



# *Canadian Environmental Protection Act*

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## Priority Substances List Assessment Report

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# **Tetrachlorobenzenes**



Government  
of Canada

Gouvernement  
du Canada

Environment  
Canada

Environnement  
Canada

Health  
Canada

Santé  
Canada



**Priority Substances List  
Assessment Report**

# **Tetrachlorobenzenes**

Government of Canada  
Environment Canada  
Health Canada

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## **Synopsis**

Tetrachlorobenzenes (of which there are 3 isomers: 1,2,4,5-, 1,2,3,5- and 1,2,3,4-tetrachlorobenzene) are not produced in Canada, and currently there is no commercial domestic demand for these substances. On the basis of limited data, the 2 most significant sources of entry of tetrachlorobenzenes into the Canadian environment are from spillage of dielectric fluids and long-range transport and deposition.

Tetrachlorobenzenes have been detected in samples of air, surface water, rain, sediment and biota collected at various locations in Canada. Tetrachlorobenzenes are not persistent in air or surface water, but can persist under anaerobic conditions in buried soil or sediment.

The highest concentration of tetrachlorobenzenes detected in Canadian surface waters is approximately 8 500 times less than the effects threshold estimated for the most sensitive aquatic species identified. For wildlife, the estimated dietary intake of tetrachlorobenzenes by piscivorous mammals is approximately 500 times less than the estimated effects threshold based on studies in laboratory animals. Although significant exposure of benthic organisms to tetrachlorobenzenes in sediment may be occurring in specific aquatic ecosystems in Canada, adequate data on the toxicological effects on these organisms were not identified. It is therefore not possible to determine whether concentrations of these substances in sediments could result in harmful effects to these biota. Similarly, because of the lack of information on concentrations in ambient soils and on the toxicological effects on soil dwelling organisms, it is not possible to determine whether these organisms are adversely affected by exposure to the levels of tetrachlorobenzenes present in Canada.

Currently, the rates of release of tetrachlorobenzenes into the environment are low. Tetrachlorobenzenes are removed from the atmosphere by photooxidation and precipitation, and, therefore, are present in low concentrations in air. As such, they are not expected to contribute significantly to global warming or to depletion of stratospheric ozone.

Based on limited available data on concentrations in ambient air, drinking water and food, the total average daily intakes for each of the isomers of tetrachlorobenzene by various age groups in the general population have been estimated. Except for the estimated intakes of breast-fed infants which are elevated for only a short period of their lifespan, these intakes are from 210 to > 34 000 times less than the tolerable daily intakes derived on the basis of the available longest term (sub-chronic) studies in laboratory animals. The tolerable daily intake is the intake to which it is believed that a person can be exposed daily over a lifetime without deleterious effect.

**Based on these considerations, it has been determined that available information is insufficient to conclude whether tetrachlorobenzenes are entering the environment in quantities or under conditions that may be harmful to the environment. It has been concluded, however, that tetrachlorobenzenes are not entering the environment in quantities or under conditions that may constitute a danger to the environment on which human life depends. It has been concluded that each of the isomers of tetrachlorobenzene is not entering the environment in quantities or under conditions that may constitute a danger in Canada to human life or health.**

## 1.0 Introduction

The *Canadian Environmental Protection Act* (CEPA) requires the federal Ministers of the Environment and of Health to prepare and publish a Priority Substances List that identifies substances, including chemicals, groups of chemicals, effluents and wastes, that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess these substances and determine whether they are "toxic" as defined in section 11 of the Act which states:

"...a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions

- (a) having or that may have an immediate or long-term harmful effect on the environment;
- (b) constituting or that may constitute a danger to the environment on which human life depends; or
- (c) constituting or that may constitute a danger in Canada to human life or health."

Substances assessed as "toxic" according to section 11 may be placed on Schedule I of the Act, and considered for possible development of regulations, guidelines or codes of practice to control any aspect of their life cycle, from the research and development stage through manufacture, use, storage, transport and ultimate disposal.

The assessment of whether the priority substance tetrachlorobenzenes (comprising the isomers 1,2,4,5-, 1,2,3,5- and 1,2,3,4-tetrachlorobenzene) are "toxic", as defined under CEPA, was based on the determination of whether they **enter** or are likely to enter the Canadian environment in a concentration or quantities or under conditions that could lead to **exposure** of humans or other biota at levels that could cause adverse **effects**.

The assessment of whether tetrachlorobenzenes are "toxic" to human health under CEPA is based principally on documentation prepared by staff of Health Canada for the International Programme on Chemical Safety (IPCS). Between 1984 and 1987, original data relevant to the assessment of risks to health associated with exposure to the chlorinated benzenes (excluding hexachlorobenzene) were reviewed by staff of Health Canada in the preparation of a draft IPCS Environmental Health Criteria (EHC) Document. The current assessment has been updated and expanded to emphasize data most relevant to the assessment of the risks associated with exposure to tetrachlorobenzenes in the general environment in Canada. Since there were sufficient

data on each isomer, the potential health effects of each of the isomers have been addressed separately. The large uncertainty factors applied in the development of the tolerable daily intakes are sufficiently conservative to account for possible additive effects of the isomers. In addition, due to limitations of the available data, it is likely that exposure of the general population to these compounds in the environment in Canada has been overestimated.

In preparation of the IPCS document, a wide variety of scientific databases was searched to update information provided in earlier contractors' reports, including an annotated bibliography on the chlorobenzenes (excluding hexachlorobenzene) by Peter Strahlendorf (1978) and a criteria document on chlorobenzenes (including hexachlorobenzene) by Michael Holliday and Associates (1984a, 1984b). Additional information was identified during peer review of the draft EHC Document by IPCS focal points and a Task Group of Experts which met in June 1990. More recently, in February 1991, a search of ENVIROLINE, Chemical Abstracts, Pollution Abstracts, Environmental Bibliography, IRIS, MEDLINE and BIOSIS databases to identify recent data relevant to the assessment of the risks to the population of Canada in particular was conducted. Data relevant to assessment of whether tetrachlorobenzenes are "toxic" to human health obtained after completion of these sections of this report (i.e., June 1992) were not considered for inclusion.

Information considered relevant to the assessment of whether tetrachlorobenzenes are "toxic" to the environment was identified from on-line searches completed in November 1990 of ASFA, BIOSIS, CAB Abstracts, Chemical Abstracts, CESARS, CIS, ENVIROLINE, Hazardous Substances and IRPTC databases. A summary of information on the environmental toxicity, fate and levels of tetrachlorobenzenes in the Canadian environment, prepared under contract by Diane Koniecki (November 1991), was also consulted in the preparation of this report. Information relevant to the assessment of environmental effects obtained after March 1993 was not considered for inclusion.

Although review articles were consulted where considered appropriate, original studies that form the basis for the determination of "toxic" under CEPA were critically evaluated by staff of Health Canada (human exposure and effects on human health) and Environment Canada (entry and environmental effects). The following officials contributed to the preparation of the report:

A.M. Bobra (Environment Canada)  
D. Boersma (Environment Canada)  
L. Brownlee (Environment Canada)  
M. Giddings (Health Canada)  
R. Gomes (Health Canada)  
M.E. Meek (Health Canada)

B. Idris and R.G. Liteplo of Health Canada also contributed to the consolidation of the Assessment Report.

In this report, a synopsis that will appear in the *Canada Gazette* is presented. A summary of the technical information that is critical to the assessment, and which is presented in greater detail in unpublished Supporting Documentation, is presented in Section 2.0. The assessment of whether tetrachlorobenzenes are "toxic" as defined under CEPA is presented in Section 3.0.

As part of the review and approvals process established by Environment Canada, the environmental sections of this Assessment Report were reviewed by D. Muir (Department of Fisheries and Oceans), B. Oliver (Zenon Environmental Laboratories) and M. Rankin (Dow Chemical Canada Inc.). Sections related to the effects on human health were approved by the Standards and Guidelines Rulings Committee of the Bureau of Chemical Hazards of Health Canada. The entire Assessment Report was reviewed and approved by the Environment Canada/Health Canada CEPA Management Committee.

Copies of this Assessment Report and the unpublished Supporting Documentation are available upon request from the:

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## 2.0 Summary of Information Critical to Assessment of "Toxic"

### 2.1 Identity, Properties, Production and Uses

Tetrachlorobenzenes are cyclic aromatic hydrocarbons with 4 chlorine atoms substituted for hydrogen atoms in the benzene ring. They comprise 3 isomers: 1,2,4,5-tetrachlorobenzene (Chemical Abstract Service Registry Number (CAS No.) 95-94-3); 1,2,3,5-tetrachlorobenzene (CAS No. 634-90-2); and 1,2,3,4-tetrachlorobenzene (CAS No. 634-66-2). The melting points of 1,2,4,5-, 1,2,3,5- and 1,2,3,4-tetrachlorobenzene are 140<sup>0</sup>C, 54.5<sup>0</sup>C and 47.5<sup>0</sup>C, respectively (Mackay and Shiu, 1981). The solid phase vapour pressures (at 25<sup>0</sup>C) of 1,2,4,5-, 1,2,3,5- and 1,2,3,4-tetrachlorobenzene are 0.72 Pa, 9.8 Pa and 5.2 Pa, respectively (Weast, 1972-73; Mackay *et al.*, 1992). The solubilities (at 25<sup>0</sup>C) of 1,2,4,5-, 1,2,3,5- and 1,2,3,4-tetrachlorobenzene in water are 1.27, 3.6 and 7.8 mg/L, respectively (Mackay *et al.*, 1992), and the log octanol/water partition coefficient (log K<sub>ow</sub>) for all 3 isomers is 4.5 (Mackay *et al.*, 1992). Tetrachlorobenzenes absorb infrared radiation, including wavelengths in the 7 to 13 µm region (Sadler Research Laboratories, 1982). Unless otherwise specified, "tetrachlorobenzenes" refer to a mixture of the 3 isomers.

Tetrachlorobenzenes can be detected by gas chromatography with flame ionization, photo-ionization or electron capture detection, or by gas chromatography/mass spectrometry (Oliver and Nicol, 1984; Bosma *et al.*, 1988).

