questions.
- MDCH, with funding from the EPA and in cooperation with local health departments of Saginaw and Bay counties, has developed targeted health education plans to increase awareness of the watershed contamination and of the Michigan Family Fish Consumption Guide.
- Dow contractors removed the top two feet of soil from residential areas and the top one foot of soil from non-residential transition zones in the EU001 area. Landscape fabric was laid down as a lower marker and then clean fill and topsoil were put in place,

followed by sod and landscaping. Contractors completed these activities on October 8, 2008.

- Dow contractors paved the dirt road and all residents' driveways with asphalt between October 14th and 15th, 2008.
- Dow contractors completed indoor activities including cleaning of upholstery, mattresses, and ductwork; and replacement of carpeting in December 2008. Non-residential areas such as workshops were cleaned as well.
- Dow is developing a post-removal monitoring plan. MDEQ will review and approve the plan.
- MDCH will remain available to assist the MDEQ and the EPA at EU001 and other high priority areas in the Tittabawassee River floodplain.

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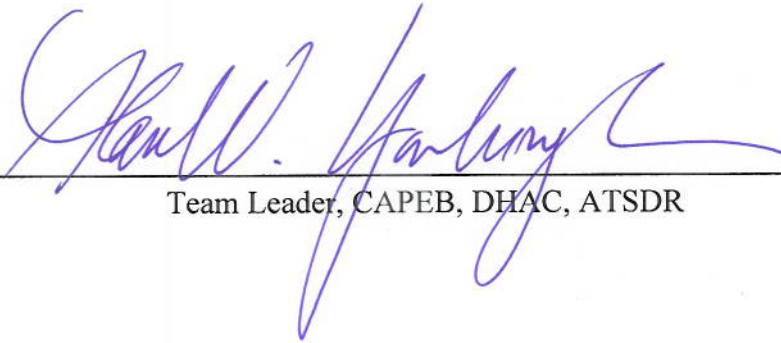
Certification

This Health Consultation was prepared by the Michigan Department of Community Health under a cooperative agreement with the Agency for Toxic Substances and Disease Registry (ATSDR). It is in accordance with approved methodology and procedures. Editorial review was completed by the cooperative agreement partner.



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The Division of Health Assessment and Consultation, ATSDR, has reviewed this public health consultation and concurs with the findings.



Team Leader, CAPEB, DHAC, ATSDR

Appendix A

Supplemental Health Effects Information

The discussion below is a brief review of additional information concerning the health effects of DLCs in animals and people that has become available since release of the ATSDR *Toxicological profile for Chlorinated Dibenzo-p-dioxins (CDDs)* in 1998 and the EPA draft Dioxin Reassessment in 2004.

Health Effects in Animals

Cancer – A 2-year rat bioassay conducted by Dow in the 1970's (Kociba 1978) has been used by the EPA, the State of Michigan, and many other agencies to evaluate the cancer potency of TCDD. Most recently, the National Toxicology Program (NTP) conducted a series of four 2-year cancer bioassays of TCDD, other DLCs including PCB-126 and 2,3,4,7,8-pentachlorodibenzofuran (PeCDF), or a mixture of all three. The purpose of these studies was to replicate results seen in the earlier rat bioassay conducted by Dow and to evaluate the TEF approach used for mixtures of multiple DLCs. The 2004 NTP bioassay confirmed that exposure of female rats to TCDD resulted in increases in the incidence of cancer of the liver, lung, and oral mucosa. Some liver cancers (cholangiocarcinomas) were seen at higher rates in the NTP study than had been observed in the earlier Dow study (Walker 2006). Additionally, these cancers were significantly and dose-dependently increased in rats exposed to PCB-126, PeCDF, and to the mixture of all three DLCs. Analysis of the dose-response modeling for each DLC and the mixture confirmed that the effects of exposure to mixtures of these chemicals are additive for these cancer endpoints. Additionally, the relative potency of PCB-126 (0.1) and PeCDF (0.3) to TCDD was found to be consistent with the WHO 2005 TEF values for these DLCs (Walker 2005).

Non-Cancer – DLCs have been widely studied in a variety of animal test subjects. TCDD has been called “the most toxic man-made chemical” because it can cause death at very low doses. The dose at which TCDD causes death in 50 percent of test animals, called the LD₅₀, varies widely between species with the guinea pig likely to be the most sensitive species tested. The TCDD dose that could kill a person is not known, but three intentional attempts to poison people suggest the lethal dose for a person is far higher than that for guinea pigs (Schechter et al. 2005).

