

Canadian Environmental Protection Act

Priority Substances List Assessment Report

1,1,2,2-Tetrachloroethane



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PRIORITY SUBSTANCES LIST ASSESSMENT REPORT

1,1,2,2-TETRACHLOROETHANE

Government of Canada Environment Canada Health and Welfare Canada

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Synopsis

1,1,2,2-Tetrachloroethane is not produced in, or imported into, Canada. 1,1,2,2-Tetrachloroethane enters the Canadian environment as a by-product in wastes generated during production of both vinyl chloride monomer and ethylene dichloride, in air emissions and leachates from waste disposal sites, and as a result of long-range atmospheric transport from other countries.

The highest concentrations of 1,1,2,2-tetrachloroethane that have been found in Canadian ambient surface waters are at least 180 times less than the estimated effects threshold for flagfish, the most sensitive aquatic species identified in long-term studies. Given the large difference between the estimated effects threshold and ambient water concentrations, no adverse effects are expected to result from exposure of freshwater organisms to 1,1,2,2-tetrachloroethane. However, as most 1,1,2,2-tetrachloroethane is released to the atmosphere and reliable data on effects to terrestrial organisms are unavailable, it is not possible to conclude whether current concentrations of 1,1,2,2-tetrachloroethane in air will adversely affect terrestrial biota in Canada.

Because of the low rate of release of 1,1,2,2-tetrachloroethane to the atmosphere, the low atmospheric concentration, and a calculated ozone depletion potential of much less than 0.001 relative to chlorofluorocarbon-l 1 (CFC-l 1), 1,1,2,2-tetrachloroethane is not expected to contribute significantly to stratospheric ozone depletion or to global warming.

Based on estimation of the total daily intake from ambient and indoor air and drinking water for various age groups of the general population, air appears to be the most significant source of human exposure to 1,1,2,2-tetrachloroethane. However, data from available studies in exposed human populations and experimental animals are considered inadequate to estimate a Tolerable Daily Intake, *i.e.*, the daily intake to which it is believed that a person may be exposed over a lifetime without deleterious effects. As a result, it is not possible to determine if current concentrations of this substance in the environment are likely to have adverse effects on human life or health in Canada.

Based on these considerations, the Minister of the Environment and the Minister of National Health and Welfare have concluded that the concentrations of 1,1,2,2-tetrachloroethane present in the Canadian environment do not constitute a danger to the environment on which human life depends. Therefore, 1,1,2,2-tetrachloroethane is not considered to be "toxic" as defined under Paragraph 11 (b) of the *Canadian Environmental Protection Act*. The Ministers have determined that available data are inadequate to conclude whether 1,1,2,2-tetrachloroethane constitutes a danger in Canada to the environment or to human life or health as defined under Paragraphs 11 (a) and 11 (c) of the *Canadian Environmental Protection Act*.

1.0 Introduction

The Canadian Environmental Protection Act (CEPA) requires the Minister of the Environment and the Minister of National Health and Welfare 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 under 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 that are assessed as "toxic" as defined under Section 11 of the Act may be placed on the List of Toxic Substances in Schedule I of CEPA (Subsection 33(1)). Consideration can then be given to developing guidelines, codes of practice, or regulations necessary to control any aspect of these substances' life cycle, including manufacture, use, storage, transport, and ultimate disposal.

The assessment of whether 1,1,2,2-tetrachloroethane is "toxic", as defined under CEPA, was based on the determination of whether it **enters** or is 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**.

Published data relevant to the assessment of whether 1,1,2,2-tetrachloroethane is "toxic" to the environment were obtained through on-line searches conducted in June, 1992 of the following commercial databases: Aquatic Sciences and Fisheries Abstracts (ASFA), BIOSIS, CHEMICAL ABSTRACTS, ENVIROLINE, International Register of Potentially Toxic Chemicals (IRPTC), Science Citation Index (SCI), and TOXLINE. In addition; trade information was voluntarily supplied by the chlorinated solvents industry. Data on Canadian sources, use patterns, and levels of 1,1,2,2-tetrachloroethane were emphasized. Data relevant to the environmental assessment of 1,1,2,2-tetrachloroethane obtained after January 1993 were not considered for inclusion.

