Health Consultation

TECHNICAL SUPPORT DOCUMENT FOR A TOXAPHENE REFERENCE DOSE (RfD) AS A BASIS FOR FISH CONSUMPTION SCREENING VALUES (FCSVs)

STATE OF MICHIGAN

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

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STATE OF MICHIGAN

Prepared By:

Michigan Department of Community Health
Under a Cooperative Agreement with the
U.S. Department of Health and Human Services
Agency for Toxic Substances and Disease Registry

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Acronyms and Abbreviations

Σ3PC	sum of the three persistent congeners (Parlars 26, 50, and 62)
ADI	acceptable daily intake
ATSDR	Agency for Toxic Substances and Disease Registry
bcl-2	B cell CLL/lymphoma-2
bw	body weight
CI	confidence interval
CLE	cod liver extract
CYP	cytochrome P450
DDT	dichlorodiphenyltrichloroethane
DMSO	dimethyl sulfoxide
EPA	Environmental Protection Agency
FARM	Factors Affecting Rural Men
FCSV	Fish Consumption Screening Value
g/mol	grams per mole
GST-p-AHF	Altered hepatic foci expressing placental glutathione-S-transferase
ha	hectare
Hp-Sed	2-endo, 3-exo, 5-endo, 6-exo, 8, 9, 10-heptachloroborane
Hx-Sed	2-exo, 3-endo, 6-exo, 8, 9, 10-hexachloroborane
IARC	International Agency for Research on Cancer
IC_{50}	inhibitory concentration 50%
Ig	immunoglobulin
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
L	liter
LOAEC	lowest observed adverse effect concentration
LOAEL	lowest observed adverse effect level
LOEC	lowest observed effect concentration
log K_{ow}	log octanol/water partition coefficient
MDCH	Michigan Department of Community Health
MFCAP	Michigan Fish Consumption Advisory Program
mg	milligram
mm	millimeter
MRL	Minimal Risk Level
ng/g	nanogram per gram
NHL	Non-Hodgkin's lymphoma
NOAEL	no observed adverse effect level
NTP	National Toxicology Program
OR	Odds ratio
PCBs	Polychlorinated biphenyls
ppm	parts per million
Rb	Retinoblastoma
RfD	reference dose
RSC	relative source contribution
TCDD	2,3,7,8-tetrachlorodibenzo-p-dioxin

TDI	tolerable daily intake
TRI	Toxics Release Inventory
TT	technical toxaphene
UF	uncertainty factors
US	United States
UV	ultraviolet
uvT	UV-treated toxaphene
WHO	World Health Organization
WT	weathered toxaphene
ww	wet weight
µg	microgram
µM	micromolar

Disclaimer

The technical support document includes and relies on scientific information that was not available to ATSDR when the Toxicological Profile for Toxaphene was finalized, and this document is not intended to replace ATSDR MRLs or recommendations.

Summary

In May 2007, the Michigan Department of Community Health (MDCH) received a letter from a Michigan resident about toxaphene contamination in the Great Lakes. He was concerned that the Michigan Fish Consumption Advisory Program was not protective for toxaphene exposure.

Toxaphene is a mixture of many chemical compounds. Over thirty years ago, this mixture was commonly used as a pesticide. Although the United States Environmental Protection Agency banned its use in 1990, toxaphene remains as a contaminant in the environment.

The waters of the Great Lakes, especially Lake Superior, contain toxaphene. Fish in those waters accumulate and store it, mainly in fatty tissues. People who eat Great Lakes sport-caught and commercial fish may be consuming these chemicals.

Since toxaphene is no longer commonly used, it is unlikely that people will have high enough exposures for immediate and severe health effects. However, eating fish contaminated with these chemicals could cause less obvious health effects in people. Animals fed toxaphene have had changes in their immune system, liver, and kidneys. Evidence exists that links toxaphene exposure to cancer. Therefore, unlimited consumption of certain sport-caught fish from the Great Lakes poses a public health hazard.

This document reviews recent information about toxaphene. The current in-use screening value for toxaphene is 5.0 parts per million (ppm). This document recommends use of the developed reference value to generate updated screening value for toxaphene.

Also recommended, is measuring three specific compounds of toxaphene instead of the total group of compounds. These three compounds represent around 90% of toxaphene found in humans. Screening values for the three toxaphene compounds would be protective of the possible cancer-causing effects of toxaphene.

Purpose and Health Issues

The Michigan Department of Community Health (MDCH) received a letter in May 2007 from a Michigan resident requesting that the toxaphene screening level used in the Michigan Family Fish Consumption Guide be reevaluated. The United States Environmental Protection Agency (EPA) banned toxaphene use in 1990 because of toxaphene's persistent toxicity in the environment. Researchers have shown that toxaphene can cause immune system alterations, developmental effects, changes in the liver and kidney, and exposure has been linked to the development of cancer. The purpose of this document is to review the recent literature on toxaphene and identify the need for changes in the Michigan Fish Consumption Advisory Program (MFCAP) that ensures that the consumption advice remains protective of public health.

Background

Introduction

Toxaphene is a pesticide made up of a mixture of over 670 chemicals with an average chlorine content of approximately 68% (Kucklick and Helm 2006). All toxaphene in the environment began as a technical toxaphene mixture containing the largest number of congeners (i.e., individual chemicals) with the most chlorination. Weathered toxaphene is technical toxaphene that has been degraded, resulting in a reduction of both the number of congeners and the chlorine present on the individual molecules.

Many studies report total toxaphene, which includes the remaining congeners from the original technical mix and the congeners created through weathering or degradation, as quantitated in comparison to a technical toxaphene standard. Unless otherwise specified, the use of the word "toxaphene" in this document refers to both technical and weathered. (For example, the phrase "toxaphene-contaminated fish" means any remnants of the original technical mixture along with congeners resulting from weathering or degradation.) When necessary, the word toxaphene will be modified to specify total, technical, or weathered. In some instances, individual chemicals that make up the toxaphene mixture will be discussed (see Chemical Nomenclature section).

Toxaphene has numerous synonyms (Appendix 1). First commercially available in the late 1940s, it was heavily utilized as an insecticide, acaricide (pesticide to kill mites), and piscicide (pesticide to kill fish). Between the 1950s and 1970s, lakes were treated with technical toxaphene to kill the unwanted fish before stocking fish for sport fishing. Technical toxaphene then became a replacement for DDT in the 1970s (Swackhamer et al. 1998). One of the first indications that toxaphene was too persistent and toxic was when the stocked sports fish died.

In 1982, toxaphene use restrictions began and the EPA completely banned toxaphene use in 1990. However, technical toxaphene was still produced in the US for export to other

countries (ATSDR 1996). Estimated world production, through 1982, of technical toxaphene was 1.2 billion kilograms with the US being the largest producer (Swackhamer et al. 1998). As of 2001, 12 suppliers of toxaphene were located in the US (NTP 2002). The EPA's Toxics Release Inventory (TRI) database listed a total of 4,616 pounds of toxaphene disposed of in 2006, with approximately 23 pounds of that amount released to the environment (EPA 2008A).