Tetrachlorobenzenes are not produced in Canada (Camford, 1991), and currently there is no domestic commercial demand for these substances. Less than 0.1 kg per year of pure tetrachlorobenzenes was imported from the United States for use as laboratory reagents (Statistics Canada, 1991; Environment Canada, 1992a). Formerly, tetrachlorobenzenes were used in combination with polychlorinated biphenyls (PCBs) in dielectric fluids for transformers and capacitors. However, after regulations prohibiting new uses of PCB-containing dielectric fluids were introduced in 1980 (*Canada Gazette*, 1980), the amount of tetrachlorobenzenes imported for this purpose declined considerably. Based on the results of a recent survey (Brien, 1992), small amounts of tetrachlorobenzenes (660 kg during the first 6 months of 1992) were still imported into Canada in dielectric fluids for use in transformer maintenance. In the United States, tetrachlorobenzenes are also used as intermediates in the production of fungicides, herbicides, defoliant and insecticides (U.S. EPA, 1980b).

## **2.2 Entry into the Environment**

There are no known natural sources of tetrachlorobenzenes. Based on recent estimates, up to 1.3 million kg of tetrachlorobenzenes are present in dielectric fluids currently in use in Canada, and up to 14 000 kg of tetrachlorobenzenes are in storage and destined for disposal by destruction (Environment Canada, 1991a). Since tetrachlorobenzenes may be formed as by-products or contaminants during the production of other chlorinated organic substances (including pentachlorobenzene, trichlorobenzenes, 1,1,1 - trichloroethane, carbon tetrachloride, trichloroethylene, perchloroethylene and ethylene dichloride [U.S. EPA, 1980b; Patty, 1981-1982]), they could enter the environment from releases of these compounds during their storage, use, transport or disposal. Estimates of the amounts of tetrachlorobenzenes in these chlorinated compounds were not identified.

Tetrachlorobenzenes have been identified in waste streams from pulp and paper mills, iron and steel mills, inorganic and organic chemical plants, a textile plant, petroleum refineries and activated sludge waste water treatment plants at concentrations ranging from not detected (detection limits ranged from 0.1 to 10 ng/L, depending upon the analytical technique) to 110 000 ng/L (Rankin, 1993; OME, 1990a, 1990b, 1991a, 1991b, 1991c, 1992a, 1992b; Merriman, 1988; King and Sherbin, 1986; Oliver and Nicol, 1982; Environment Canada, 1979). Concentrations were highest in effluents from pulp and paper mills, inorganic chemical plants and iron and steel mills.

No quantitative data on releases of tetrachlorobenzenes into the Canadian environment were identified; however, amounts released from the most likely sources were estimated and are summarized in Table I. On the basis of limited data, the 2 most significant sources of entry result from spillage of dielectric fluids and from long-range transport and deposition.

**Table 1**  
**Estimated Major Releases of Tetrachlorobenzenes**  
**into the Canadian Environment**

Sources	Releases kg/year
Tetrachlorobenzenes Released Due to Dielectric Fluid Spills (After Clean-up) <sup>a</sup>	1 200
Tetrachlorobenzenes Released from Dielectric Fluid Incineration <sup>b</sup>	133
Manufacture of Chlorinated Solvents <sup>c</sup>	
(Before April 1992)	(24-70)
(After April 1992)	none expected
Use of Chlorinated Solvents <sup>d</sup>	4
From Other Chlorinated Compounds	unknown
Degradation and Metabolism of Other Chlorinated Compounds <sup>e</sup>	unknown
Long Range Transport and Deposition <sup>f</sup>	1 016
Effluents from Activated Sludge Wastewater Treatment Plants, a Textile Plant, Pulp and Paper Mills, Iron and Steel Mills, Inorganic and Organic Chemical Plants and Petroleum Refineries <sup>g</sup>	greater than 28
From Landfill Sites <sup>h</sup>	greater than 1

- a. Based on 12 200 kg for a 10-year period and 67% removal from the initial spill due to recovery efforts (Menzies, 1992); of this total, 1 100 kg would be 1,2,3,4-tetrachlorobenzene and 100 kg would be 1,2,4,5-tetrachlorobenzene (Environment Canada, 1984). These estimates do not include fugitive releases which can be substantial (Western Research, 1991).
- b. Assumes a destruction efficiency of 99.99% (Dibbs, 1991); annual quantities not known. Assuming 100% release of tetrachlorobenzenes in one year.
- c. Before April 1992, approximately 24 to 70 kg were released annually from incineration of waste by-products (based on 1990 production figures [CPI, 1990a, 1990b, 1990c], emission factors by the U.S. EPA [Brooks and Hunt, 1984], and incineration efficiency of 99.99% [Environment Canada, 1991c, Jacoff *et al.*, 1986]). Since April 1992, chlorinated solvents were no longer produced in Canada other than in one plant in Ontario which manufactures carbon tetrachloride. No tetrachlorobenzenes are expected to be released into the environment from this source (ICI, 1993).
- d. Based on domestic demand in Canada (Camford, 1991) multiplied by an upper limit concentration of 1 mg/L, and assuming 10% release.
- e. Tetrachlorobenzenes can be released into the environment through the metabolism and degradation of other chlorinated compounds, such as lindane (Reed and Forgash, 1970; Karapally *et al.*, 1973; U.S. EPA, 1980b), pentachloronitrobenzene (Ware and Weast, 1977), gamma-pentachlorocyclohexane (U.S. EPA, 1980b) and pentachlorobenzene (Menzie, 1978).
- f. Transboundary entry from waste disposal sites (Oliver, 1984, 1985; Oliver and Kaiser, 1986) and in Canadian rainfall (Muir, 1993; Strachan, 1993) and snow (Welch *et al.*, 1991).
- g. Loadings from Ontario Iron and Steel Mills; for the other plants, loadings are unknown (Environment Canada, 1979; OME, 1990a, 1990b, 1991a, 1991b, 1991c, 1992a, 1992b; Rankin, (1993; Merriman, 1988; King and Sherbin, 1986).
- h. Loading from only one site (a chemical company landfill in Sarnia, Ontario, at which chlorinated solvents were disposed [King and Sherbin, 1986]).

## 2.3 Exposure-related Information

### 2.3.1 Fate

The fate of tetrachlorobenzenes in the environment is governed by transport processes such as volatilization and adsorption, and transformation processes such as photo-oxidation and aerobic biodegradation. Although tetrachlorobenzenes are removed from aerobic environments (e.g., air and surface water) by degradative processes, they persist and accumulate under anaerobic conditions in buried sediments and soils.

Based on their physical/chemical properties, it is anticipated that tetrachlorobenzenes released into the atmosphere will be distributed between air and water, with smaller amounts in soil and sediment (Mackay *et al.*, 1992). Wash-out from the atmosphere in rainwater also occurs (Muir, 1993; Strachan, 1993). Tetrachlorobenzenes can be photooxidized in the atmosphere, largely through reactions with photochemically-produced hydroxyl (OH) radicals (Atkinson, 1987; Howard *et al.*, 1991) with estimated half-lives ranging from 32 to 329 days for 1,2,4,5- and 1,2,3,4-tetrachlorobenzene (Howard *et al.*, 1991; Mackay *et al.*, 1992; Singleton, 1993), and up to 139 days for 1,2,3,5-tetrachlorobenzene (Singleton, 1993). These half-lives are sufficient to permit long-range transport. The presence of 1,2,4,5- and 1,2,3,4-tetrachlorobenzene in air masses over the Pacific Ocean (Atlas and Schaufli, 1990) indicate that these substances may be transported over long distances.

Based on their physical/chemical properties, tetrachlorobenzenes released into water are expected to adsorb to sediment and particulate matter (Kuntz and Warry, 1983; Oliver, 1987b, 1987c; Oliver and Nicol, 1984), with some volatilization to the atmosphere (Oliver, 1984; Oliver and Carey, 1986). The half-lives for volatilization of tetrachlorobenzenes from river water (1 m deep, flowing at 1 m/s at 20°C and with a wind velocity of 3 m/s) calculated according to the method described by Thomas (1982) are approximately 4.5 hours for all 3 isomers. In water, biodegradation appears to be the only significant biotransformation process of tetrachlorobenzenes (Howard *et al.*, 1991). The half-life of 1,2,4,5-tetrachlorobenzene in surface water was estimated to range from 28 to 417 days (Howard *et al.*, 1991; Mackay *et al.*, 1992); the half-life for the anaerobic biodegradation of 1,2,4,5-tetrachlorobenzene in deeper waters ranges from 120 to 720 days (Howard *et al.*, 1991; Mackay *et al.*, 1992). 1,2,4,5- and 1,2,3,4-Tetrachlorobenzene were not biodegraded after incubation in sewage sludge under anaerobic conditions for 32 days (Kirk *et al.*, 1989).

Tetrachlorobenzenes released to soil are expected to be persistent and immobile, based on their organic carbon sorption coefficients ( $K_{oc}$ ) which are greater than 100 (Kenaga, 1980). Half-lives in soil ranging from 28 to 417 days were estimated by Mackay *et al.* (1992) and Howard *et al.* (1991).

Based on their physical/chemical properties, tetrachlorobenzenes are expected to persist in sediment (Mackay *et al.*, 1992). Although tetrachlorobenzenes strongly adsorb to sediment, some can be removed by resuspension (Oliver, 1984, 1985; Oliver *et al.*, 1989) through biological activities, such as bioturbation (Karickhoff and Morris, 1985), or through desorption into pore water and subsequent diffusion into overlying water (Charlton, 1983; Oliver and Charlton, 1984). The half-life for the biodegradation of 1,2,4,5-tetrachlorobenzene in sediment was estimated to range from 56 to 1 250 days (Howard *et al.*, 1991; Mackay *et al.*, 1992). On the basis of an analysis of samples of core sediment obtained from Lake Ontario and a lake near Kenora, Ontario, tetrachlorobenzenes have been released into the environment for more than 60 years (Oliver and Nicol, 1982; Oliver, 1984; Durham and Oliver, 1983; Oliver *et al.*, 1989; Muir, 1993), without significant anaerobic degradation in sediment (Oliver and Nicol, 1983).