To identify toxicological data relevant to the preparation of the human health-related sections of the assessment, in April 1992, literature searches were conducted on the computerized databases TOXLINE [MEDLINE, BIOSIS, and

National Technical Information Service (NTIS)], TOXLIT, EMBASE, Hazardous Substances Data Bank (HSDB), Registry of Toxic Effects of Chemical Substances (RTECS), Integrated Risk Information System (IRIS), Chemical Carcinogenesis Research Information System (CCRIS), Environmental Bibliography, ENVIROLINE, POLLUTION ABSTRACTS, Environment Canada Departmental Library Catalogue (ELIAS), AQUAREF, Canadian Research Index (MICROLOG), and the Cooperative Documents Project (CODOC). In addition, computer literature searches were conducted biweekly on the MEDLINE and TOXLINE databases to identify any references incorporated since April 1992. Data obtained after the period of peer review (i.e., September 1992) were not considered in the preparation of the health-related sections of this report.

A review of available toxicological and epidemiological data on 1,1,2,2-tetrachloroethane published by the Agency for Toxic Substances and Disease Registry (1989) and a background report on toxicokinetics and health effects prepared under contract by Global-Tox International Corporation in September 1991, were consulted in the preparation of this report.

All original scientific studies that form the basis for determining whether 1,1,2,2-tetrachloroethane is "toxic" under CEPA were critically evaluated by the following Environment Canada staff (entry, exposure, and effects on the environment) and Health and Welfare Canada staff (human exposure and effects on human health):

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T. Dann	I. Caldwell
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K. Lloyd	
L. Shutt	

In this report, an overview of findings concerning 1,1,2,2-tetrachloroethane that will appear in the *Canada Gazette* is presented. Section 2.0 is an extended summary of the technical information that is critical to the assessment. This information is presented in greater detail in supporting documentation that is available upon request. The assessment of "toxic" under CEPA is presented in Section 3.0.

As part of the review and approvals process established by Environment Canada, the environmental portions of the Assessment Report were reviewed by Dr. P. Cammer (Cammer and Associates), Dr. D. Muir (Fisheries and Oceans), Dr. D. Singleton (National Research Council Canada), and Dr. K. Woodburn (Dow Chemical Canada Inc.). Sections related to the assessment of human exposure and health effects were peer reviewed by Dr. J. Domoradzki (Dow Chemical Company, U.S., supporting documentation only), Dr. R. Bull (Washington State University, U.S.), and BIBRA Toxicology International, U.K., and subsequently approved by the Standards and Guidelines Rulings Committee of the Bureau of Chemical Hazards of Health and

Welfare Canada. The final Assessment Report was reviewed and approved by the Environment Canada/Health and Welfare Canada CEPA Management Committee.

Copies of this Assessment Report and the unpublished supporting documentation are available upon request from:

Commercial Chemicals Branch Environment Canada 14th Floor, Place Vincent Massey 351 St. Joseph Blvd Hull, Quebec K1A 0H3 Environmental Health Centre Health and Welfare Canada Room 104 Tunney's Pasture Ottawa, Ontario K1A 0L2

2.0 Summary of Information Critical to Assessment of "Toxic"

2.1 Identity, Properties, Production, and Uses

- 1,1,2,2-Tetrachloroethane (CAS # 79-34-5) is a colourless, nonflammable liquid at room temperature, having the molecular formula $\text{Cl}_2\text{CHCHCI}_2$ (Verschueren, 1983). It is a highly volatile, synthetic chemical having a relatively high vapour pressure (0.65 kPa at 20°C) and water solubility (2900 mg/L at 20°C), and low partition coefficients (log K_{oc} = 1.66 and log K_{ow} = 2.39) (Verschueren, 1983; Chiou *et al.*, 1979; Hansch and Leo, 1985).
- 1,1,2,2-Tetrachloroethane is produced by direct chlorination or oxychlorination of ethylene and is not usually purified but rather is used as an intermediate in the production of other chlorinated compounds (Archer, 1979). This chemical is detected and quantified in environmental samples by gas chromatography using either electron capture or mass spectrometric detectors.
- 1,1,2,2-Tetrachloroethane has not been produced in Canada since early 1985 (CPI, 1991a). At that time, 1,1,2,2-tetrachloroethane was manufactured at a facility in Shawinigan, Quebec for use as an intermediate in the production of trichloroethylene and tetrachloroethylene. These latter two substances have not been manufactured in Canada since 1986 and 1992, respectively (CPI, 1990; Dow Chemical Canada News Release, 1992)

Globally, 1,1,2,2-tetrachloroethane is used primarily as a feedstock in the production of tri- and tetra-chloroethylene (Archer, 1979). Small amounts of 1,1,2,2-tetrachloroethane are also used as specialty solvents.