Toxaphene has been found globally, in North America, Central America, Europe, Scandinavia, Russia, and the high Arctic. Due to its physical/chemical properties, it is transported in the air over long distances via the cold condensation effect (Swackhamer et al. 1998). The cold condensation effect is when the chemical is heated by the sun, evaporates into the air where it cools and returns to the ground, only to repeat the process many times. This effect has moved toxaphene from southeastern US agricultural fields, where it was commonly used, to the waters of the Great Lakes. Recent studies modeling this transport have estimated 78-88% of the deposition into the Great Lakes basin is from the southeastern states. The authors determined the second major source region to be the northeastern states (Ma et al. 2005A). Ma et al. (2005B) also investigated events of increased transport, again with the major source region determined as the southern US. The increased transport of toxaphene was attributed to a specific weather pattern and was believed to be responsible for increasing the annual average daily air concentration of toxaphene.

Technical toxaphene released to the environment results in two major and multiple minor degradation products. The major ones are: 2-exo, 3-endo, 6-exo, 8, 9, 10-hexachlorobornane (Hx-Sed) and 2-endo, 3-exo, 5-endo, 6-exo, 8, 9, 10-heptachlorobornane (Hp-Sed). Both of these rapidly leave the human body and do not accumulate. Hx-Sed and Hp-Sed occur in larger amounts in the soil than the minor products. Minor products include Parlars 26, 40, 41, 44, 50, and 62 (see Chemical Nomenclature section below). Minor products are less abundant in the soil, but accumulate in humans and other animals, including fish.

The accumulation of these minor products in humans raises public health questions. In Michigan, consumption of toxaphene-contaminated fish is a known pathway of human exposure and toxaphene is included in the MFCAP.

Chemical Nomenclature

Along with the IUPAC names, there are four systems for naming toxaphene congeners: Parlar numbers, Andrews-Vetter code, Wester code, and the Nikoforov code. The Parlar numbers are the most commonly used system. They represent the order in which the chemical is detected by the laboratory equipment (elution order). The Andrews-Vetter system, also popularly used, employs a computer to assign numbers to chlorine-substituted bornanes. The Wester system has two sets of codes, one for chlorine number and another for chlorine position. The Nikoforov code is a four digit number based on a 13-digit binary code using the position of chlorines and hydrogens (Kucklick and Helm

2006). Table 1 presents the Parlar names, Andrews-Vetter code, Wester code, Nikoforov code, and IUPAC names for three toxaphene congeners.

Table 1: Examples of different systems used to name the three selected chemicals that are part of the toxaphene mixture.

Parlar Name	Andrews–Vetter code	Wester code	Nikoforov code	IUPAC names of both chiral forms
p-26 (P26)	B8-1413	B[12012]-[202]r	OCB-4921	2-endo, 3-exo, 5-endo, 6-exo, 8,8,10,10-octachlorobornane
		B[12012]-[202]s		2-exo, 3-endo, 5-exo, 6-endo, 8,8,10,10-octachlorobornane
p-50 (P50)	B9-1679	B[12012]-[212]r	NCB-4925	2-endo, 3-exo, 5-endo, 6-exo, 8,8,9,10,10-nonachlorobornane
		B[12012]-[212]s		2-exo, 3-endo, 5-exo, 6-endo, 8,8,9,10,10-nonachlorobornane
p-62 (P62)	B9-1025	B[30030]-(122)	NCB-6551	2,2,5,5,8,9,9,10,10-nonachlorobornane

(Simon and Manning 2006, Wester et al. 1997)

Physical and Chemical Parameters

Toxaphene is a yellow to amber waxy solid that smells like turpentine (ATSDR 1996). Technical toxaphene consists mainly of polychlorinated boranes with six to nine chlorines attached (EPA 2005). Toxaphene compounds dechlorinate in the presence of alkali, sunlight (ultraviolet [UV] radiation around 290 nm [de Geus et al. 1999]), or temperatures above 120°C. They are soluble in common organic solvents, but practically insoluble in water (0.4-3 ppm) (WHO 1990).

The chemical formula (average) for toxaphene is $C_{10}H_{10}Cl_8$, and it has a molecular weight (average) of 414 g/mol. The vapor pressure for toxaphene is 0.2 to 0.4 mm Hg at 20°C, and it has a log octanol/water partition coefficient (log K_{ow}) of 5.5 [MDEQ 2006] although lower numbers have been reported for both vapor pressure and log K_{ow} (ATSDR 1996).

Analytical Methods

The EPA Method 8081 can be used to detect toxaphene in environmental media by identifying five major peaks in a technical toxaphene sample. Since the degradation products differ from the original technical mixture, using this EPA method may not accurately detect the degradation products (EPA 2005) (Figure 1).

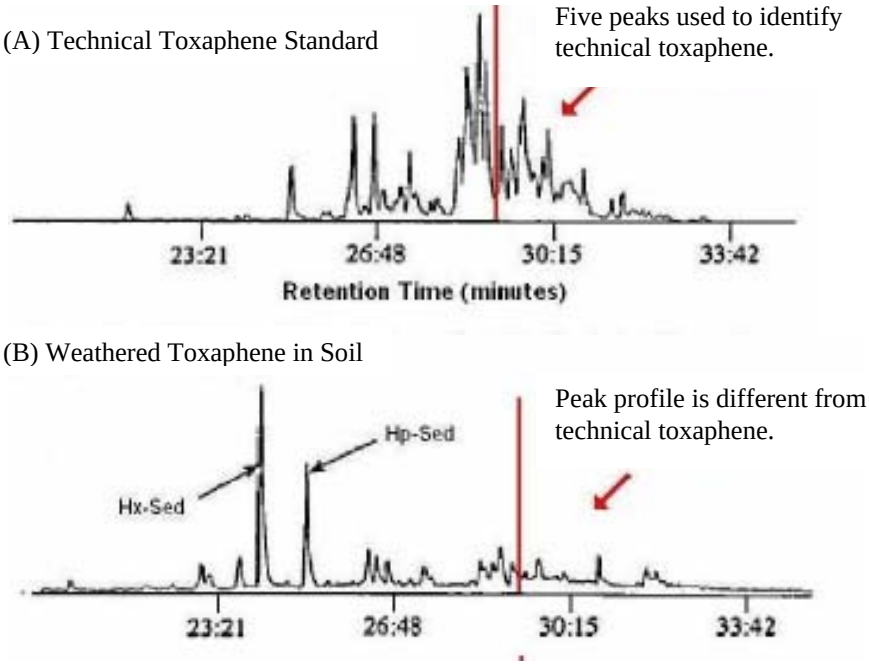

Figure 1: Chromatograms for technical (A) and weathered (B) toxaphene using EPA Method 8081 (EPA 2005).