Bioaccumulation factors (whole-body) for tetrachlorobenzenes in fish range from 1 778 (fathead minnow, *Pimaphales promelas*) [Veith *et al.*, 1979] to 12 883 (rainbow trout, *Oncorhynchus mykiss*) [Oliver and Niimi, 1983]; bioaccumulation factors (lipid content) range from 14 125 (guppy, *Poecilla reticulata*) [Konemann and van Leeuwen, 1980] to 134 896 (rainbow trout, *Oncorhynchus mykiss*) [Oliver and Niimi, 1983]. A bioaccumulation factor for tetrachlorobenzenes of 84 000 has been reported for earthworms (*Eisenia andrei*) [Belfroid *et al.*, 1993]. Tetrachlorobenzenes from sediments can be available to benthic invertebrates. Concentrations of tetrachlorobenzenes in field populations of oligochaete worms and amphipods were related to levels in the sediments (Fox *et al.*, 1983). The accumulation of tetrachlorobenzenes by oligochaete worms from sediments in Lake Ontario in laboratory aquaria was demonstrated by Oliver (1987a). The extent of bioaccumulation from sediments appeared to be controlled by the concentration of tetrachlorobenzenes in sediment pore water rather than from ingestion of contaminated sediment particles (Oliver, 1987a; Markwell *et al.*, 1989). Although tetrachlorobenzenes are bioaccumulative compounds, no aquatic food chain magnification has been reported (Thomann, 1989; Oliver and Niimi, 1988).

Based on studies conducted in the Upper Great Lakes region of Ontario, air-plant concentration factors (air-lichen) for tetrachlorobenzenes range from  $1.4 \times 10^7$  to  $1.12 \times 10^8$  (Muir *et al.*, 1993). Though there is potential for the uptake of tetrachlorobenzenes by terrestrial plants through both roots and foliage, it is probably limited (Topp *et al.*, 1986; Trapp *et al.*, 1990).

### 2.3.2 Concentrations

Tetrachlorobenzenes have been detected in samples of ambient air, surface water, drinking water, sediment and biota in Canada. Data on concentrations in soil were limited to those determined at a single contaminated site. Data on the concentrations of tetrachlorobenzenes in indoor air, estuarine or marine waters in Canada were not identified.

Information on concentrations of the individual isomers of tetrachlorobenzene in ambient air in Canada has not been identified. The mean concentration of total tetrachlorobenzenes in samples of ambient air taken between August 1988 and October 1989 in Windsor, Ontario, was  $0.2 \text{ ng/m}^3$  (detected on all 32 days of sampling; detection limit =  $0.03 \text{ ng/m}^3$ ). In samples obtained between September 1988 and October 1989 at Walpole Island, the mean concentration was  $0.14 \text{ ng/m}^3$  (detected on 26 of 30 days of sampling) [Environment Canada, 1990]. The maximum concentration of tetrachlorobenzenes at Windsor and Walpole Island, Ontario, were  $0.44 \text{ ng/m}^3$  and  $0.31 \text{ ng/m}^3$  respectively (Environment Canada, 1990). The sampling locations in Windsor were located approximately 6 km from a municipal waste incinerator plant in Detroit, Michigan, while Walpole Island is a rural site located 55 km from the same plant. These concentrations are considerably less than those reported for 1,2,4,5- and 1,2,3,5-tetrachlorobenzene (combined) and 1,2,3,4-tetrachlorobenzene in samples of air obtained from 12 sites in Hamburg, Germany, between April 1986 and April 1987 ( $0.5$  to  $20.9 \text{ ng/m}^3$  and  $0.3$  to  $28.4 \text{ ng/m}^3$  respectively [Bruckmann *et al.*, 1988]). Information on concentrations of tetrachlorobenzenes or the individual isomers in indoor air in Canada (or elsewhere) was not identified.

The mean concentration of 1,2,4,5- and 1,2,3,4-tetrachlorobenzene in samples of rain collected from various locations across Canada between 1987 and 1991 was  $0.55$  and  $0.016 \text{ ng/L}$ , respectively; the levels ranged from  $0.32$  to  $0.78 \text{ ng/L}$  and from not detected (detection limit =  $0.01 \text{ ng/L}$ ) to  $0.19 \text{ ng/L}$ , respectively (Muir, 1993; Strachan, 1993).

Mean concentrations of tetrachlorobenzenes in samples of water collected from various lakes and rivers in Canada between 1980 and 1991 were less than  $4 \text{ ng/L}$  for both the 1,2,4,5- and 1,2,3,5-isomers, and less than  $15 \text{ ng/L}$  for the 1,2,3,4-isomer; the levels ranged from not detected (detection limits ranged from  $0.01$  to  $1 \text{ ng/L}$  depending upon the analytical technique) to  $21 \text{ ng/L}$ , for both the 1,2,4,5- and 1,2,3,5-isomers, and to  $125 \text{ ng/L}$  for the 1,2,3,4-isomer (Oliver and Nicol, 1982, 1984; Fox *et al.*, 1983; Oliver, 1984; Oliver and Charlton, 1984; Fox and Carey, 1986, 1989; Chan and Kohli, 1987; Biberhofer and Stevens, 1987; Carey and Fox, 1987; Merriman, 1988; Oliver and Niimi, 1988; Data Interpretation Group River Monitoring Committee, 1988, 1990; Stevens and Neilson, 1989; Muir, 1993). The maximum concentrations were highest in

samples of water collected in the early 1980s from the Niagara River (Carey and Fox, 1987; Oliver and Nicol, 1982) and Lake Ontario at the mouth of the Niagara River (Fox and Carey, 1986); however, concentrations have subsequently declined. The maximum concentration of 1,2,3,4-tetrachlorobenzene in samples of water collected from the Niagara River at Niagara-on-the-Lake during 1988 and 1989 was 1.08 ng/L (Data Interpretation Group River Monitoring Committee, 1990).

Available data on the levels of tetrachlorobenzenes in Canadian drinking water supplies are limited. 1,2,4,5-Tetrachlorobenzene was detected in the drinking water supplies of 3 cities bordering on Lake Ontario; concentrations ranged from not detected (detection limit = ~ 0.05 ppt [ng/L]) to 0.3 ppt (ng/L) and the mean concentration was 0.2 ppt (ng/L) [Oliver and Nicol, 1982]. In a survey of 602 samples of drinking water collected from 139 locations throughout the 4 Atlantic provinces between 1985 and 1988, 1,2,4,5-tetrachlorobenzene was detected (detection limit = 2 ng/L) in a single sample at a concentration of 3 ng/L (Environment Canada, 1989a, 1989b, 1989c, 1989d). 1,2,3,5-Tetrachlorobenzene was not detected (detection limit = ~ 0.05 ppt [ng/L]) in the drinking water supplies of 3 cities bordering on Lake Ontario (Oliver and Nicol, 1982), nor in a survey of 602 samples of drinking water collected from 139 locations in the 4 Atlantic provinces between 1985 and 1988 (detection limit = 2 ng/L) [Environment Canada, 1989a, 1989b, 1989c, 1989d]. 1,2,3,4-Tetrachlorobenzene was detected in the drinking water supplies of 3 cities bordering on Lake Ontario at concentrations ranging from 0.1 to 0.4 ppt (ng/L); the mean concentration was 0.3 ppt (ng/L) [Oliver and Nicol, 1982]. However, this isomer was not detected (detection limit = 2 ng/L) in a survey of 602 samples of drinking water collected from 139 locations in the Atlantic provinces between 1985 and 1988 (Environment Canada, 1989a, 1989b, 1989c, 1989d).

The concentration of tetrachlorobenzenes in samples of surficial sediments collected from various lakes and rivers in Canada between 1979 and 1991 ranged from not detected (detection limits ranged from 0.2 to 2 ng/g, depending upon the analytical technique) to 7 000 ng/g (dry weight) [Environment Canada, 1979; Oliver and Nicol, 1982; Fox *et al.*, 1983; Oliver and Charlton, 1984; Oliver and Bourbonniere, 1985; Oliver and Pugsley, 1986; Merriman, 1987; Oliver and Niimi, 1988; Oliver *et al.*, 1989; Fox and Carey, 1989; Kaiser *et al.*, 1990; Welch *et al.*, 1991; OME, 1993]. The mean concentrations were less than 10 ng/g (dry weight), with the exception of the levels in samples collected from Lake Ontario, the St. Clair River and sites near point sources. Concentrations were highest in samples collected in 1985 from the St. Clair River near a waste disposal site at a chemical plant, and an effluent outfall from an industrial area of Sarnia; the level of total tetrachlorobenzenes ranged from 17 to 7 000 ng/g (data on individual isomers were not available). The concentration of 1,2,4,5- and 1,2,3,5-tetrachlorobenzene in samples collected from the St. Clair River in 1990 ranged from not detected to 1 140 ng/g and 510 ng/g, respectively; 1,2,3,4-tetrachlorobenzene was not detected (Oliver and Pugsley, 1986; OME, 1993).

The level of tetrachlorobenzenes in suspended sediments collected from various locations in southern Ontario and Quebec between 1980 and 1989 ranged from not detected (detection limits ranged from 0.2 to 5 ng/g, depending upon analytical technique) to 320 ng/g (dry weight) [Fox *et al.*, 1983; Kuntz and Warry, 1983; Oliver and Charlton, 1984; Sylvestre, 1987; Merriman, 1987, 1988; Oliver and Niimi, 1988; Data Interpretation Group River Monitoring Committee, 1988, 1990; Fox and Carey, 1989; Oliver *et al.*, 1989; Kaiser *et al.*, 1990]. Concentrations of tetrachlorobenzenes were highest in samples obtained in 1981 from the Niagara River at Niagara-on-the-Lake; for 1,2,4,5- and 1,2,3,4-tetrachlorobenzene the levels ranged up to 160 ng/g (dry weight) and 320 ng/g (dry weight), respectively (Sylvestre, 1987).

Information on the concentration of tetrachlorobenzenes in soil was limited to a single study in which tetrachlorobenzenes were detected in samples of soil collected at a depth of 0 to 3 m, near a transformer manufacturing facility where dielectric fluids had been spilled; the concentrations ranged from not detected (detection limit = 3 ng/g) to 6 300 ng/g (dry weight) [NRCC, 1980].