2.2 Entry into the Environment

Since 1,1,2,2-tetrachloroethane is no longer produced in, or imported into Canada (CPI, 1991a), it is unlikely that any additional entry of this substance to the Canadian environment will occur through its production and use.

The manufacture of other chlorinated hydrocarbons, specifically vinyl chloride monomer (VCM), ethylene dichloride (EDC), and methyl chloroform, also generates detectable quantities of 1,1,2,2-tetrachloroethane as a by-product (U.S. EPA, 1981) and represents an indirect source of 1,1,2,2-tetrachloroethane release to the environment.

There is only one Canadian manufacturer of VCM and EDC, with plants located in Fort Saskatchewan, Alberta and in Sarnia, Ontario. Based on a Canadian VCM and EDC production of 416.8 and 922 kt, respectively, for 1990 (CPI, 1991b; CPI, 1991c), and a waste-to-product ratio of 0.008 (Tsang and Bisson, 1992), the total waste generated by these plants would be 10.7 kt. An analysis of the combined liquid waste streams from both the VCM plant and the EDC plant revealed a 1,1,2,2-tetrachloroethane content of 23% by weight, or 2.5 kt of 1,1,2,2- tetrachloroethane (Tsang and Bisson, 1992). These waste products are usually treated to recover the organic compounds present and then

incinerated (McPherson *et al.*, 1979). Since there is no market for 1,1,2,2-tetrachloroethane, however, no recovery process for 1,1,2,2-tetrachloroethane is undertaken (Dow Chemical Canada Inc., 1992). Assuming an incineration destruction efficiency of 99.99% (U.S. EPA, 1986), approximately 0.246 t (or 246 kg) of 1,1,2,2-tetrachloroethane from VCM and EDC wastes are emitted to the atmosphere every year.

Waste materials from the manufacture of methyl chloroform also contain small amounts of 1,1,2,2-tetrachloroethane. Estimates of quantities released from this source are not available; however, as of June 1992, methyl chloroform is no longer manufactured in Canada (Dow Chemical Canada Inc., 1992).

1,1,2,2-Tetrachloroethane has also been found to enter the environment in air emissions and leachates from waste disposal sites (Lesage *et al.*, 1990; Ghassemi *et al.*, 1984; Harkov *et al.*, 1985; Shah and Singh, 1988). Furthermore, 1,1,2,2-tetrachloroethane may be entering the Canadian environment by long- range atmospheric transport from other countries that continue to produce tri- and tetra-chloroethylene, vinyl chloride, and ethylene dichloride (SRI, 1988) and release 1,1,2,2-tetrachloroethane as a by-product (see Subsection 2.3.1). The contribution of these sources to the total release of 1,1,2,2-tetrachloroethane to the Canadian environment could not be estimated.

2.3 Exposure-related Information

2.3.1 *Fate*

Based on its vapour pressure, 1,1,2,2-tetrachloroethane is expected to exist entirely in the vapour phase in ambient air (Verschueren, 1983; Eisenreich *et al.*, 1981). The principal removal process of 1,1,2,2-tetrachloroethane from the troposphere is expected to be photo-oxidation (Singh *et al*, 1982), although studies of competing fate processes have not been identified.

The calculated reaction rates of 1,1,2,2-tetrachloroethane with hydroxyl (OH) radicals derived from the Structure-Activity Relations (SAR) model of Atkinson (1987) [3 x 10⁻¹³ cm³/(mol·s)] and from the model of Nimitz and Skaggs (1992) [5.4 x 10⁻¹³ cm³/(mol·s)] are similar to the experimental value determined by Qiu *et al.* (1992) [2.3 x 10⁻¹³ cm³/(mol·s)]. Therefore, using these reaction rates and assuming an atmospheric OH concentration representative of a moderately polluted area, the estimated atmospheric lifetime of 1,1,2,2-tetrachloroethane is between 43_{calculated} and 100_{experimental} days (Finlayson-Pitts and Pitts, 1986). Since the atmospheric lifetime of 1,1,2,2-tetrachloroethane is greater than one month, there is potential for long-range transport (LRT) of this compound. Further evidence of long-range transport is provided in a 1985 monitoring study by Class and Ballschmiter (1986) who detected 1,1,2,2-tetrachloroethane in the lower troposphere over the northern Atlantic Ocean.