Compounding the issue, Kucklick and Helm (2006) reported that only approximately 25% of the toxaphene congeners found in Lake Superior lake trout are commercially available for use as analytical standards. However, for the assessment of human health, Parlars 26 and 50 are more relevant than the other congeners in fish (marine mammals and humans primarily retain Parlars 26 and 50).

Maruya et al. (2001) analyzed seafood samples collected near a former technical toxaphene production plant in Georgia to determine if the EPA Method 8081 was acceptable for measuring both technical toxaphene and weathered toxaphene. The authors concluded that the actual toxaphene amount was underestimated when using the EPA Method 8081 because that method was not optimal for detecting weathered toxaphene.

It is possible that other chlorinated hydrocarbons, such as PCBs, interfere with the detection of toxaphene. (Gill et al. 1996).

Discussion

Environmental Contamination

Fish Tissue Concentrations

Most Great Lake fish fillets sampled have detectable levels of toxaphene (Table 2). The highest average concentrations reported by either the Michigan Fish Contaminant Monitoring Program (MFCMP) or the US EPA were in siscowet trout (2.6 ppm) and Lake Trout (4.9 ppm) both from Lake Superior. The most current results (2000-2006) have average concentrations that appear to be lower than older data.

Table 2: Total toxaphene levels in Great Lakes fish.

Great Lake	Fish species (number of fillets[1] tested)	Year[2]	Range (ppm)	Mean ± standard error (ppm)
Lake Superior	Brown Trout (10)	1984-1999	All below 0.05 (MDCH detection limit)	NA
	Smelt	1992-1994	NA	0.16 ± 0.04
	Burbot (13)	2000-2006	All below 0.05	NA
	Chinook (17)	1984-1999	0.125-2.0	1.11 ± 0.14
	Chinook (10)	2000-2006	0.175-0.425	0.28 ± 0.04
	Coho (41)	1984-1999	Below 0.05-0.3	0.10 ± 0.01
	Lake Herring (20)	1984-1999	Below 0.05-0.35	0.18 ± 0.02
	Lake Herring (6)	2000-2006	Below 0.05-0.125	0.06 ± 0.01
	Lake Sturgeon (3)	2000-2006	0.075-0.316	0.23 ± 0.08
	Lake Trout	1992-1994	NA	4.9 ± 1.4
	Lake Trout (146)	1984-1999	Below 0.05-8.6	1.20 ± 0.11
	Lake Trout (10)	2000-2006	0.052-0.444	0.11 ± 0.04
	Lake Whitefish (42)	1984-1999	Below 0.05-0.475	0.23 ± 0.03
	Lake Whitefish (33)	2000-2006	Below 0.05-0.45	0.17 ± 0.02
	Longnose (10)	1984-1999	0.125-0.425	0.22 ± 0.03
	Rainbow Smelt (12)	1984-1999	0.075	0.075 ± 0
	Rainbow Trout (9)	2000-2006	All below 0.05	NA
	Siscowet Trout (100)	1984-1999	Below 0.05-10	2.63 ± 0.23
	Siscowet Trout (30)	2000-2006	Below 0.05-2.264	0.41 ± 0.10
	Walleye (16)	2000-2006	All below 0.05	NA
	Yellow Perch (10)	1984-1999	All below 0.05	NA
Lake Michigan	Lake Trout	1992-1994	NA	1.5 ± 0.3
	Smelt	1992-1994	NA	0.059 ± 0.006
Lake Huron	Lake Trout	1992-1994	NA	2.4 ± 0.5
Lake Erie	Walleye	1992-1994	NA	0.13 ± 0.02
Lake Ontario	Lake Trout	1992-1994	NA	0.54 ± 0.2

[1] = Fillets are either skin-on or skin-off and varies by species (EPA 1999)

[2] = Data Source: 1984-1999 (Joe Bohr, MDEQ, MFCMP database, 2008), 1992-1994 (EPA 1999), and 2000-2006 (Joe Bohr, MDEQ, MFCMP database, 2008)

NA = not available

Total toxaphene measurements include a majority of the toxaphene congeners in fish. Recent studies have quantitated specific toxaphene congeners. This quantitation may provide a more precise amount of toxaphene in the fish by focusing on congeners that may not be completely included in the total toxaphene measurement (see Analytical Methods section above). It has the added advantage of allowing measurement of the congeners that tend to accumulate in people (see Introduction above and Toxicological Evaluation section below).

Fish tested from waters near the Yukon First Nations, in northern Canada, were assessed for both total toxaphene and relative concentrations of specific toxaphene congeners. People of the First Nations collected 19 fish samples (eight marine [three salmon species, dogfish, halibut, and ooligan] and two freshwater species [trout and whitefish]) and prepared them as they would to eat. Total toxaphene was between 0.042 and 0.242 ppm with a mean of 0.107 ± 0.061 ppm. Three congeners, Parlars 26, 50, and 62, represented 8-25% of the total toxaphene found in the fish. Based on this data and the lack of commercially available congeners, the authors recommended that both the total toxaphene and the sum of the three specific congeners be assessed to accurately determine the toxaphene present in samples (Chan and Yeboah 2000).

Ekici et al. (2008) recently evaluated toxaphene levels (Parlars 26, 40 + 41 [measured together], 44, 50, and 62) in commercially available fish from Germany. Fish species that were tested were: Alaska pollock, bonitos, cod, eel, hake, halibut, herring, mackerel, redfish, saith, salmon, sardines, and trout. Specific congener toxaphene levels in these fish ranged from 0.0003-0.1077 ppm with the largest amounts in halibut, herring, and salmon (0.1077, 0.0465, and 0.0503 ppm, respectively). For most of the samples, Parlars 40 + 41 and 44 only added a negligible amount to the levels found (Ekici et al. 2008).

Exposure Pathways Analysis

An exposure pathway contains five elements: (1) the contaminant source, (2) contamination of environmental media, (3) an exposure point, (4) a human exposure route, and (5) potentially exposed populations. An exposure pathway is complete if there is a high probability or evidence that all five elements are present. Table 3 describes human exposure to toxaphene from ingestion of fish.

Table 3: Exposure pathway for human exposure to toxaphene.

Source	Environmental Medium	Exposure Point	Exposure Route	Exposed Population	Time Frame	Status
Historical usage and atmospheric deposition in the Great Lakes	Fish (contamination from the water and sediments magnifying in the food web)	Great Lakes fish	Ingestion	Anyone who eats Great Lakes fish (residents and tourists)	Past, Present, and Future	Complete

Fish Advisories and Specific Screening Levels

Humans are primarily exposed to toxaphene from ingestion of fish (~80-90% relative source contribution [RSC]) and drinking water or surface water (~10% RSC) with air and soil exposure negligible (EPA 2005). In 1998, there were 6 fish consumption advisories in 4 US states and by 2004 that number increased to 28 advisories in 7 US states (Table 4) with Canada issuing 57 advisories that recommended restricted or no consumption due to toxaphene (EPA 1999).