The concentration of 1,2,4,5-, 1,2,3,5- and 1,2,3,4-tetrachlorobenzene in samples of biota collected from various lakes and rivers in Canada between 1980 and 1991 ranged from less than 0.01 ng/g (wet weight) up to 46.2, 0.5 and 28.6 ng/g (wet weight), respectively (Oliver and Nicol, 1982; Oliver and Niimi, 1983, 1988; Fox *et al.*, 1983; Jaffe and Hites, 1986; Niimi and Oliver, 1989; Metcalfe and Charlton, 1990; Muir, 1993). The concentration of tetrachlorobenzenes in aquatic invertebrates collected from Lake Ontario (near the mouth of the Niagara River) ranged from less than 0.01 to 46.2 ng/g (wet weight) for 1,2,4,5-tetrachlorobenzene, from 0.06 to 0.5 ng/g (wet weight) for 1,2,3,5-tetrachlorobenzene, and from less than 0.01 to 28.6 ng/g (wet weight) for 1,2,3,4-tetrachlorobenzene (Fox *et al.*, 1983; Oliver and Niimi, 1988). The concentration of tetrachlorobenzenes in lichens collected from Ontario was less than 1 ng/g (wet weight) [Muir *et al.*, 1993].

The concentration of tetrachlorobenzenes in various species of upper trophic level fish obtained in 1980 from lakes Superior, Huron, Erie and Ontario ranged from 0.2 to 5 ng/g (wet weight) for 1,2,4,5-tetrachlorobenzene, from 0.05 to 1 ng/g (wet weight) for 1,2,3,5-tetrachlorobenzene, and from 0.5 to 12 ng/g (wet weight) for 1,2,3,4-tetrachlorobenzene; the highest levels were in fish obtained from Lake Ontario near the Niagara River (Oliver and Nicol, 1982). The concentrations of tetrachlorobenzenes in various species of lake-dwelling fish collected in northwestern Ontario during 1990 and 1991 were relatively low (i.e., < 1 ng/g [wet weight]) [Muir, 1993].

Between the early 1980s and 1990, the mean concentrations of 1,2,4,5- and 1,2,3,4-tetrachlorobenzene in herring gull (*Larus argentatus*) eggs collected from the Niagara and Detroit rivers have declined from 20 and 53 ng/g (wet weight), respectively, to 1 ng/g (i.e., the detection limit) for both isomers (Bishop *et al.*, 1992). Tetrachlorobenzenes are included in the routine monitoring of chlorinated organic compounds in wildlife by Environment Canada and were detected in approximately 20% to 30% of the samples collected in 1990 and 1991. Concentrations were rarely above 2 ng/g (detection limits ranged from 0.1 to 2.0 ng/g), except in samples collected from known contaminated areas (such as pulp mills on the Columbia River in British Columbia) in which levels ranged from 1 ng/g (detection limit) to 37.4 ng/g (wet weight) [Environment Canada, 1992b]. The mean concentrations of 1,2,4,5-tetrachlorobenzene in eggs from bald eagles (*Haliaeetus leucocephalus*) and osprey (*Pandion haliaetus*), and in samples of liver from mink (*Mustela vison*) and otter (*Lutra canadensis*) from this contaminated area were 3.3, 6.2 and 2.4 ng/g, respectively; the mean concentration of 1,2,3,4-tetrachlorobenzene in these tissues was less than 1 ng/g. Concentrations of 1,2,4,5- and 1,2,3,4-tetrachlorobenzene in samples of arctic char, and blubber from narwhal and beluga were less than 1 and 10 ng/g (wet weight), respectively (Muir, 1993).

Available data on concentrations of the individual isomers of tetrachlorobenzene in food are limited. 1,2,4,5-, 1,2,3,5- and 1,2,3,4-Tetrachlorobenzene were not detected in a limited survey of fresh food composites (leafy vegetables, fruit, 2% cows' milk, root vegetables [including potatoes] and eggs/meat) obtained in Ontario (detection limit = 0.01 ng/g) [Davies, 1988]. Food composites were prepared from samples obtained in 4 retail grocery stores and analysed for all 3 isomers. The concentration of 1,2,4,5-tetrachlorobenzene in trout (whole fish) obtained from 5 sites in the Great Lakes ranged from 0.2 ppb (ng/g) [detection limit] to 5 ppb (ng/g) [wet weight]; reported concentrations of 1,2,3,5-tetrachlorobenzene ranged from 0.05 to 1 ppb (ng/g), and concentrations of 1,2,3,4-tetrachlorobenzene ranged from 0.3 to 12 ppb [ng/g] (detection limit = 0.2 ppb [ng/g]) [Oliver and Nicol, 1982]. In a market basket survey conducted by the U.S. Food and Drug Administration, the concentration of tetrachlorobenzenes ranged from 0.1 ng/g in mixed canned vegetables to 0.4 ng/g in garden fruit (Johnson *et al.*, 1984; Prodrebarac, 1984; Gunderson, 1987).

1,2,4,5-, 1,2,3,5- and 1,2,3,4-Tetrachlorobenzene were not detected in samples of breast milk from the general (n = 210) and indigenous (n = 18) populations of Canada obtained 3 to 4 weeks after parturition (detection limit was not unspecified) [Mes *et al.*, 1986; Davies and Mes, 1987]. In a recent unpublished survey, 1,2,4,5-, 1,2,3,5- and 1,2,3,4-tetrachlorobenzene were detected in 0%, 36% and 37% of 412 samples of breast milk from Canadian women, respectively (minimum detectable levels ranged from 0.3 to 1.2 ng/g) [Mes, 1992]. The mean and maximum concentrations of 1,2,3,5- and 1,2,3,4-tetrachlorobenzene were 0.3 and 2.1 ng/g, and

0.2 and 1.7 ng/g, respectively. These mean concentrations are about an order of magnitude lower than those reported in a survey of breast milk obtained from women in Yugoslavia (Jan, 1983).

## 2.4 Effects-related Information

### 2.4.1 Experimental Animals and In Vitro

Data on the acute toxicity of the tetrachlorobenzenes are restricted to studies in which the compounds were administered orally. LD<sub>50</sub>s for 1,2,4,5-, 1,2,3,5- and 1,2,3,4-tetrachlorobenzenes in male Sprague-Dawley rats were 3 105, 2 297 and 1 470 mg/kg bw, respectively; in females, LD<sub>50</sub>s were 1 727 and 1 167 mg/kg bw for 1,2,3,5- and 1,2,3,4-tetrachlorobenzene, respectively (Chu *et al.*, 1983, 1984b).

In the most extensive short-term study completed to date, the administration of diets containing each of the isomers of tetrachlorobenzene [at concentrations of 0, 0.5, 5.0, 50 or 500 ppm [mg/kg] (0, 0.056, 0.54, 5.4 or 54 mg/kg bw/day)] to rats for 28 days produced no clinical signs of toxicity or effects on body weight gain or food consumption; however, dose-dependent effects in the liver, thyroid, kidney and lungs were observed in exposed animals (Chu *et al.*, 1983). 1,2,4,5-Tetrachlorobenzene was the most toxic isomer; concentrations were highest in fat and liver. The relative toxicity of the tetrachlorobenzenes, which correlated with concentrations in tissues, was 1,2,4,5-tetrachlorobenzene > 1,2,3,4-tetrachlorobenzene or 1,2,3,5-tetrachlorobenzene.

In a study in which rats were administered diets containing 1,2,4,5-tetrachlorobenzene (at concentrations of 0, 30, 100, 300, 1 000 or 3 000 ppm [mg/kg] [up to 287 mg/kg bw/day] for 14 days, compound-related clinical changes were observed in the high-dose group; food consumption and mean body weights were decreased, and liver weights increased at the highest dose levels, compared to controls; abnormal hyaline droplets in the renal cortical epithelium of exposed males were also observed (NTP 1991). The administration of diets containing 0, 30, 100, 300, 1 000 or 3 000 ppm (mg/kg) 1,2,4,5-tetrachlorobenzene to mice (dose on a body weight basis not reported) for 14 days produced mortality in all animals in the highest dose group; significant increases in liver weights at the high doses and depletion and necrosis of lymphoid tissue of the spleen, thymus, and lymph nodes in both sexes, particularly in early death or moribund animals were also observed (NTP, 1991).

The longest term studies of adequate design conducted to date for each of the tetrachlorobenzenes are sub-chronic studies in which the compounds were administered in the diet. F344 rats and B6C3F<sub>1</sub> mice were administered diets containing 0, 30, 100, 300, 1 000 or 2 000 ppm (mg/kg) 1,2,4,5-tetrachlorobenzene (mixed in 1% corn oil) for 13 weeks (NTP, 1991). In exposed rats, body weights were

reduced, and compound-related clinical symptoms, histopathological changes in the liver and haematological effects were observed in the highest dose groups, compared to unexposed controls. Increased kidney and liver weights, and histopathological effects in the kidney and thyroid were observed in animals exposed to lower levels of 1,2,4,5-tetrachlorobenzene. The spectrum of renal lesions observed in male rats was characterized by "hyaline droplet nephropathy". Compared to unexposed controls, decreased levels of free thyroxine and total thyroxine in the serum, indicative of a primary hypothyroid state, were observed in rats of both sexes which were administered lower levels of 1,2,4,5-tetrachlorobenzene. The no-observed-effect-level (NOEL) for histopathological effects in both sexes was 30 ppm (mg/kg) 1,2,4,5-tetrachlorobenzene in the diet (i.e., NOEL = 2.1 mg/kg bw/day) [NTP, 1991]. Although no effects were observed in males which were administered 30 ppm (mg/kg) 1,2,4,5-tetrachlorobenzene in the diet, there was a significant increase in the relative but not absolute liver weight and concentration of thyroxine in the serum in females at this level. Therefore, 30 ppm (mg/kg) 1,2,4,5-tetrachlorobenzene in the diet is considered the no-observed-adverse-effect-level (NOAEL) in this sex (i.e., NOAEL = 2.1 mg/kg bw/day).