While LD₅₀ values can vary widely, other adverse effects observed in test animals occur at similar doses in multiple mammalian species. Exposure of test animals to DLCs has resulted in reproductive and developmental abnormalities, immune system effects, nervous system effects, endocrine disruption, diabetes, thyroid disorders, liver damage, dental abnormalities, and blood effects such as elevated cholesterol and triglycerides (ATSDR 1998, Schechter et al 2005). Results from animal studies suggest that the perinatal period, before and just after birth, is the most critical period for DLC exposure and that the endocrine (hormonal) system is likely the most sensitive target. (Nishimura et al. 2008; Bell et al. 2007a; Bell et al. 2007b).

There is a large body of compelling information that supports the assumption that people and other mammals respond to DLCs in similar ways at the cellular level via the aryl hydrocarbon receptor (AhR). Activation of the AhR by TCDD and other DLCs that bind to it sets off a cascade of cellular events that are thought to be responsible for the health effects associated with

these compounds (Walker 2006). Therefore, it is reasonable to assume that people may experience the same health effects as those seen in studies of other mammals.

Human Health Effects

Studies of people who were exposed to high levels of DLCs at their work place, through industrial accidents, and in contamination incidents have demonstrated adverse effects, but there are not always consistent results among these studies. Only three instances of intentional human poisonings have been reported. For a severe acne-like skin condition called chloracne, the effect of dioxin exposure is obvious and occurs soon after exposure. For other effects (e.g., cancer and chronic diseases like diabetes), it may take many years before health effects, if any, are seen and it may be difficult to determine if the effect is from exposure to DLCs.

Human studies are often difficult to interpret because every person lives differently and people may be exposed to multiple chemicals at the same time. It takes a lot of exposed people in a well designed study to see increases in common conditions such as heart disease, diabetes and some types of cancer. Recent studies that will be discussed further below confirm the need to carefully define exposure groups (e.g., non-exposed vs. highly exposed). In many older studies, people were assigned to exposure groups based on assumptions about occupational duties that could result in exposure to dioxins. More recent analysis of serum blood dioxin levels in workers revealed that high dioxin exposures may occur unexpectedly and that comparison groups must be carefully chosen based on measured dioxin body levels (Collins et al. 2005).

Some studies of exposed populations that showed little health impact or uncertain results were conducted within a few years after exposure, but many of the potential health effects of DLCs such as cancer are not seen until 15 or 20 years following exposure. Offspring of exposed people may show effects of dioxin exposure at levels that do not affect the health of the parents. More recent analysis of the data is finding significant health impacts in these exposed people.

Cancer - The WHO International Agency for Research on Cancer (IARC), the United States Department of Health and Human Services (DHHS) National Toxicology Program 9th Report on Carcinogens (NTP 2001), and the EPA have all classified TCDD as a human carcinogen. The EPA has characterized the mixture of DLCs to which people are commonly exposed as "likely to be carcinogenic to humans" (EPA 2000). The NAS, the WHO, and DHHS concur that the other DLCs and mixtures of those compounds are likely to cause cancer.

The NAS in its 2006 evaluation of the EPA Dioxin Reassessment recommended that the EPA reevaluate its conclusions regarding whether TCDD is "carcinogenic to humans" or "likely to be carcinogenic to humans." The difference between these two conclusions relies primarily on the strength of the evidence. However, the NAS stated that the "public health implications of the two terms appeared to be identical." This means that, regardless of the classification used, people should take precautions to limit their exposure to this chemical. Recent studies in human populations exposed to TCDD have confirmed the association of cancer incidence with dioxin exposure. The most consistent findings from human studies of TCDD exposure show an increase in all cancers combined.

In 1997, IARC classified TCDD as “carcinogenic to humans” based on limited evidence in humans, sufficient evidence in animals, and extensive evidence that TCDD acts through a similar mechanism, binding to the AhR, in both humans and animals. IARC relied on studies of people who were occupationally exposed to TCDD in chemical production (including workers at Dow’s Midland plant site) or pesticide application as well as residents of Seveso, Italy where an accident exposed local residents (IARC 1997).