Table 4: Number of advisories due to toxaphene issued per US state.

State	Number of fish advisories due to toxaphene (2004)
Arizona	6
Delaware	2
Georgia	6
Louisiana	1
Mississippi	9
Oklahoma	2
Texas	2

(Information current as of 2004 for all states except Delaware, which has information current as of 2006. [EPA 2008B])

Along with states issuing advisories, several other states screen fish tissue for toxaphene. Table 5 presents the action or screening levels for several US states and Ontario, Canada. Not all states that have action or screening levels have had or currently have fish consumption advisories due to toxaphene.

Table 5: Levels of total toxaphene (ppm) in fish tissue for action levels for additional monitoring or screening levels used to set fish consumption advisories.

Location	Value	Category	Reference
Virginia [1]	0.098 ppm	Screening value	VDH 2003
Maine	0.778 ppm	Action level	MBH 2001
	0.02 ppm	Action level [1]	
Ontario, Canada	Greater than 0.235 ppm	Restrict consumption	MoE 2007
	Greater than 1.877 ppm	No consumption	
California [1, 2]	Less than or equal to 0.2 ppm [3]	Restrict consumption	CA EPA 2008
	Greater than 0.61 ppm	No consumption	
Mississippi	Greater than 0.4 ppm	Restrict consumption	Mississippi DEQ 2007
	Greater than 2.0 ppm	No consumption	
Ohio	Greater than or equal to 1.094 ppm	Restrict consumption	SoO 2006
	Greater than 9.45 ppm	No consumption	

1 = based on cancer risk
2 = based on a 72.5 kg person
3 = eight ounce meal prior to cooking, six ounces after cooking

Toxicological Evaluation

Toxicokinetics

The human body burden consists of five persistent toxaphene congeners, with the three major congeners Parlars 26, 50, and 62 (Simon and Manning 2006). Absorption of toxaphene occurs in the intestinal tract and lungs in laboratory animals and preferentially distributes to fat compared to other organs (ATSDR 1996). Toxaphene excretion

(approximately 70%) happens through both feces and urine (ATSDR 1996), but low levels remain in fat. Metabolism of toxaphene, in the body, is due to dechlorination, dehydrodechlorination, and oxidation (ATSDR 1996).

Development of a pharmacokinetic model used two data sets, with one from male and one from pregnant rats, for technical toxaphene absorption, tissue distribution, and elimination. Absorption rate was rapid in fat, whole body, carcass (everything else but the stomach), and blood. The rate was slower in the liver and muscle, and slowest in the brain. Tissue burden was highest in fat (around 63% of total dose), carcass (around 23% of total), and blood and muscle (both about 6% of total). The tissue burden was lowest in liver and brain (both less than 2%). Elimination rates overall were much slower than the absorption rates, but were rapid in whole body, muscle, and blood. Moderately rapid elimination rates were obtained for carcass and brain. Slow elimination rates occurred in liver and were very slow rates occurred in fat. Feces and urine were the excretion routes, with feces as the dominant excretion pathway and urine as a minor route in male rats. Fecal toxaphene levels were twenty times higher than urine levels. In contrast to the male rats, pregnant rats had similar levels of excretion in both feces and urine attributed to physiological differences because of pregnancy and/or gender differences in fat content. A positive relationship was noted between lipid content of tissue and toxaphene tissue burden (Wen and Chan 2000).

Human Biomonitoring

Recent tests of human milk, adipose tissue, and serum have had measurable levels of toxaphene congeners, which demonstrates that people's bodies retain these chemicals. Toxaphene congeners were assessed in human milk and adipose tissue from Germany collected in 1992-1993 and 1998-1999. Parlars 26, 41, 42, 44, 50, 63, B7-1453 (Andrews-Vetter code), and B8-1412 were found in human breast milk. Approximately 50-80% of the total toxaphene was Parlar 50 with Parlar 26 being the second most abundant. A range of 4.4-13.0 μg/kg lipid weight was found for Parlar 50 and 1.5-7.2 μg/kg lipid weight for Parlar 26. Parlars 41 + 44 had a range of 0.4-2.8 μg/kg lipid weight. These amounts were similar to the ranges detected in two other studies the authors cited, one from Russia and one from Southern Canada. After comparing the current results to eight other studies, the authors concluded that, in general, samples from the Arctic region were higher than samples from more temperate regions (Skopp et al. 2002).

Newsome and Ryan (1999) surveyed human milk samples from Canada for toxaphene and other persistent chemicals. Samples, collected from Keewatin, northern Canada, (12 samples) in 1996-1997, were compared to samples from southern Canada, collected in 1986 (30 samples) and 1992 (54 samples). Human milk from Keewatin had significantly higher levels of total toxaphene as well as significantly higher levels of Parlars 26 and 50 than the human milk samples from southern Canada collected in either 1992 or 1986. Comparing the two sample sets from southern Canada, samples in 1992 had significantly lower levels of total toxaphene than the samples from 1986. Parlars 26 + 50 were 86% of

the total toxaphene in the Keewatin samples, with samples from southern Canada in 1986 samples having 47% and 1992 having 61%. Even though samples from Keewatin were the highest of those assayed in this study for total toxaphene, the authors noted that they were still lower than samples collected in Sweden, Finland, and Northern Quebec, Canada (Newsome and Ryan 1999).

Aboriginal people of northern Canada are exposed to larger amounts of toxaphene due to their traditional diet (Health Canada 2003) with the Inuit people the most highly exposed group in the Canadian Arctic (VanOostdam et al. 2005). Traditional diets of these groups include fish, marine mammal muscle, fat, and organs with aboriginal peoples obtaining approximately 12-40% of their energy requirements from traditional foods. The Inuit located around the Arctic have around ten times greater levels of toxaphene (total toxaphene and Parlars 26 and 50) in maternal blood as compared to Caucasians with inland Inuit people having levels lower than the Inuit around the Arctic. Mean intakes of the Inuit exceed Health Canada's provisional tolerable daily intake (TDI) of 0.2 μg/kg bw day (Health Canada 2003).

Pooled human blood serum, collected by the American Red Cross in Atlanta in 1987, Chicago in 1992, and Cincinnati in 1994, was assessed in 2003 for toxaphene congeners (Barr et al. 2004). Parlars 26 and 50 were found with Parlars 40/41 (measured together, but not differentiated), 44, and 62 being tentatively identified. Parlars 26 and 50 were quantitated and ranged from 0.7-6.6 ng/g lipid and 2.01-5.7 ng/g lipid, respectively (Barr et al. 2004). Gill et al. (1996) found Parlars 26, 40/41, 44, and 50 representing around 90% of the total toxaphene in serum from Canadian Native communities.