In the study in which B6C3F<sub>1</sub> mice were administered diets containing 0, 30, 100, 300, 1 000 or 2 000 ppm (mg/kg) 1,2,4,5-tetrachlorobenzene (mixed in 1 % corn oil) for 13 weeks, compound-related clinical changes, decreased body weights and food consumption, increased liver weights and circulating hepatic enzymes, and haematological effects were observed in animals exposed to the higher concentrations; histopathological changes in the liver included centrilobular hepatocellular hypertrophy and necrosis of individual hepatocytes (NTP, 1991). The NOEL for histopathological effects in both sexes was considered by the National Toxicology Program to be 300 ppm (mg/kg) [i.e., NOEL = 45.2 mg/kg bw/day (males); 56.6 mg/kg bw/day (females)] (NTP 1991). However, in view of the minor effects observed at lower concentrations (a significant increase in absolute but not relative liver weights in females at concentrations as low as 30 ppm (mg/kg), and in both in males at 100 ppm [mg/kg]), 300 ppm (mg/kg) 1,2,4,5-tetrachlorobenzene in the diet is considered a NOAEL for both sexes (i.e., NOAEL = 45.2 mg/kg bw/day [males], 56.6 mg/kg bw/day [females]).

In a study in which rats were administered diets containing each of the isomers of tetrachlorobenzene (at concentrations of 0, 0.5, 5.0, 50 or 500 ppm [mg/kg]) for a period of 90 days, increased organ weights and effects on haematological parameters were observed in animals receiving diets containing 500 ppm (mg/kg) 1,2,4,5-tetrachlorobenzene, compared to controls (Chu *et al.*, 1984a). Dose dependent increases in the severity and incidence of histopathological changes in the kidney (extensive epithelial necrosis with large intratubular casts at 500 ppm (mg/kg) for 1,2,4,5-tetrachlorobenzene) and liver (accentuation of zonation, increase in cytoplasmic homogeneity, aggravated basophilia, anisokaryosis and pyknotic nuclei)

were also observed (Chu *et al.*, 1984a). The 1,2,4,5-isomer was the most toxic of the tetrachlorobenzenes, likely due to its relatively slower metabolism and greater accumulation in fat and liver<sup>1</sup>. In animals which were administered diets containing 1,2,3,5- or 1,2,3,4-tetrachlorobenzene, the renal lesions were considered moderate even at the highest dose levels, and histopathological effects in the liver, although similar to those caused by the 1,2,4,5-tetrachlorobenzene, were less severe.

In the study conducted by Chu *et al.* (1984a) the statistical significance of the incidence of the renal and hepatic histopathological lesions was not addressed; however, based on subsequent statistical analysis by the one sided Fisher's exact test, there were no significant increases in the incidence of renal lesions, though there appeared to be an increase in severity with increasing dose, particularly in animals exposed to 1,2,4,5-tetrachlorobenzene in the diet. The incidence of hepatic lesions was increased significantly ( $p = 0.05$ ) only in males and females exposed to 500 ppm (mg/kg) 1,2,4,5-tetrachlorobenzene and in females exposed to 500 ppm (mg/kg) 1,2,3,5-tetrachlorobenzene. The severity of the histopathological effects in the liver was greatest in these groups. The NOAEL in rats administered 1,2,4,5-tetrachlorobenzene is, therefore, considered to be 50 ppm (mg/kg) in the diet (i.e., NOAEL = 3.4 mg/kg bw/day [males]; 4.1 mg/kg bw/day [females]). In male and female rats administered 1,2,3,5-tetrachlorobenzene, the NOAEL is considered to be 500 ppm and 50 ppm (mg/kg), respectively (i.e., NOAEL = 34 mg/kg bw/day [males]; 4.1 mg/kg bw/day [females]). In male and female rats administered 1,2,3,4-tetrachlorobenzene, the NOAEL is considered to be 500 ppm (mg/kg) [i.e., NOAEL = 34 mg/kg bw/day (males), 41 mg/kg bw/day (females)].

One limited study (in which beagle dogs were administered 1,2,4,5-tetrachlorobenzene in the diet) on the chronic toxicity of the tetrachlorobenzenes has been identified (Braun *et al.*, 1978). However, this study is inadequate for the assessment of chronic toxicity or carcinogenicity owing to several limitations including small group sizes, no concurrent control group and lack of examination of urinary, haematological or clinical chemistry parameters, or the conduct of histopathological examinations.

Investigations of the reproductive effects of tetrachlorobenzenes have not been identified. The results of available studies on the embryotoxicity, foetotoxicity and teratogenicity of tetrachlorobenzenes are limited to a study in rats in which all 3 isomers were administered (Kacew *et al.*, 1984) and additional investigations in rats

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1. The toxicokinetics of the isomers of tetrachlorobenzene have been investigated in several species (rats, rabbits, monkeys, beagle dogs) following oral administration (Schwartz *et al.*, 1985, 1987; Chu *et al.*, 1983, 1984b; Braun *et al.*, 1978; Jondorf *et al.*, 1958). Available data indicate that 1,2,4,5-tetrachlorobenzene is not significantly metabolized and accumulates in tissues (primarily fat) to a greater extent than either 1,2,3,5- or 1,2,3,4-tetrachlorobenzene (Chu *et al.*, 1983, 1984b; Jondorf *et al.*, 1958).

involving the 1,2,4,5- and 1,2,3,4-isomers (Kitchin and Ebron, 1983a, 1983b). None of the isomers was teratogenic in these studies. Generally, each of the isomers was foetotoxic only at doses which were toxic to the mothers; however, the administration of 200 mg/kg bw/day 1,2,3,5- or 1,2,3,4-tetrachlorobenzene to rats produced a reduction in the number of live foetuses without adverse effects on the dams (Kacew *et al.*, 1984). [These doses were higher than those reported to induce adverse effects in sub-chronic studies].

Based on limited available data on mutagenicity in *S. typhimurium* and *E. coli* with and without metabolic activation, and effects on chromosomes in Chinese Hamster ovary cells exposed *in vitro*, tetrachlorobenzenes (mixed and the 1,2,4,5- and 1,2,3,5-isomers) do not appear to be genotoxic.

#### 2.4.2 Humans

Case reports of adverse effects in individuals exposed to tetrachlorobenzenes were not identified. In one epidemiological study, there was an increase in chromosomal aberrations in peripheral lymphocytes of workers employed in a pesticide manufacturing complex producing 1,2,4,5-tetrachlorobenzene, compared to 14 workers minimally exposed to chemicals and 49 individuals from the local community (Kiraly *et al.*, 1979).

#### 2.4.3 Ecotoxicology

The acute and chronic toxicity of the tetrachlorobenzenes have been studied in several aquatic species; however, data concerning the toxicity of these compounds to any other biota including sediment- and soil-dwelling organisms, terrestrial invertebrates, aquatic vascular plants, birds or wild mammals were not identified.

In aquatic organisms, the tetrachlorobenzenes have a common mode of toxic action (i.e., narcosis) [Veith *et al.*, 1983; Bobra *et al.*, 1985; Abernathy *et al.*, 1986].

In acute toxicity studies, bacteria and algae were exposed to various levels of tetrachlorobenzenes (Hutchinson *et al.*, 1980; U.S. EPA, 1980a; Ribo and Kaiser, 1983; Wong *et al.*, 1984; Blum and Speece, 1991). The lowest identified effect levels were for the marine alga (*Skeletonema costatum*) exposed to 1,2,3,5-tetrachlorobenzene, 96-hour EC<sub>50</sub>s of 830 µg/L (for chlorophyll a) and 700 µg/L (for cell numbers) have been reported (U.S. EPA, 1980a). Reproductive effects were the most sensitive end-point identified for the water flea (*Daphnia magna*), following exposure to 90 µg/L 1,2,3,4-tetrachlorobenzene; the corresponding 16-day no-observed-effect-concentration (NOEC) [for reproductive and growth effects] was 55 µg/L (DeWolf *et al.*, 1988).

Following the acute exposure of fish to 1,2,3,4-tetrachlorobenzene, lethality was the most sensitive end-point identified with a 96-hour LC<sub>50</sub> of 365 µg/L reported for the guppy (*Poecilia reticulata*) [van Hoogen and Opperhuizen, 1988]. van Leeuwen *et al.* (1990) reported a chronic 28-day LC<sub>50</sub> of 410 µg/L for zebra fish (*Brachydanio rerio*) exposed to 1,2,3,4-tetrachlorobenzene; the corresponding 28-day NOEC (inhibition of growth) was 100 µg/L. A 33-day NOEC of 250 µg/L was reported for the fathead minnow (Carlson and Kosian, 1987). Following the exposure of early life stage American flagfish (*Jordanella floridae*) to 1,2,4,5-tetrachlorobenzene, the 28-day maximum acceptable tolerance concentration (MATC) for fry growth and survival were 85 µg/L and 138 µg/L, respectively (Smith *et al.*, 1991).

## 3.0 Assessment of "Toxic" under CEPA

### 3.1 CEPA 11(a): Environment

Tetrachlorobenzenes are not produced in Canada, and currently there is no domestic commercial demand for these substances. On the basis of limited information, the 2 most significant sources of entry of these substances into the Canadian environment result from spillage of dielectric fluids and from long-range transport and deposition.

Tetrachlorobenzenes have been detected in air, surface water, rain, sediment and biota within Canada. They are removed from air and surface water by degradation processes but can persist under anaerobic conditions in buried sediments and soils.

Differences between effects thresholds for organisms exposed to the different isomers of tetrachlorobenzene are typically small, and since the mode of action for their toxic effects is similar (i.e., narcosis), effects of exposure to mixtures of tetrachlorobenzene isomers can be considered to be additive. Thus, exposure of biota was estimated by summing environmental concentrations reported for the 3 tetrachlorobenzene isomers. Estimated effects thresholds were based on data for the isomer with the lowest observed adverse effect level.