In 1976, an explosion at a trichlorophenol plant in Seveso, Italy released several kilograms of TCDD and contaminated a large populated area. Studies of health effects in the exposed populations began almost immediately after the accident, however initial findings in 1984 identified only chloracne as a certain effect (Consonni et al. 2007). The Seveso population, divided into three zones of exposure, has been followed over the intervening years to assess cancer incidence and mortality. After 20 years, all cancer mortality in the most polluted area, Zone A, showed a 60 percent increase among males. Lung cancer mortality was also elevated in males in Zone A 15 years after the accident (Consonni et al. 2007). These findings are consistent with those seen in occupational studies of men exposed to TCDD at their jobs. Additionally, rectal cancer incidence and mortality was increased in males in the exposed Seveso population.

Among exposed females, liver cancer incidence was elevated in females 15 years after the accident (Steenland et al. 2004). Breast cancer incidence was found to increase 2-fold with a 10-fold increase in serum TCDD in Zone A women (Warner et al. 2002).

The Seveso population also shows an excess of lymphatic and hematopoietic neoplasms in both males and females, in both Zone A and Zone B (Consonni et al. 2007). The lymphatic system includes lymph nodes, ducts and lymph vessels, whose function is to produce and carry lymph fluid around the body. The hematopoietic system includes the bone marrow, spleen, tonsils, and lymph nodes, and is involved in the production of all types of blood cells.

More recent analyses of occupational data conducted after the 1997 IARC classification of TCDD, have relied on better methods to estimate the level of TCDD in blood serum thus allowing for more accurate predictions of the exposure-response relationship. These newer studies all benefited from the availability of measurements of serum blood TCDD levels for at least a subset of the workers, which allowed researchers to predict the blood levels in workers who had performed similar tasks for the same length of time. These analyses show an increasing risk for all cancers as exposure to TCDD increases. In a study of Dutch workers, those in the medium and high exposure groups had a 5-fold increase in cancer mortality compared with workers at the same manufacturing plant who were in the low exposure group (Steenland et al. 2004). Newer analyses of United States worker data that include several years of additional follow-up indicate a significant trend in all cancer mortality with increasing dioxin exposure (Crump 2003, Steenland 1999). A strength of these newer studies is that they compare cancer rates between the workers (who are likely to be similar in lifestyle, availability of health care, and socioeconomic class) rather than to the general population that includes the elderly and people who may be less healthy than the actively employed (Steenland et al. 2004).

During the Vietnam War, the United States Air Force used the herbicides 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) in an equal mixture to

clear jungle foliage. This mixture, called Agent Orange because of orange labels on the containers, was contaminated with TCDD. Operation Ranch Hand was the Air Force unit that handled and loaded the Agent Orange onto aircraft, and flew those aircraft in aerial spraying missions. In 2006, the NAS Institute of Medicine concluded that there is sufficient evidence of an association between exposure to herbicides and TCDD and soft-tissue sarcoma, non-Hodgkin's lymphoma, chronic lymphocytic leukemia (CLL), Hodgkin's disease, and chloracne. The NAS also found limited or suggestive evidence of an association of herbicide and TCDD exposure and the following: cancer of the larynx, lung, bronchus, trachea, prostate; multiple myeloma; primary amyloidosis; early-onset transient peripheral neuropathy; porphyria cutanea tarda; hypertension; Type 2 diabetes (mellitus), and spina bifida in offspring of exposed people (IOM 2007).

Recently, researchers have further defined which Vietnam veterans were most highly exposed to TCDD and examined disease incidence in veterans as a function of the timing and duration of exposure (Akhtar et al. 2004; Michalek and Pavuk 2008). Veterans' exposure was stratified by their calendar period of service (during and before 1968 or after 1968), the number of days spraying, and the duration of their service in Southeast Asia. The calendar period of service is important because TCDD contamination present in Agent Orange is thought to have been higher before 1969. The number of days spraying and the duration of service are important because people who are exposed for longer periods of time will likely have more dioxin in their bodies than people who are exposed for shorter periods of time. When the Ranch Hand veterans were stratified in this way, cancer risk estimates were significantly increased for the entire group and for the high exposure category in particular (Michalek and Pavuk 2008). These results likely differ from earlier reports because exposure was more accurately defined and because more time had elapsed since exposure.