Genotoxicity

Toxaphene was genotoxic in mammalian cells and carcinogenic in rats and mice (de Geus et al. 1999). Additionally, in other testing technical toxaphene was positive in the *Salmonella* mutagenicity assay, sister chromatid exchange, and micronucleus test (Choi et al. 2004).

A study by Samosh (1974) observed chromosomal aberrations in eight women occupationally exposed to a single massive dose of technical toxaphene. Aircraft had sprayed a field with 2 kilograms per hectare (2.47 acres) of polychlorocamphene (technical toxaphene). Due to weather conditions (rain after the spraying and warm temperatures the next day), the technical toxaphene evaporated from the soil (volatilized). Women inhaled the volatilized compounds in the field and reported mild to moderate symptoms four to five hours after starting work. The women were hospitalized, given Vitamins B and C and intravenous glucose. Some women required treatment with cardiac stimulants. Blood was drawn eight days after the exposure. Examination of metaphases from white blood cells revealed that 13% were aberrant in the exposed women as compared to 3% in the unexposed controls. Additionally, breaks per aberrant metaphases were larger in the exposed group with a wider range of damage present in the exposed group as compared to the control group (Samosh 1974).

Recently, genotoxicity of degradation products was assessed and compared to technical toxaphene. Technical toxaphene reduced the growth of *Escherichia coli* strain PQ37 at 10, 20, and 40 mg/L but not *Salmonella*. UV irradiation (six or nine hours) of technical toxaphene caused a reduction of growth in *Salmonella*, possibly due to increased toxicity of the UV-degraded toxaphene (Bartos et al. 2005).

Another more recent study compared the mutagenicity of technical to weathered toxaphene. Young et al. (2008) exposed *Salmonella typhimurium* strain TA100 in the presence and absence of a rat-liver extract (S9), which contains microsomal enzymes, to technical, soil-weathered, or fish-weathered toxaphene. The author found no difference in the mutagenicity of either soil- or fish-weathered toxaphene as compared to technical toxaphene.

Toxicity in Human Derived Cell Lines

Researchers conducted two studies on toxaphene using human derived cell lines. One study examined CYP19, an aromatase responsible for the rate-limiting step in converting androgens to estrogens, in the human placental epithelial JEG-3 cell line. Aromatase expression occurs in multiple tissues at tissue-specific levels in humans. JEG-3 cells were exposed to technical toxaphene for 2 or 24 hours. Aromatase activity was inhibited only after the 24 hour exposure to 10 μM (about 4.14 ppm, lowest observed effect concentration [LOEC]) technical toxaphene with an inhibitory concentration of 50% (IC_{50}) of 11 μM (Laville et al. 2006).

Human CEM x 174 lymphoblasts, a hybrid human T and B cell line were used by Rought et al. (1999) to examine retinoblastoma expression after exposure to technical toxaphene (0, 10, 25, or 50 μM in 0.1% dimethyl sulfoxide [DMSO]). Retinoblastoma (Rb) is a tumor suppressor gene with loss of function or expression associated with many cancers, including lymphocytic leukemia and monocytic leukemia. A 24 hour toxaphene exposure (10-50 μM; about 4.14-20.7 ppm) reduced Rb protein expression in the hybrid cell line (Rought et al. 1999).

Observational Epidemiology Studies

Several epidemiological studies have been conducted on individuals that may have been occupationally exposed to toxaphene. The FARM (Factors Affecting Rural Men) study investigated a chromosomal translocation, t(14; 18), present in Non-Hodgkin's lymphoma (NHL). The translocation, t(14; 18), moved the B cell CLL/lymphoma-2 (bcl-2) gene to the immunoglobulin (Ig) heavy chain gene. This resulted in increased expression of bcl-2, an anti-apoptotic protein, which could result in increased survival of neoplastic or aberrant cells. Toxaphene exposure was associated with t(14; 18) positive NHL (odds ratio [OR] = 3.7, 95% Confidence Interval [CI] = 1.9-7.0). It was also

mentioned that chromosomal damage has been reported to be higher in peripheral blood lymphocytes during the peak spraying season (Schroeder et al. 2001).

Mills et al. (2005) surveyed United Farm Workers of America between 1988 and 2001 for lymphohematopoietic cancer. The authors found that California farm workers that used mancozeb (OR = 2.35, 95% CI = 1.12-4.95) or toxaphene (OR = 2.20, 95% CI = 1.04–4.65) had a statistically significant increase in their risk of leukemia. Also elevated was their risk for granulocytic leukemia after exposure to mancozeb (OR = 3.35, 95% CI = 1.09-10.31), toxaphene (OR = 3.24, 95% CI = 1.01-10.41), or trifluralin (OR = 2.90, 95% CI = 1.00-8.46). The authors noted that this was a small study, without interviews and additional information on the subjects, including age and smoking status. The authors also noted that the exposure was estimated, based on the time that these individuals were working and the crop that was being grown at that time (Mills et al. 2005).

Purdue et al. (2006) surveyed 22,409 subjects with interviews and/or questionnaires assessing the total lifetime exposure days to various pesticides. The authors excluded those with existing cancer and relied on cancer incidence registries. A statistically significant increase ($p < 0.05$) in cancer risk for rectal cancer (rate ratio [RR] = 2.0, 95% CI = 1.1-3.5) was identified for individuals reporting toxaphene exposure, with the cancer risk being the same for all ages. Unlike the previous study, these authors did not find a statistically significant link between toxaphene use and leukemia (RR = 1.5, 95% CI = 0.8-2.9) or NHL (RR = 1.5, 95% CI = 0.9-2.5). The authors noted that a large number of statistical comparisons were performed, which may cause some findings to be significant by chance (Purdue et al. 2006).

Cantor et al. (1992) examined pesticides, including toxaphene, and the occurrence of NHL. The authors found what was termed a “notable, though nonsignificant” elevated risk for developing NHL after handling toxaphene (OR = 1.5, 95% CI = 0.6-3.5). However, Cantor et al. (1992) mentioned that there was a potential for exposure misclassification due to reliance on the subject’s recall of their exposure.

In Iceland, plasma toxaphene levels were measured to determine if there was a correlation with semen quality. All men selected were seeking services of assisted reproduction from March 1999 to May 2001 and were categorized in one of three groups, two with fertility issues and one with normal semen (control). Parlar 50 was present in greater than 85% of the plasma samples (72 total samples from all groups) and while there was a statistically significant positive correlation of Parlar 50 levels with age, no correlation was found with semen quality (Magnusdottir et al. 2005).