The lowest identified chronic effect level for freshwater organisms is 90 µg/L 1,2,3,4-tetrachlorobenzene for the water flea (*Daphnia magna*) [16-day EC<sub>50</sub> for reduced reproduction]. Dividing this value by a factor of 10 to account for interspecies sensitivity, to extrapolate laboratory results to field conditions and to convert the chronic lowest effect level to a chronic no effect level, results in an estimated effects threshold of 9.0 µg/L. The highest total concentration of the 3 isomers of tetrachlorobenzene in surface waters in Canada (i.e., 146 ng/L in a sample collected from Lake Ontario near the mouth of the Niagara River in 1982), is approximately 62 times less than the estimated effects threshold. Based on more recent data, the concentration of tetrachlorobenzenes in surface waters in Canada (i.e., a maximum concentration of 1.08 ng/L 1,2,3,4-tetrachlorobenzene detected in samples of water collected in 1988 and 1989 from the Niagara River), is approximately 8 500 times less than the estimated effects threshold. Therefore, no adverse effects are expected to result from exposure of aquatic organisms to tetrachlorobenzenes in Canadian surface waters.

Benthic organisms are exposed to tetrachlorobenzenes in sediments in the Canadian Great Lakes and their connecting channels, the St. Lawrence River, Hawk and Far lakes in the Northwest Territories, and Abercrombie Point and Truro in Nova Scotia. However, no toxicological data that would permit estimation of an effects threshold for these biota were identified. Similarly, because of the lack of information on ambient concentrations and effects in soils, it is not possible to determine whether soil-dwelling organisms are adversely affected by exposure to the levels of tetrachlorobenzenes present in Canada.

The potential for adverse effects to wildlife resulting from exposure to tetrachlorobenzenes has been evaluated based on a "worst case" scenario involving the multimedia exposure of mink (*Mustela vison*), a terrestrial mammal having a diet consisting in part of aquatic prey. A daily intake of 420 ng/kg bw/day was estimated for mink living in the area near the mouth of the Niagara River where the levels of tetrachlorobenzenes in Canadian waters were the highest (Table 2). The uptake of tetrachlorobenzenes from air and water is negligible compared to that from food. In the absence of identified data on the effects on wildlife, the estimated effects threshold for mink exposed to 1,2,4,5-tetrachlorobenzene was based on the results of a sub-chronic study in which rats were exposed orally to this isomer (NTP, 1991). In this study, the NOAEL was considered to be 2.1 mg/kg bw/day (based on thyroid follicular cell hypertrophy observed at higher doses). Dividing this value by a factor of 10 (to account for interspecies differences and to extrapolate from the laboratory to the field), results in an estimated effects threshold of 210 µg/kg bw/day. The estimated total daily intake of tetrachlorobenzenes by mink is approximately 500 times less than the estimated effects threshold. Thus, no adverse effects are expected to result from exposure of mammalian wildlife to levels of tetrachlorobenzenes present in Canada.

**Table 2**  
**Estimated Worst-case Total Daily Exposure of a Piscivorous Mammal**  
**around the Niagara Region, Ontario**

Exposure Route	Environmental Levels <sup>a</sup>	Daily Rate of Consumption (per kg-bw) <sup>b</sup>	Daily Intake (ng/kg bw/day)
Air	0.31 ng/m <sup>3</sup>	0.55 m <sup>3</sup>	0.17
Surface Water	1.08ng/L	0.1 L	0.11
Biota (Fish)	2.71 ng/g	155 g	420
Total	-	-	420

- a. The level in air is the maximum level measured in a rural environment (Walpole Island, Ontario) between 1988 and 1989 (Environment Canada, 1990); the level in surface water is the maximum concentration of 1,2,3,4-tetrachlorobenzene (the most abundant isomer) in samples of water obtained from Niagara-on-the-Lake between 1988 and 1989 (Data Interpretation Group River Monitoring Committee, 1990); the level in fish is that predicted based on a log bioaccumulation factor of 3.4 for fathead minnow, a trophic level 3 fish, and the maximum level of 1,2,3,4-tetrachlorobenzene in surface water.
- b. Inhalation rate from Stahl (1967); drinking rate from Calder and Braun (1983); and ingestion rate from Nagy (1987), assuming a diet of 75% fish.

**Although, on the basis of available data, the levels of tetrachlorobenzenes present in Canadian surface waters are not expected to cause adverse effects in aquatic biota or wildlife, adequate data upon which to evaluate the significance of exposure in sediment and soil were not identified. Therefore, there is insufficient information to conclude whether tetrachlorobenzenes are entering the environment in quantities or under conditions that may be harmful to the environment.**

### **3.2 CEPA 11(b): Environment on Which Human Life Depends**

Although tetrachlorobenzenes are present as gases in the troposphere and absorb infrared radiation in wavelengths ranging from 7 to 13  $\mu\text{m}$ , their low rate of release and relatively rapid removal from the atmosphere by photooxidation (half-lives ranging from 32 to 329 days) and precipitation result in low concentrations in the atmosphere (i.e.,  $<0.01 \mu\text{g}/\text{m}^3$ ). As such, tetrachlorobenzenes are not expected to contribute significantly to global warming or depletion of stratospheric ozone.

**Therefore, on the basis of available data, it has been concluded that tetrachlorobenzenes are not entering the environment in quantities or under conditions that may constitute a danger to the environment on which human life depends.**

### **3.3 CEPA 11(c): Human Life or Health**

Identified data on the exposure of the general population and potential health effects were sufficient to permit assessments for each of the isomers of tetrachlorobenzene. Uncertainty factors applied in the development of tolerable daily intakes for each of the isomers are also sufficiently conservative to account for possible additive effects of the isomers. In addition, due to limitations of the available data, it is likely that exposure of the general population to these compounds in the environment in Canada has been overestimated.

#### *Population Exposure*

The limitations of available information on concentrations of the individual isomers of the tetrachlorobenzenes in environmental media are such that estimates of exposure must be considered to be highly uncertain (Tables 3 to 5). For example, data on concentrations of the individual isomers of tetrachlorobenzene in ambient air in Canada were not identified and it was necessary, therefore, to calculate intake from this medium for each of the isomers on the basis of total tetrachlorobenzene concentrations determined at Windsor and Walpole Island (Environment Canada, 1990); intake from air, therefore, most likely has been overestimated. It has also been assumed that concentrations of the individual isomers of tetrachlorobenzene in indoor air are similar to those in ambient air owing to a lack of identification of relevant data. Moreover, the estimates of intake of each of the isomers in food are based principally on a small study of a limited number of food composites in which they were not detected (Davies, 1988). Intake from this source has been calculated, therefore, on the basis of detection limits and is likely overestimated. In addition, the intake of 1,2,4,5-tetrachlorobenzene in breast milk for suckling infants has been calculated on the basis of the results of a Canadian survey in which it was not detected (Mes, 1992) so that intake of this isomer from this source (calculated based on detection limits) is probably also overestimated. The calculated intake of 1,2,3,5-tetrachlorobenzene from drinking water was also based on a small survey of samples from 3 cities bordering on Lake Ontario in which it was not detected, leading to probable overestimation of exposure (calculated on the basis of detection limits) from this source.

**Table 3**  
**Estimated Daily Intake ( $\mu\text{g}/\text{kg}$ ) of 1,2,4,5-Tetrachlorobenzene by**  
**Canadians from Various Sources**

Medium	Estimated Intake $\mu\text{g}/\text{kg}$ bw/day				
	0-6 mo <sup>a</sup>	7 mo-4 yr <sup>b</sup>	5-11 yr <sup>c</sup>	12-19 yr <sup>d</sup>	20-70 yr <sup>e</sup>
Ambient Air <sup>f</sup>	0.00004- 0.00006	0.00005- 0.00008	0.00006- 0.00009	0.00005- 0.00007	0.00005- 0.00007
Drinking Water <sup>g</sup>	-	0.00001- 0.0002	0.000007- 0.0001	0.000005- 0.00007	0.000004- 0.00006
Breast Milk <sup>h</sup>	<0.13	-	-	-	-
Food <sup>i</sup>	-	<0.0003- <0.0007	<0.0002- <0.0004	<0.0001- <0.0002	<0.00007- <0.0002
Total Intake <sup>j</sup>	<0.13	<0.0004- <0.001	<0.0003- <0.0006	<0.0002- <0.0003	<0.0001- <0.0003

- a. Assumed to weigh 7 kg, breathe 2 m<sup>3</sup> air per day, and drink 750 mL of breast milk (as food) per day (Environmental Health Directorate, 1992).
- b. Assumed to weigh 13 kg, breathe 5 m<sup>3</sup> air per day, and drink 0.8 L of water per day (Environmental Health Directorate, 1992).
- c. Assumed to weigh 27 kg, breathe 12 m<sup>3</sup> air per day, and drink 0.9 L of water per day (Environmental Health Directorate, 1992).
- d. Assumed to weigh 57 kg, breathe 21 m<sup>3</sup> air per day, and drink 1.3 L of water per day (Environmental Health Directorate, 1992).
- e. Assumed to weigh 70 kg, breathe 23 m<sup>3</sup> air per day, and drink 1.5 L of water per day (Environmental Health Directorate, 1992).
- f. Based on a range of mean atmospheric concentrations of total tetrachlorobenzenes (0.00014 - 0.0002  $\mu\text{g}/\text{m}^3$ ) measured at Walpole Island, Ontario, and Windsor, Ontario, assuming that concentrations in indoor air are similar to those in ambient air (Environmental Health Directorate, 1992). Though concentrations of 1,2,4,5- and 1,2,3,5-tetrachlorobenzene (combined) have been determined in ambient air in Hamburg, Germany (Bruckmann *et al.*, 1988), mean values were, in some cases, considerably higher than those reported in Canada for total tetrachlorobenzenes and were not considered suitable, therefore, for incorporation into these estimates of exposure.
- g. Based on a range of concentrations of 1,2,4,5-tetrachlorobenzene in Canadian drinking water of 0.0002  $\mu\text{g}/\text{L}$  (mean value in Oliver and Nicol, 1982) to 0.003  $\mu\text{g}/\text{L}$  (detected in one sample in Environment Canada, 1989a, 1989b, 1989c, 1989d).
- h. Based on the maximum value of the range of minimum detection limits (1.2  $\mu\text{g}/\text{kg}$ ) for the tetrachlorobenzenes in breast milk from Canadian mothers (1,2,4,5-tetrachlorobenzene was not detected) [Mes, 1992], assuming the density of breast milk is equal to 1.0 g/mL.
- i. Estimated daily intake from food based on levels in milk, eggs and meat, fish, leafy and root vegetables, and fruit (Davies, 1988; Oliver and Nicol, 1982) and intake of these foodstuffs by each age group (Environmental Health Directorate, 1992).
- j. Data were insufficient to estimate intake from soil.