In the stratosphere, 1,1,2,2-tetrachloroethane undergoes photolysis to produce chlorine radicals that may react with ozone (Callahan *et al*, 1979; Spence and Hanst, 1978). However, a simple method developed by Nimitz and Skaggs (1992), indicates

that 1,1,2,2-tetrachloroethane is not expected to contribute significantly to the depletion of the stratospheric ozone layer. Based on either the experimental (Qiu *et al.*, 1992) or predicted (Atkinson, 1987; Nimitz and Skaggs, 1992) rates of reaction between OH and 1,1,2,2-tetrachloroethane, the ozone depletion potential (ODP) for 1,1,2,2-tetrachloroethane is very much less than 0.001 relative to the chlorofluorocarbon, CFC- 11.

Volatilization is the major removal process of 1,1,2,2-tetrachloroethane from the aquatic environment (Dilling *et al.*, 1975; Lyman *et al.*, 1982). Based on a calculated Henry's Law constant of 47.6 Pa (Mackay and Shiu, 1981) and a modeling scenario representing a 1-m deep river flowing 1 m/s with a wind speed of 3 m/s at 25 °C (Mackay and Leinonen, 1975), the volatilization half-life of 1,1,2,2-tetrachloroethane was estimated to be 6.2 hours (Lyman *et al.*, 1982).

Neither hydrolysis nor biodegradation is considered a significant removal process for 1,1,2,2-tetrachloroethane at concentrations found in ambient surface waters; however, on the basis of experimental data, hydrolysis and biodegradation play a role in removing 1,1,2,2-tetrachloroethane from groundwater (Hallen *et al.*, 1986; Haag and Mill, 1988; Agency for Toxic Substances and Disease Registry, 1989). When the hydrolysis rate was measured under experimental conditions similar to groundwater (e.g., higher ionic strength), the half-lives at pH 6.05, 7.01, and 9.0 were reported to be 573 days, 36 days, and 6.6 to 12.8 hours, respectively (Haag and Mill, 1988). Six weeks of simulated anaerobic growing conditions of landfills resulted in the dechlorination of 1,1,2,2-tetrachloroethane to lesser chlorinated ethanes and to chloroethenes including vinyl chloride (Hallen *et al.*, 1986). Since anaerobic biodegradation depends on the availability and acclimation of micro-organisms capable of biodegrading 1,1,2,2-tetrachloroethane, it is, therefore, a site-specific process and as such would be an important degradation process where 1,1,2,2-tetrachloroethane or related chlorinated compounds have been discharged over time (Agency for Toxic Substances and Disease Registry, 1989).

In an anoxic sediment-water system (pH unreported), the half-life of 1,1,2,2-tetrachloroethane due to both chemical hydrolysis and biotic degradation was 6.6 days (Jafvert and Wolfe, 1987). In contrast, the hydrolytic half-life of 1,1,2,2-tetrachloroethane in sediment-extracted pore water was 29 days in a laboratory study where 1,1,2,2-tetrachloroethane was in contact with low-carbon sediment at a pH of 7 and at 25 °C (commonly associated with groundwater) (Haag and Mill, 1988).

1,1,2,2-Tetrachloroethane is not expected to adsorb appreciably to soil, suspended solids, or sediment, based on its partition coefficients. This is confirmed by two partitioning experiments in which the sorption coefficient of 1,1,2,2-tetrachloroethane in a silt loam soil and in a low organic carbon soil were found to be 46 and 0.05, respectively (Chiou *et al.*, 1979; Whitehead, 1987). 1,1,2,2-Tetrachloroethane would be expected to leach readily from soil surfaces into the subsurface soil and groundwater (Agency for Toxic Substances and Disease Registry, 1989). Sorption may be significant in dry soils having a high clay content (Agency for Toxic Substances and Disease Registry, 1989). When subsurface soil conditions (anaerobic, methanogenic) were

simulated in a laboratory with a continuous influent concentration of $27 \mu g/L$ for four months, 97% of the 1,1,2,2-tetrachloroethane was dehydrohalogenated to 1,1,2-trichloroethane (Bouwer and McCarty, 1983).