In addition, recent studies conducted in California have confirmed the link between exposure to Agent Orange and prostate cancer in Vietnam veterans. Researchers stratified veterans receiving care at the Northern California Veteran Affairs Health System as either exposed or unexposed, and examined demographic data and prostate health status. Twice as many exposed veterans had been diagnosed with prostate cancer. In addition, exposed veterans had been diagnosed at an earlier age and were more likely to have cancer that has spread to other parts of the body (Chamie 2008).

Chloracne - This severe acne-like disease is known to be associated with high levels of exposure to DLCs. However, not everyone who is exposed to high levels will have chloracne and its absence cannot be taken as proof that no exposure has occurred. Chloracne may be disfiguring and can persist for years, sometimes clearing only to recur several years later. Workers exposed on the job; adults and especially children exposed by the accident at Seveso, Italy; and the three people known to have been intentionally poisoned with TCDD have all developed chloracne. (Schechter 2005).

Diabetes - As previously discussed, the NAS found evidence of an association of TCDD herbicide exposure and Type 2 diabetes (sometimes called adult onset diabetes) in Vietnam veterans. Recent analysis of diabetes incidence in Operation Ranch Hand veterans provides

further strength for this association when exposure is adjusted for calendar period of service and for number of days spraying Agent Orange herbicides (Michalek and Pavuk 2008).

Studies of the relationship of DLC exposure and diabetes incidence in occupational settings have yielded mixed results. Calvert et al. (2005) found that workers with very high (> 1500 ppt) serum TCDD levels were at greater risk of developing diabetes. However, no difference was found in diabetes incidence between other exposed workers with lesser TCDD levels and a referent group with TCDD serum levels below 20 ppt.

Women who had been exposed to DLCs (polychlorinated biphenyls and polychlorinated dibenzofurans) during the 1970's Yucheng accidental rice oil poisoning event in Taiwan were 2.1 times more likely to develop diabetes than women in an unexposed referent group (Wang et al. 2008). Similarly, women in all exposure zones in Seveso, Italy, were found to have slightly higher mortality rates from diabetes when compared to a non-exposed population (Consonni 2008).

People who lived adjacent to a TCDD-contaminated site in Arkansas were studied by Cramer et al. (2000) to determine if blood serum levels of the DLC were associated with biomarkers of diabetes and insulin resistance. People whose blood level of TCDD was in the highest 10 percent of those studied were more likely to have higher plasma insulin concentrations after a glucose load, suggesting that higher levels of TCDD in blood serum is associated with insulin resistance.

Other researchers have used human blood serum and survey results from the National Health and Nutrition Examination Surveys (NHANES) to investigate the association between background exposures to DLCs and diabetes. These investigations are limited because only a few DLCs could be measured in the blood of many of the people who participated. Lee et al. (2006) reported that diabetes incidence was positively associated with serum lipid levels of a group of six measured pollutants that included two chlorinated dioxins.

Developmental Effects - The 1976 explosion in Seveso, Italy provides a unique, albeit unfortunate, opportunity to assess the effects of dioxin exposure on human development. Children in Seveso who were exposed to TCDD had higher levels of the DLCs in their blood compared to adults. Approximately 20 percent of exposed children developed chloracne following the accident (Alaluusua et al. 2004).

Reports on the 1970's Yucheng event in Taiwan suggested that children born to women exposed to DLCs while pregnant had dental abnormalities that persisted into adult life (Guo et al. 2003). Therefore, Seveso children who were younger than nine and a half years at the time of the accident were examined 25 year later for dental defects. People who had lived in the contaminated zones showed a higher prevalence (42%) of development defects in their tooth enamel compared to people who had not lived there (26%). People with higher serum TCDD levels as children showed these effects more often than people who had lower levels. More people from the contaminated zones (12.5%) also had missing permanent teeth than people from the non-contaminated zones (4.6%) (Alaluusua et al. 2004).