**Table 4**  
**Estimated Daily Intake ( $\mu\text{g}/\text{kg}$ ) of 1,2,3,5-Tetrachlorobenzene by**  
**Canadians from Various Sources**

Medium	Estimated Intake $\mu\text{g}/\text{kg}$ bw/day				
	0-6 mo <sup>a</sup>	7mo-4 yr <sup>b</sup>	5-11 yr <sup>c</sup>	12-19 yr <sup>d</sup>	20-70 yr <sup>e</sup>
Ambient Air <sup>f</sup>	0.00004- 0.00006	0.00005- 0.00008	0.00006- 0.00009	0.00005- 0.00007	0.00005- 0.00007
Drinking Water <sup>g</sup>	-	<0.000003	<0.000002	<0.000001	<0.000001
Breast Milk <sup>h</sup>	0.03	-	-	-	-
Food <sup>i</sup>	-	<0.0003- <0.0004	<0.0002	<0.0001	<0.00007- <0.00009
Total Intake <sup>j</sup>	0.03	<0.0004- <0.0005	<0.0003	<0.0002	<0.0001- <0.0002

- a. Assumed to weigh 7 kg, breathe 2 m<sup>3</sup> air per day, and drink 750 mL of breast milk (as food) per day (Environmental Health Directorate, 1992).
- b. Assumed to weigh 13 kg, breathe 5 m<sup>3</sup> air per day, and drink 0.8 L of water per day (Environmental Health Directorate, 1992).
- c. Assumed to weigh 27 kg, breathe 12 m<sup>3</sup> air per day, and drink 0.9 L of water per day (Environmental Health Directorate, 1992).
- d. Assumed to weigh 57 kg, breathe 21 m<sup>3</sup> air per day, and drink 1.3 L of water per day (Environmental Health Directorate, 1992).
- e. Assumed to weigh 70 kg, breathe 23 m<sup>3</sup> air per day, and drink 1.5 L of water per day (Environmental Health Directorate, 1992).
- f. Based on a range of mean atmospheric concentrations of total tetrachlorobenzenes (0.00014- 0.0002  $\mu\text{g}/\text{m}^3$ ) measured at Walpole Island, Ontario, and Windsor, Ontario, assuming that concentrations in indoor air are similar to those in ambient air (Environmental Health Directorate, 1992). Though concentrations of 1,2,4,5- and 1,2,3,5-tetrachlorobenzene (combined) have been determined in ambient air in Hamburg, Germany (Bruckmann *et al.*, 1988), mean values were, in some cases, considerably higher than those reported in Canada for total tetrachlorobenzenes and were not considered suitable, therefore, for incorporation into these estimates of exposure.
- g. Based on a concentration of 1,2,3,5-tetrachlorobenzene in Canadian drinking water of 0.00005  $\mu\text{g}/\text{L}$  (limit of detection in Oliver and Nicol, 1982). 1,2,3,5-Tetrachlorobenzene was also not detected in a recent survey of a large number of samples in the Atlantic provinces (Environment Canada, 1989a, 1989b, 1989c, 1989d), but the detection limit (0.002  $\mu\text{g}/\text{L}$ ) was considerably higher than that reported by Oliver and Nicol (1982).
- h. Based on the mean concentration (0.3  $\mu\text{g}/\text{kg}$ ) of 1,2,3,5-tetrachlorobenzene in breast milk from Canadian mothers (Mes, 1992), assuming the density of breast milk is equal to 1.0 g/mL.
- i. Estimated daily intake from food based on levels in milk, eggs and meat, fish, leafy and root vegetables, and fruit (Davies, 1988; Oliver and Nicol, 1982) and intake of these foodstuffs by each age group (Environmental Health Directorate, 1992).
- j. Data were insufficient to estimate intake from soil.

**Table 5**  
**Estimated Daily Intake ( $\mu\text{g}/\text{kg}$ ) of 1,2,3,4-Tetrachlorobenzene by**  
**Canadians from Various Sources**

Medium	Estimated Intake $\mu\text{g}/\text{kg}$ bw/day				
	0-6 mo <sup>a</sup>	7 mo- 4 yr <sup>b</sup>	5-11 yr <sup>c</sup>	12-19 yr <sup>d</sup>	20-70 yr <sup>e</sup>
Ambient Air <sup>f</sup>	0.00004- 0.00006	0.00005- 0.00008	0.00006- 0.00009	0.00005- 0.00007	0.00005- 0.00007
Drinking Water <sup>g</sup>	-	0.00002	0.00001	0.000007	0.000006
Breast Milk <sup>h</sup>	0.02	-	-	-	-
Food <sup>i</sup>	-	<0.0003- <0.001	<0.0002- <0.0007	<0.0001- <0.0003	<0.00007- <0.0003
Total Intake <sup>j</sup>	0.02	<0.0004- <0.001	<0.0003- <0.0008	<0.0002- <0.0004	<0.0001- <0.0004

- a. Assumed to weigh 7 kg, breathe 2 m<sup>3</sup> air per day, and drink 750 mL of breast milk (as food) per day (Environmental Health Directorate, 1992).
- b. Assumed to weigh 13 kg, breathe 5 m<sup>3</sup> air per day, and drink 0.8 L of water per day (Environmental Health Directorate, 1992).
- c. Assumed to weigh 27 kg, breathe 12 m<sup>3</sup> air per day, and drink 0.9 L of water per day (Environmental Health Directorate, 1992).
- d. Assumed to weigh 57 kg, breathe 21 m<sup>3</sup> air per day, and drink 1.3 L of water per day (Environmental Health Directorate, 1992).
- e. Assumed to weigh 70 kg, breathe 23 m<sup>3</sup> air per day, and drink 1.5 L of water per day (Environmental Health Directorate, 1992).
- f. Based on a range of mean atmospheric concentrations of total tetrachlorobenzenes of 0.00014 - 0.0002  $\mu\text{g}/\text{m}^3$  measured at Walpole Island, Ontario, and Windsor, Ontario, assuming that concentrations in indoor air are similar to those in ambient air (Environmental Health Directorate, 1992). Though concentrations of 1,2,3,4-tetrachlorobenzene have been determined in Hamburg, Germany (Bruckmann *et al.*, 1988), mean values were, in some cases, considerably higher than those reported in Canada for total tetrachlorobenzenes and were not considered suitable, therefore, for incorporation into these estimates of exposure.
- g. Based on a concentration of 1,2,3,4-tetrachlorobenzene in Canadian drinking water of 0.0003  $\mu\text{g}/\text{L}$  (mean value in Oliver and Nicol, 1982). 1,2,3,4-Tetrachlorobenzene was not detected in a recent survey of a large number of samples in the Atlantic provinces (Environment Canada, 1989a, 1989b, 1989c, 1989d), however, the detection limit was relatively high (0.002  $\mu\text{g}/\text{L}$ ) in comparison to the mean concentration reported by Oliver and Nicol (1982).
- h. Based on the mean concentration of 1,2,3,4-tetrachlorobenzene (0.2  $\mu\text{g}/\text{kg}$ ) in breast milk from Canadian mothers (Mes, 1992), assuming the density of breast milk is equal to 1.0 g/mL.
- i. Estimated daily intake from food based on levels in milk, eggs and meat, fish, leafy and root vegetables, and fruit (Davies, 1988; Oliver and Nicol, 1982) and intake of these foodstuffs by each age group (Environmental Health Directorate, 1992).
- j. Data were insufficient to estimate intake from soil.

On the basis of the limited available information, however, it is likely that the general population in Canada is exposed to the tetrachlorobenzenes principally in food (breast milk for suckling infants). The estimated total daily intakes for various age groups in the population (older than 6 months of age) for each of the isomers of tetrachlorobenzene are as follows: 1,2,4,5-tetrachlorobenzene: <0.0001 to <0.001 µg/kg bw/day; 1,2,3,5-tetrachlorobenzene: <0.0001 to < 0.0005 µg/kg bw/day; 1,2,3,4-tetrachlorobenzene: <0.0001 to < 0.001 µg/kg bw/day. Based on the concentrations in breast milk, the total intake for suckling infants aged 0 to 6 months are as follows: 1,2,4,5-tetrachlorobenzene: <0.13 µg/kg bw/day; 1,2,3,5-tetrachlorobenzene: 0.03 µg/kg bw/day; 1,2,3,4-tetrachlorobenzene: 0.02 µg/kg bw/day.

### **Effects**

Available data on the toxicity of the tetrachlorobenzenes are limited. Epidemiological studies of exposed populations are limited and information on chronic toxicity or carcinogenicity in adequate studies in experimental animals has not been identified. None of the tetrachlorobenzenes (mixed and the 1,2,4,5- and 1,2,3,5-isomers) was genotoxic in *in vitro* studies of a very limited range of end-points, though clastogenic effects in an occupationally-exposed population have been associated with exposure to 1,2,4,5-tetrachlorobenzene in a single epidemiological study (Kiraly *et al.*, 1979). All 3 tetrachlorobenzenes (1,2,4,5-, 1,2,3,5- and 1,2,3,4-isomers) have been classified, therefore, in Group V (inadequate data for evaluation) of the classification scheme for carcinogenicity developed for use in the derivation of the “Guidelines for Canadian Drinking Water Quality” (Environmental Health Directorate, 1989).

With the exception of one inadequate chronic study on the effects of 1,2,4,5-tetrachlorobenzene in dogs (Braun *et al.*, 1978), the longest term studies of the effects of the tetrachlorobenzenes are sub-chronic investigations. Sub-chronic studies in which the tetrachlorobenzenes have been administered by the principal route of exposure of the general population (i.e., oral) have been identified for all 3 isomers.