Animal Toxicity Studies

An initial oral study used four cynomolgus monkeys (*Macaca fascicularis*, two male/two female) given technical toxaphene at 1.0 mg/kg bw/day in glycerol/corn oil for 52 weeks. Mild toxic effects, such as increased relative organ weights, increased hepatic microsomal activity, and inflammation/enlargement of tarsal glands (similar to Aroclor

exposure), were observed after the 52 week treatment, classifying 1.0 mg/kg bw/day as the lowest observed adverse effect level (LOAEL). Two previously obtained no observed adverse effects levels (NOAELs), 0.7 mg/kg bw/day (NOAEL from von Rumker et al. 1974) and 10 ppm (around 0.6 mg/kg/d; NOAEL from the Kettering Lab report, a two year two female monkey study [Lehman 1965]) were noted as being lower than the LOAEL from the above described study (Bryce et al. 2001).

In a companion report from the Bryce et al. (2001) feeding study, Andrews et al. (1996) examined toxaphene congeners in blood and adipose tissue throughout the course of the treatment. Blood levels of toxaphene plateaued at 40 ppb, around 10 weeks, and adipose levels plateaued at 4000 ppb, between 15 and 20 weeks. Interestingly, there were a reduced number of congeners in the blood and adipose tissue as compared to the technical mix. Four congeners were detected: Parlars 26, 44, 50, and 62.

Monkeys from the Bryce et al. (2001) feeding study were also examined for immune function alteration in a study published by Tryphonas et al. (2000). Immune effects were measured after 34 weeks of exposure to the technical toxaphene mixture. There were no statistically significant effects, but mild immunomodulatory effects were observed. The authors noted that due to large inter-animal variability, more animals were necessary.

Tryphonas et al. (2001) conducted a larger study using young adult female cynomolgus monkeys (*Macaca fascicularis*, 10 per group) fed 0.1, 0.4, 0.8 mg/kg bw/day technical toxaphene or 10 female control monkeys fed glycerol/corn oil. Male monkeys (5 per group) were also fed (0.8 mg technical toxaphene/kg bw/day or glycerol/corn oil) for a total of 75 weeks. Immune function testing started after 33 weeks of treatment, when steady state blood and adipose levels of toxaphene were estimated to have been reached (based on data in Andrews et al. [1996]). A reduced response to sheep red blood cells was identified in both the 0.4 and 0.8 mg/kg bw/day groups. The reduction in the 0.8 mg/kg bw/day group was statistically significant. There was no change to the delayed-type hypersensitivity response, lymphocyte proliferation, natural killer cell activity, or leukocyte numbers (except absolute B cell number in the 0.8 mg/kg bw/day treatment group). The NOAEL from this study was 0.1 mg/kg bw/day for female monkeys.

Based on the shift toward examining the toxicity of individual congeners, Calciu et al. (1997) investigated the effects of Parlar 26 and/or Parlar 50 compared to technical toxaphene or a control group *ex vivo* in embryos. Embryos were treated *ex vivo*, by removal from the uterus and submerging in a solution composed of technical toxaphene, Parlars 26, 50, or 26 + 50 at 0, 0.10, 1.0, or 5.0 ppm in 0.01% DMSO. Statistically significant differences were noted in all treatment groups as compared to the control (0.10 ppm = lowest observed adverse effect concentration [LOAEC] for technical toxaphene, Parlars 26, 50, and 26 + 50). Defects noted for all toxaphene treatment groups included central nervous system and morphological alterations. Results from this study were due to treatment of embryos outside of the mother. As this does not represent a real exposure, the authors calculated a dose necessary for a feeding study in order for an embryo to be exposed to 0.10 ppm *in utero* to be approximately 10 mg toxaphene/kg day.

A second study was done by Calciu et al. (2002), again treating embryos *ex vivo* with 0, 0.10, 1.0, or 5.0 ppm in 0.01% DMSO of technical toxaphene, Parlars 26, 50, or 26 + 50, but this time hyperglycemic conditions were also examined. Again, as in the previous study, all treatment groups had significant differences as compared to the control. Hyperglycemic conditions made the toxaphene-induced neural tube and limb defects worse as compared to toxaphene treated groups under normal glucose conditions. The effects of Parlars 26 and 50 appeared to be differentially impacted by the hyperglycemia, as the defect pattern was different in embryos treated with Parlar 26 or Parlar 50.

Simon and Manning (2006) chose the NOAEL from a relatively new study treating rats with weathered toxaphene (WT) to calculate a proposed reference dose (RfD). Partially hepatectomized rats were subcutaneously injected each week for 20 weeks with multiple doses of technical toxaphene (TT), UV-treated toxaphene (uvT), cod liver extract (CLE) containing WT, corn oil (negative control), or 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD; positive control) (Besselink et al. 2008 [peer-reviewed version of Besselink et al. 2000]). CLE was from farm-raised cod exposed to TT for 2 months. There was a smaller percentage of Parlars 26, 50, and 62 (sum of three persistent congeners [Σ3PC]) in the CLE than reported in surveys of other fish, which Simon and Manning (2006) attributed to the short weathering time of the technical toxaphene. The rats treated with the TCDD had a significantly increased number of altered hepatic foci expressing placental glutathione-S-transferase (GST-p-AHF), which is an indication of tumor promotion (Besselink et al. 2008). Other studies have reported effects, inhibition of intercellular communication, that indicate toxaphene is a tumor promoter (Kang et al. 1996; Besselink et al. 2008). There was no difference in GST-p-AHF numbers in any toxaphene treatment group (TT, uvTT, or CLE) as compared to the negative control. Besselink et al. (2008) selected the highest dose of their CLE groups, 12.5 mg/kg/week (1.79 mg/kg/day), for the NOAEL even though there was a significant reduction in GST-p-AHF as compared to the negative control. The NOAEL that Simon and Manning (2006) chose from the Besselink et al. (2008) study was 0.0021 mg/kg/day for the Σ3PC and 0.60 mg/kg/day for the CLE that contained all congeners of WT.

Reference Values or Regulatory Levels

The EPA has set the limit on the amount of toxaphene in drinking water to 0.003 mg/L (EPA 2005). Additional values utilized by other countries or agencies, including numerous tolerable daily intakes (TDIs), are in Table 6.

Table 6: Examples of regulatory or reference values for toxaphene.