1,1,2,2-Tetrachloroethane has a low bioaccumulation potential. A measured bioconcentration factor (BCF) of 8 and a depuration half-life in tissues of less than one day were observed in freshwater bluegill (*Lepomis macrochirus*) exposed to 9.6 μ g/L of 1,1,2,2-tetrachloroethane for 14 days (Barrows *et al.*, 1980). The experimental BCF is consistent with the calculated BCF of 21 to 72 estimated by regression analysis with K_{ow} (Veith *et al.*, 1980). Similarly, in another study in which rainbow trout (*Oncorhynchus mykiss*) were exposed to up to 1 mg/L of 1,1,2,2-tetrachloroethane, 1,1,2,2-tetrachloroethane was found to partition preferentially to fatty tissue by approximately 8 times that in blood; exposed trout were close to steady-state in 48 hours (Nichols *et al.*, 1991).

2.3.2 Concentrations

1,1,2,2-Tetrachloroethane was detected in Canadian ambient and indoor air, surface waters, and groundwaters but not detected in food. No studies were identified that measured 1,1,2,2-tetrachloroethane in human breast milk, precipitation, sediments, soil, and aquatic or terrestrial biota in Canada.

Based on preliminary results of a pilot study, the mean concentration of 1,1,2,2-tetrachloroethane in indoor air in approximately 750 homes from 10 provinces across Canada in 1991 was 1.8 μ g/m³, with a maximum single value of 11 μ g/m³ (Otson *et al.*, 1992).

Environment Canada has been monitoring volatile organic chemicals in the ambient air of 12 Canadian cities since 1989 and has detected 1,1,2,2-tetrachloroethane at all sites with a detection frequency of approximately 50%. In 1989 and 1990, the mean concentrations at these Canadian sites ranged from non-detectable (below $0.1~\mu g/m^3$) to $0.25~\mu g/m^3$, with a maximum single value of $0.86~\mu g/m^3$ in Ottawa, Ontario (Environment Canada, 1992). In contrast, 1,1,2,2-tetrachloroethane was infrequently detected (18%) above the detection limit of $0.1~\mu g/m^3$ in 385 samples from several cities in Ontario between 1989 and 1991 (OME, 1992a; 1992b; 1992c). In addition, a report to the International Joint Commission focused on the ambient air quality of five sites in the vicinity of the Ontario/Michigan border during 1987 and 1988 and found only one sample (N=1825) above the minimum detectable level of $0.02~\mu g/m^3$ at a concentration of $0.76~\mu g/m^3$ (D-W/PH-S APAB, 1990).

1,1,2,2-Tetrachloroethane was not detected in more than 2000 samples of drinking water in Ontario in 1991 (detection limit $0.05 \,\mu g/L$) (Lachmaniuk, 1991) or in 171 samples of drinking water from across New Brunswick in 1990 (detection limit $1.0 \,\mu g/L$) (Ecobichon and Allen, 1990). It was found only once in treated drinking water in a 1979 survey of 30 potable water treatment facilities across Canada at a concentration of 1 $\,\mu g/L$ (Quantitation limit $1 \,\mu g/L$) (Otson *et al.*, 1982).

In 1985, numerous volatile chemicals were monitored in the St. Clair River and 1,1,2,2-tetrachloroethane was identified downstream of Sarnia, Ontario (COARGLWQ, 1986). The levels of 1,1,2,2-tetrachloroethane ranged from non-detectable (1.0 μ g/L) to 4.0 μ g/L for surface waters, and to 2.0 μ g/L for bottom waters. In a 1981 survey of the Welland River in Ontario, concentrations ranged from non-detectable (0.005 μ g/L) to 0.06 μ g/L (Kaiser and Comba, 1983).

- 1,1,2,2-Tetrachloroethane is not frequently detected in groundwater and appears primarily in leachates from hazardous waste sites. Laboratory organic solvents were the primary wastes deposited in a Gloucester, Ontario landfill site and, although the site has been abandoned since 1980, concentrations of 1,1,2,2-tetrachloroethane in groundwater were reported to range between 5 and $15 \mu g/L$ in 1988 (Lesage *et al.*, 1990). A hazardous waste site in Ville Mercier, Quebec had a maximum 1,1,2,2-tetrachloroethane concentration of $1600 \mu g/L$ in groundwater in 1988 (Pakdel *et al.*, 1992).
- 1,1,2,2-Tetrachloroethane has not been detected in two surveys of samples of 34 food groups in Canada (detection limits of $1.0 \,\mu\text{g/L}$ for liquids in both surveys, and 50 and 5 $\,\mu\text{g/kg}$ for solid food in the first and second survey, respectively) (Enviro-Test Laboratories, 1991; 1992), or in a survey of 231 food items in the U.S. (quantitation limits of 13 or $20 \,\mu\text{g/kg}$) (Daft, 1988). No data were identified on levels of 1,1,2,2-tetrachloroethane in human breast milk in Canada or elsewhere.