#### *1,2,4,5-tetrachlorobenzene*

For 1,2,4,5-tetrachlorobenzene, the lowest doses at which compound-related effects were observed in the 2 available sub-chronic bioassays which both involved dietary administration of the compound (mixed in corn oil and added to the diet) were similar. In male and female F344 rats in the NTP bioassay, the NOAEL was 2.1 mg/kg bw/day, based on thyroid follicular cell hypertrophy observed at higher doses (NTP, 1991). In the study by Chu *et al.* (1984a), the NOAELs in male and female Sprague-Dawley rats were 3.4 and 4.1 mg/kg bw/day, respectively, based on effects on haematological parameters and a significant increase in the incidence of histopathological lesions of

the liver at the next highest dose. (Hepatic and renal lesions were also more severe at the highest dose.) On the basis of the lowest of these values, a tolerable daily intake (TDI) is conservatively (owing to the paucity of available data) derived as follows:

$$\begin{aligned} \text{TDI} &= \frac{2.1 \text{ mg/kg bw/day}}{10\,000} \\ &= 0.00021 \text{ mg/kg bw per day (0.21 } \mu\text{g/kg bw per day)} \end{aligned}$$

where:

- 2.1 mg/kg bw/day is the lowest NOAEL or LOAEL in adequate sub-chronic studies conducted to date (NOEL in males and NOAEL in female F344 rats in the sub-chronic bioassay conducted by NTP (1991))
- 10 000 is the uncertainty factor (x 10 for intraspecies variation; x 10 for interspecies variation; x 10 for less than chronic study; x 10 for limited database including lack of adequate data on carcinogenicity and chronic and reproductive toxicity)

In developmental studies in which 1,2,4,5-tetrachlorobenzene was administered by gavage, it did not induce adverse effects at concentrations below those upon which the TDI derived above is based (Kitchin and Ebron, 1983b; Kacew *et al.*, 1984).

The total daily intake of 1,2,4,5-tetrachlorobenzene for various age groups in the Canadian population is estimated to range from <0.0001 to < 0.13  $\mu\text{g/kg bw/day}$ . It should be noted, however, that these estimates of intake are highly uncertain and are, most likely, greater than actual values owing to the incorporation of data on concentrations of total tetrachlorobenzenes in ambient air in Canada (Environment Canada, 1990), the lack of data on concentrations of tetrachlorobenzenes in indoor air, the estimation of intake in food being based principally on the lack of detection of the individual isomers in a limited study of food composites in Ontario (Davies, 1988), and the reliance on data from a Canadian survey of breast milk in which the 1,2,4,5-isomer was not detected (Mes, 1992), necessitating calculation on the basis of detection limits.

The estimated average daily intakes (though based on limited data) for various age groups of the Canadian population are from 1.6 to > 2 100 times less than the TDI derived above, on the basis of a very conservative uncertainty factor (i.e., 10 000). It should also be noted, though, that with the exception of breast-fed infants whose intakes are elevated for only a short period of their lifespan, and for which the intake is probably overestimated owing to calculation on the basis of the detection limits in a Canadian survey in which 1,2,4,5-tetrachlorobenzene was not detected in breast milk, the calculated average daily intakes (which are also likely overestimated owing to limitations of the data) are from 210 to > 2 100 times less than the TDI.

**Therefore, on the basis of currently available data, it has been concluded that 1,2,4,5-tetrachlorobenzene is not entering the environment in quantities or under conditions that may constitute a danger in Canada to human life or health.**

*1,2,3,5-tetrachlorobenzene*

For 1,2,3,5-tetrachlorobenzene, the lowest dose at which compound-related effects were observed in the only sub-chronic bioassay identified for this isomer in which this compound was administered orally (mixed with corn oil in the diet) to Sprague-Dawley rats was approximately 41 mg/kg bw/day; at this dose, there was a significant increase in the incidence of histopathological lesions in the liver in female rats (Chu *et al.*, 1984a). (Hepatic lesions were also more severe at this dose.) Based on the NOAEL in female rats observed in this study (4.1 mg/kg bw/day), a TDI is conservatively (owing to the paucity of available data) derived as follows:

$$\begin{aligned} \text{TDI} &= \frac{4.1 \text{ mg/kg bw/day}}{10\,000} \\ &= 0.00041 \text{ mg/kg bw per day (0.41 } \mu\text{g/kg bw per day)} \end{aligned}$$

where:

- 4.1 mg/kg bw/day is the lowest NOAEL in the only sub-chronic study conducted to date (NOAEL in female rats in study conducted by Chu *et al.* [1984a]);
- 10 000 is the uncertainty factor (x 10 for intraspecies variation; x 10 for interspecies variation; x 10 for less than chronic study; x 10 for limited database including lack of adequate data on carcinogenicity and chronic and reproductive toxicity).

In developmental studies in which 1,2,3,5-tetrachlorobenzene was administered by gavage, it did not induce adverse effects at concentrations below those upon which the TDI derived above is based (Kacew *et al.*, 1984).

The total daily intake of 1,2,3,5-tetrachlorobenzene for various age groups in the Canadian population is estimated to range from < 0.0001 to 0.03  $\mu\text{g/kg bw/day}$ . It should be noted, however, that these estimates of intake are highly uncertain and are, most likely, greater than actual values owing to the incorporation of data on concentrations of total tetrachlorobenzenes in ambient air in Canada (Environment Canada, 1990), the lack of data on concentrations of tetrachlorobenzenes in indoor air, the estimation of intake in food being based principally on the lack of detection of the individual isomers in a limited study of food composites in Ontario (Davies, 1988), and the estimation of intake from water being based on a small survey of samples from 3 cities on Lake Ontario in which it was not detected (Oliver and Nicol, 1982), necessitating calculation on the basis of detection limits.

The estimated average daily intakes (though based on limited data) for various age groups in the Canadian population are from 13.7 to > 4 100 times less than the TDI derived above, on the basis of a very conservative uncertainty factor (i.e., 10 000). It should also be noted, though, that with the exception of breast-fed infants whose intakes are elevated for only a short period of their lifespan, the calculated average daily intakes (which are likely overestimated owing to limitations of the data) are from 820 to > 4 100 times less than the TDI.

**Therefore, on the basis of currently available data, it has been concluded that 1,2,3,5-tetrachlorobenzene is not entering the environment in quantities or under conditions that may constitute a danger in Canada to human life or health.**

#### *1,2,3,4-tetrachlorobenzene*

For 1,2,3,4-tetrachlorobenzene, significant compound-related effects were not observed at any dose in the only sub-chronic bioassay identified for this isomer in which the compound was administered orally (mixed with corn oil in the diet) to Sprague-Dawley rats (i.e., NOAEL = 34 mg/kg bw/day [males]; 41 mg/kg bw/day [females]) [Chu *et al.*, 1984a]. On the basis of the lower of these values, a TDI is conservatively (owing to the paucity of available data) derived as follows:

$$\begin{aligned} \text{TDI} &= \frac{34 \text{ mg/kg bw/day}}{10\,000} \\ &= 0.00034 \text{ mg/kg bw per day (3.4 } \mu\text{g/kg bw per day)} \end{aligned}$$

where:

- 34 mg/kg bw/day is the lowest NOAEL or LOAEL in the only sub-chronic study conducted to date (NOAEL in male rats in study conducted by Chu *et al.* [1984a]);
- 10 000 is the uncertainty factor (x 10 for intraspecies variation; x 10 for interspecies variation; x 10 for less than chronic study; x 10 for limited data base including lack of adequate data on carcinogenicity and chronic and reproductive toxicity).

In developmental studies in which 1,2,3,4-tetrachlorobenzene was administered by gavage, it did not induce adverse effects at concentrations below those upon which the TDI derived above is based (Kitchin and Ebron, 1983a; Kacew *et al.*, 1984).

The total daily intake of 1,2,3,4-tetrachlorobenzene for various age groups in the Canadian population is estimated to range from <0.0001 to 0.02  $\mu\text{g/kg bw/day}$ . It should be noted, however, that these estimates of intake are highly uncertain and are, most likely, greater than actual values owing to the incorporation of data on concentrations of total tetrachlorobenzenes in ambient air in Canada (Environment Canada, 1990), the lack of data on concentrations of tetrachlorobenzenes in indoor air,

and the estimation of intake in food being based principally on the lack of detection of the individual isomers in a limited study of food composites in Ontario (Davies, 1988), necessitating calculations on the basis of the detection limits.

The calculated average daily intakes (which are likely to be overestimated owing to limitations of the available data) are from 170 to > 34 000 times less than the TDI derived above, on the basis of a very conservative uncertainty factor (i.e., 10 000).

**Therefore, on the basis of currently available data, it has been concluded that 1,2,3,4-tetrachlorobenzene is not entering the environment in quantities or under conditions that may constitute a danger in Canada to human life or health.**

### **3.4 Conclusion**

**Based on available data, there is insufficient information to conclude whether tetrachlorobenzenes are entering the environment in quantities or under conditions that may be harmful to the environment. It has been concluded that tetrachlorobenzenes are not entering the environment in quantities or under conditions that may constitute a danger to the environment on which human life depends. It has been concluded that each of the isomers of tetrachlorobenzene is not entering the environment in quantities or under conditions that may constitute a danger in Canada to human life or health.**

## 4.0 Recommendations

To enable an assessment of the environmental effects of tetrachlorobenzenes, it is recommended that the following additional data be acquired on a high priority basis:

- (i) concentrations of tetrachlorobenzenes in soil and sediment, particularly near point sources; and
- (ii) toxicity tests (chronic and acute) with benthic organisms representative of those in the Canadian environment to determine the effects of tetrachlorobenzenes associated with sediment.

In addition, to permit a more complete assessment of the exposure of the general population in Canada to tetrachlorobenzenes, additional monitoring data are desirable, particularly for indoor (all isomers) and ambient (individual isomers) air and food (all isomers). Investigations of the chronic toxicity, carcinogenicity and reproductive toxicity of all of the tetrachlorobenzenes in laboratory animals exposed by ingestion are also required to permit a more complete assessment of the toxicity of these compounds. The priority for this research is considered to be moderate.

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