Authority	Category	Value	Total toxaphene or specific Parlars	Reference and notes
Germany	Maximum Residue Limit	0.1 mg/kg ww	Parlars 26, 50, and 62	McHugh et al. 2004; Matrix: Fish/fish products
Nordic Council of Ministers	TDI	0.2 μg/kg bw day	Total	Health Canada 2003; Only if carcinogenic effects are indirect mechanisms
European Union	TDI (tumor promotion)	0.41 mg/d[1]	Total weathered	McHugh et al. 2003
Canada	Provisional TDI	0.2 μg/kg bw day	Total	Health Canada 2003
US EPA	TDI (chronic toxicity)[2]	0.015 mg/d[1]	Total	McHugh et al. 2003
ATSDR	Acute oral MRL	0.005 mg/kg/day	Total	ATSDR 1996
	Intermediate oral MRL	0.001 mg/kg/day	Total	
California EPA	Non-cancer critical value	0.00035 mg/kg day	Total	CA EPA 2008

1 = based on a 60 kg person
2 = calculated based on RfD

Toxaphene is classified as a probable human carcinogen (B2) by the EPA (EPA 1991) and the International Agency for Research on Cancer (IARC) (IARC 2001). Table 7 provides a summary of cancer slope factors from various sources. Studies with technical toxaphene exposure in rodents are the basis for all of these values.

Table 7: Cancer slope factors (CSFs) for toxaphene.

Source	CSF value
EPA 1991	1.1 per mg/kg day
Goodman et al. 2000	0.1 per mg/kg day
CA EPA 2008	1.2 per mg/kg day

Development of the RfD for toxaphene fish contaminant screening values (FCSVs)

Currently (September 2008), the MDCH screening level for restricted fish consumption due to toxaphene contamination is 5 ppm. Toxaphene in fish is currently measured at the MDCH lab as apparent toxaphene, which is an estimate of total toxaphene as compared to a technical standard. Any peaks with less than a 32 minute retention time are not included in the estimate due to potential interference by other pesticides. Lab personnel are currently working to optimize methods for detection of individual Parlars, including 26, 50, and 62. In the interim, it is likely that samples will be assessed for both total (apparent) toxaphene and individual Parlars.

Simon and Manning (2006) recently reviewed the available information on toxaphene and suggested an RfD based on the tumor promotion effect of toxaphene. They selected a NOAEL of 0.0021 mg/kg day for Σ3PC and 0.60 mg/kg day for the CLE that contained all congeners of WT based on the Besselink et al. (2008) study treating rats subcutaneously for 20 weeks (See Animal Toxicity Studies section for further discussion). The authors utilized uncertainty factors of 10 (animal to human) and 10 (human to human) for a combined uncertainty factor (UF) of 100. Using the NOAEL and above UF the RfD for Σ3PC is 0.000021 (2.1×10^{-5}) mg/kg/day.

MDCH recommends an additional uncertainty factor (10) to account for the length of the study (subchronic), which is less than a chronic exposure. With this additional modifying factor, the RfD for Σ3PC would be 0.0000021 (2.1×10^{-6}) mg/kg/day. As the MDCH lab is still determining its capabilities for measurement of individual Parlars, this value cannot be put into use at this time, but should be considered once method optimization and preliminary sample assessment is completed.

Even though Simon and Manning (2006) calculate a total toxaphene amount in the CLE, there is a more comprehensive study for development of a technical toxaphene RfD. Female monkeys were treated for over a year (75 weeks, subchronic exposure) with multiple doses of technical toxaphene (Tryphonas et al. 2001). After feeding the monkeys for 33 weeks, immune function assessment began (See Animal Toxicity Studies section for the discussion of Tryphonas et al. [2001]). The authors found a NOAEL of 0.1 mg/kg day from this subchronic study. Applying the UFs utilized by ATSDR (1996) in calculation of their intermediate oral MRL (10 for animal to human, 10 for human to human, and a modifying factor of 3 for possible developmental effects) and including an uncertainty factor for subchronic to chronic (10) the RfD is 0.000033 mg/kg/day.

The two studies above have several shared and individual advantages for use in development of an RfD and FCSVs. Shared advantages include:

- NOAELs determined based on sensitive endpoints, either tumor promotion or immune function alteration.
- Incorporation of weathering into the study design, either by treatment of animals with weathered toxaphene or by assessment after steady-state blood levels and accumulation of the persistent congeners were achieved.

Advantages specific to the Tryphonas et al. (2001) study are:

- Toxaphene exposure to people is through ingestion of fish; oral treatment is a route closer to actual exposure, rather than subcutaneous injection.
- Use of monkeys, which may be a better model for humans than rats as both monkeys and humans are primates.

Advantages specific to the Simon and Manning (2006) utilized Besselink et al. (2008) study:

- The endpoint for this RfD is tumor promotion, which will enable FCSVs developed to be protective of carcinogenic effects.
- It only covers the Σ3PC, which appears to be responsible for toxicity in people.

Children's Health Considerations

Children can be at greater risk than adults from certain kinds of exposure to hazardous substances. A child's lower body weight and higher intake rate results in a greater dose of hazardous substance per unit of body weight. Fetuses would be exposed during development to any toxaphene-contaminated fish that the mother eats. If toxic exposure levels are high enough during critical growth stages, the developing body systems of children can sustain permanent damage. Further exposure to a newborn and older babies could occur through the mother's breast milk. Breast milk may contain higher levels of toxaphene than certain species of fish due to the high levels of fat (lipids) present in breast milk.

Conclusions

Unlimited consumption of certain sport-caught fish from the Great Lakes, especially Lake Superior, is a public health hazard. Based on current information, fish consumption advisories may be required for certain fish species.

Recommendations

Use the proposed RfDs to develop updated toxaphene FCSVs and utilize these values to issue fish consumption advice in Michigan.

Continual monitoring of Lake Superior fish for toxaphene. However, fish from inland lakes in Michigan's Upper Peninsula and Lakes Michigan and Huron, from locations already utilized in the MFCMP, should be checked for toxaphene every other or every third sampling collection to confirm that it is not a concern. If fish consumption needs to be restricted, or if levels of toxaphene are increasing in Lake Michigan or Lake Huron

fish, Lower Peninsula inland lakes fish should be checked, again from locations already utilized by the MFCMP.

Develop analytical capabilities to screen for the three persistent congeners (Σ3PC = Parlars 26, 50, and 62). Conversion to FCSVs based on an RfD for the Σ3PC can then occur.

Provide the Fish and Wildlife Contaminant Advisory Committee (FAWCAC) and other relevant groups (Great Lakes Sport Fish Advisory Task Force and Great Lakes Human Health Network) with a copy of this document.

Public Health Action Plan

1. Using new toxaphene FCSVs, MDCH will issue advisories in the Michigan Family Fish Consumption Guide if fish tissue toxaphene exceeds the FCSVs (see Appendix 2 for sample FCSVs).

2. The MDCH Analytical Chemistry Laboratory will continue to screen fish, collected for the MFCMP (DEQ/DNR) for toxaphene.

3. The MDCH Analytical Chemistry Laboratory will develop methods to determine congener levels, in particular Parlars 26, 50, and 62.