Animal studies suggest that development of the male reproductive system is a sensitive target for DLC effects (Bell et al. 2007a, 2007b). Studies of these effects in Seveso males exposed as children or young adults confirm that the human male reproductive system is similarly sensitive. Mocarelli et al. studied three age groups 22 years after the Seveso accident: infancy/prepuberty age 1-9 years, puberty age 10-17 years, and adults age 18-26 years. Men who were exposed before puberty showed reductions in sperm concentration, progressive motility, and total motile sperm count, as well as increased levels of estradiol and follicle-stimulating hormone. These effects were seen at 1976 blood levels of 68 ppt TCDD; the median blood level of the first quartile of men exposed at age 1-9 years. Men who were exposed at ages 10-17 years showed opposite effects including increased sperm counts, total motile sperm count, and FSH; and decreased estradiol. Effects seen in the two younger age groups persisted into adulthood despite a return to background TCDD levels in blood serum by 1998. Men who were exposed as adults showed no effects on these measures (Mocarelli et al. 2008). This study demonstrates that effects of DLCs on the developing male reproductive system are permanent and measurable in adulthood even when blood levels had returned to concentrations consistent with background estimates for this dioxin congener. Once established, the male reproductive system appears to be less sensitive to the effects of DLCs.

Neonatal thyroid function may also be a sensitive target for DLC effects related to maternal exposure. Changes in neonatal (around the time of birth) thyroid hormone function may result in long term effects including cognitive disability and neurodevelopmental impairment (Giacomini et al. 2006).

Baccarelli et al. (2008) assessed thyroid function in 1,014 children born between 1994 and 2005 to women who were of reproductive age and lived in the two zones of highest contamination (A and B) at the time of the Seveso accident. Thyroid function in these children was compared to that of children from an uncontaminated reference area. Blood thyroid-stimulating hormone (b-TSH) at levels greater than 5 micro units per milliliter of blood ($\mu\text{U}/\text{ml}$) is an indication of low thyroid function. The mean b-TSH levels were 0.98 $\mu\text{U}/\text{ml}$, 1.35 $\mu\text{U}/\text{ml}$, and 1.66 $\mu\text{U}/\text{ml}$ for the reference area, zone B and, zone A respectively. The percentage of children in the reference area whose b-TSH exceeded 5 $\mu\text{U}/\text{ml}$ was 2.8, in Zone B the percentage was 4.9, and in Zone A the percentage was 16.1. In addition, the relationship of b-TSH levels in children to current TCDD levels in the mothers was studied in 51 mother-child pairs. Neonatal b-TSH levels were found to be positively correlated with current TCDD levels in the blood of the mothers (Baccarelli et al. 2008).

In contrast to the effects seen in the Seveso population, studies of the relationship of background DLC exposures and neonatal thyroid function have provided inconsistent results. Studies conducted in the Netherlands suggested that babies born to mothers with higher DLC blood concentrations had higher b-TSH levels at 11 weeks of age (Pluim et al. 1993), but this effect was not observed at two and half years of age, nor at 7-12 years (ten Tusscher et al. 2008). A more recent study conducted in Duisburg, Germany also failed to find any relationship between background blood DLC concentrations of 3.8 to 58.4 ppt in mothers and thyroid function or neurodevelopment in children assessed through 24 months of age (Wilhelm 2008). However, a negative association was found in the Duisburg, Germany study between maternal exposure to DLCs and sex steroids in infants as measured in cord blood (Cao et al. 2008).

In addition to thyroid function, the studies conducted in the Netherlands investigated the effects of perinatal exposure to DLCs and immunological function. While no health effects were seen in infancy, DLC exposure was associated with a decrease in the number of white blood cells. Health effects were reassessed in these children at preschool age (Pluim 1994). Higher DLC exposure was associated at this age with an increased incidence of ear infections, viral diseases like chicken pox, coughing, chest congestion and phlegm. However, white blood cell numbers were found to be normal (Weisglas-Kuperus et al. 2000). At 8 years of age, children from this group were again assessed for health status and blood factors. In this report, prenatal exposure to DLCs was associated with a decrease in allergies, which may be a result of immune system impairment. Levels of blood factors were within normal ranges, however exposure to DLCs was associated with lower levels of blood clotting cells (thrombocytes and platelets) (ten Tusscher et al. 2003).

Spatial abilities are typically better developed in boys than girls. Changes in spatial abilities of male offspring born to women exposed to high levels of PCBs and furans during the Yucheng event suggests that prenatal exposure to DLCs may result in demasculinated behavior in boys (Guo et al. 2003). Additional studies conducted in the Netherlands investigated the effects of background exposures to PCBs and dioxins on play behavior at school age. Play behavior was assessed on three subscales: masculine, feminine, and composite. The results indicated an association between higher prenatal exposure to DLCs and more feminized play behavior in both girls and boys (Vreugdenhil et al. 2002). This study suggests that sex hormones (steroids) may be affected by prenatal exposure to these compounds.