4. MDCH will share a copy of this document so that FAWCAC and other relevant groups will have this information.

Preparers of Report

Michigan Department of Community Health
Division of Environmental Health

Jennifer Gray
Toxicology and Response Section

Kory Groetsch
Toxicology and Response Section

ATSDR Region 5 Office

Mark Johnson
Office of Regional Operations

ATSDR Division of Health Assessment and Consultation

Trent LeCoultre, Technical Project Officer
Cooperative Agreement Program Evaluation Branch

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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.

Technical Project Officer, Cooperative Agreement Program Evaluation Branch (CAPEB), Division of Health Assessment and Consultation (DHAC), ATSDR

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 1: Synonyms for Toxaphene (CAS #8001-35-2)

Agricide Maggot Killer
Agricide maggot killer (F)
Agro-Chem Brand Torbidan 28
Agro-Chem Brand Toxaphene 6E
Agsco toxaphene
Agway toxaphene 6E
Alltex
Alltox
Anatox
Attac 4-2
Attac 4-4
Attac 6
Attac 6-3
Attac 8
CCRIS 600
Camphechlor
Camphechlore [ISO-French]
Camphochlor
Camphofene huileux
Caswell No. 861
Chem-Phene
Chlorinated camphene
Chlorocamphene
Clor Chem T-590
Clor Chem T-590 Insecticide
Compound 3956
Coopertox
Cotton-Tox MP 82
Crestoxo
Cristoxo 90
Dr Roger's TOX-ENE
EINECS 232-283-3
ENT 9,735
EPA Pesticide Chemical Code 080501
Estonox
Fasco-terpene
Felco/Land O'Lakes Toxaphene
Geniphene
Grower Service Toxaphene 6E
Grower Service Toxaphene MP
Gy-phene
HSDB 1616
Hercules 3956
Hercules Toxaphene Emulsifiable Concentrate
Kamfochlor
Latka 3956 [Czech]
M 5055
Melipax
Motox
NCI-C00259
Octachlorocamphene
PchK
PCC
Penphene
Phenacide
Phenatox
Polychlorcamphene
Polychlorocamphene
RCRA waste number P123
Red Top Toxaphene 8 Spray
Rigo Toxaphene 8
Royal Brand Bean Tox 82
Security Motox 63 cotton spray
Security Tox-MP cotton spray
Security Tox-Sol-6
Strobane T-90
Strobane-T
Synthetic 3956
Toxadust
Toxafeen [Dutch]
Toxakil
Toxaphen
Toxaphen [German]
Toxaphene
Toxaphene (technical)
Toxaphene 8 EC
Toxaphene 8 Emulsifiable Insecticide
Toxaphene 90-10
Toxaphene E-8
Toxon 63
Toxyphen
Vertac 90%
Vertac toxaphene 90

Appendix 2: Development of Example Toxaphene Fish Contaminant Screening Values (FCSVs)

Using the RfD of 0.0000021 [2.0 x 10^{-6}] mg/kg/day for Σ3PC, developed from the Besselink et al. (2008) study, FCSVs were determined for both the general population and a sensitive population. The general population includes adult men and women no longer of childbearing age. The sensitive population consists of women of childbearing age and children under 15 years of age. One body weight was used to represent the sensitive population for both FCSV calculations.

Restrictions on consumption would begin around 1.7 ppb of Σ3PC. See Table 8 for example FCSVs using this RfD.

Table 8: Toxaphene (sum of the three persistent congeners [Σ3PC]) FCSVs using Simon & Manning (2006) RfD.

Population	Fish Σ3PC Concentration (ppb)	Fish Meals
General Population	≤ 1.2	Unrestricted
	> 1.2 to ≤ 5.1	One meal/week
	> 5.1 to ≤ 22.2	One meal/month
	> 22.2 to ≤ 44.3	Six meals/year
	> 44.3	Do not eat
Sensitive Population (women of childbearing age and children under 15)	≤ 1.0	Unrestricted
	> 1.0 to ≤ 4.3	One meal/week
	> 4.3 to ≤ 18.6	One meal/month
	> 18.6 to ≤ 37.3	Six meals/year
	> 37.3	Do not eat

- All calculated values rounded to 1 decimal place
- RfD = 0.0000021 (2.1 x 10^{-6}) mg/kg/day for Σ3PC
- Adapting EPA's equation for consumption limit of fish (contaminant amount [mg/kg] = (RfD*BW)/Fish consumption [kg/day] [mg/kg = ppm]) (EPA 2000)
    - Body weight (EPA 1997)
        - General population body weight (BW) = 78.1 kg
        - Sensitive population BW = 65.4 kg
    - Fish Consumption:
        - Unrestricted = 225 meals/year (140 g fish/day)
        - One meal/week = 52 meals/year (32 g fish/day)
        - One meal/month = 12 meals/year (7.4 g fish/day)
        - Six meals/year = 3.7 g fish/day

Using the RfD of 0.0000333 mg/kg/day for total toxaphene, developed from the Tryphonas et al. (2001) study, FCSVs were determined for both the general population

and a sensitive population (defined above). Restrictions on consumption would begin around 0.027 ppm of toxaphene. See Table 9 for example FCSVs using this RfD.

Table 9: Toxaphene (total) FCSVs using calculated RfD from Tryphonas et al. (2001).

Population	Fish Toxaphene Concentration (ppm)	Fish Meals
General Population	≤ 0.019	Unrestricted
	> 0.019 to ≤ 0.081	One meal/week
	> 0.081 to ≤ 0.351	One meal/month
	> 0.351 to ≤ 0.703	Six meals/year
	> 0.703	Do not eat
Sensitive Population (women of childbearing age and children under 15)	≤ 0.016	Unrestricted
	> 0.016 to ≤ 0.069	One meal/week
	> 0.069 to ≤ 0.297	One meal/month
	> 0.297 to ≤ 0.595	Six meals/year
	> 0.595	Do not eat

- All calculated values rounded to 3 decimal places
- RfD = 0.0000333 (3.33×10^{-6}) mg/kg/day for total toxaphene
- Adapting EPA's equation for consumption limit of fish (contaminant amount [mg/kg] = (RfD*BW)/Fish consumption [kg/day] [mg/kg = ppm]) (EPA 2000)
    - Body weight (EPA 1997)
        - General population body weight (BW) = 78.1 kg
        - Sensitive population BW = 65.4 kg
    - Fish Consumption:
        - Unrestricted = 225 meals/year (140 g fish/day)
        - One meal/week = 52 meals/year (32 g fish/day)
        - One meal/month = 12 meals/year (7.4 g fish/day)
        - Six meals/year = 3.7 g fish/day

It is unlikely that MDCH will use the updated toxaphene FCSVs with the current comparison method to generate fish consumption advisories. Several updated comparison methods are under consideration. MDCH will select a method after an assessment of each one. After selection of an updated comparison method, MDCH will implement the updated toxaphene FCSVs.