2.4 Effects-related Information

2.4.1 Experimental Animals and In Vitro

Based on limited data, 1,1,2,2-tetrachloroethane does not appear to be highly acutely toxic in experimental species. Hepatic effects, including congestion, fatty degeneration, histological changes, alterations in levels of enzymes, and increased DNA synthesis have been reported in rodents following short-term inhalation or ingestion of 1,1,2,2-tetrachloroethane in the few available, principally limited, studies (Horiuchi *et al.*, 1962; Gohlke and Schmidt, 1972; Schmidt *et al.*, 1972; Hanley *et al.*, 1988).

Only a few limited studies have been identified on the effects in experimental animals following subchronic exposure to 1,1,2,2-tetrachloroethane. Ingestion of up to 316 mg/[kg (b.w.)·day] had no effects on body weight gain or mortality in mice, while doses of 100 (females) or 178 (males) mg/[kg (b.w.)·day] and above resulted in decreased body weight gain in rats in subchronic studies preliminary to longer term bioassays (no other endpoints appear to have been examined) (National Cancer Institute, 1978). Histopathological damage was reported in the liver, kidney, testicles, and thyroid gland of rats administered oral doses of 3.2 to 50 mg/[kg (b.w.)·day] of 1,1,2,2-tetrachloroethane for periods ranging from 2 to 150 days (Gohlke *et al.*, 1977), although the poor documentation of results in this study precludes validation of an effect level. Exposure to 50 mg/m³ for approximately 5 weeks resulted in neurological effects, and alterations in biochemical parameters and organ weights in rats, although no "morphological changes" were noted upon examination (the nature and extent of which

were unspecified) (Schmidt *et al.*, 1975). Hepatic effects, including a transient increase in DNA synthesis, reversible histopathological changes, and an increase in relative liver weight were reported in female Sprague-Dawley rats exposed to 560 mL/m³ (890 000 mg/m³) for 15 weeks (Truffert *et al.*, 1977); however, the results of this study are inconsistent with those of other investigations, as the concentration to which the animals were exposed was extremely high, and would likely have been lethal.

The chronic toxicity of 1,1,2,2-tetrachloroethane has not been extensively investigated; available studies are not adequate to determine an effect level for non-neoplastic effects. An increase in the incidence of hepatocellular carcinomas was reported in male and female B6C3F₁ mice administered time-weighted average daily doses of 142 or 284 mg/[kg (b.w.)·day] of 1,1,2,2-tetrachloroethane in corn oil by gavage for 78 weeks (1/18, 13/50, and 44/49 in males, and 0/20, 30/48, and 43/47 in females in the vehicle controls, low and high dose group, respectively) (National Cancer Institute, 1978). There were no significant increases in the incidence of any type of tumor in male or female Osborne-Mendel rats similarly administered 62 or 108 mg/[kg (b.w.)·day] and 43 or 76 mg/[kg (b.w.)·day] of 1,1,2,2-tetrachloroethane, respectively, for 78 weeks, although there were two males with hepatocellular carcinomas and one with a hepatic neoplastic nodule in the high dose group (National Cancer Institute, 1978). Intraperitoneally administered 1,1,2,2-tetrachloroethane did not increase the number of pulmonary adenomas per animal in a limited bioassay designed to investigate the potential of the compound to induce these tumors in mice; however, mortality was high in this study (Theiss *et al.*, 1977).

Increased adrenocorticotropic hormone activity of the hypophysis was observed in rats exposed to 13.3 mg/m³ of 1,1,2,2-tetrachloroethane by inhalation for up to 325 days; there was also a reversible decrease in body weight, an increase in lipid content of the liver, and alterations in hematological parameters, which were only significantly different from controls at one point in time during the study (Schmidt *et al.*, 1972). However, histopathological effects were apparently not examined in this study.

1,1,2,2-Tetrachloroethane acted as a potent promoter in rats initiated with diethylnitrosamine in an initiation/promotion bioassay in rats (Milman *et al.*, 1988; Story *et al.*, 1986). Although inadequately tested *in vivo* (results have been negative or equivocal), some potential for genotoxicity of 1,1,2,2-tetrachloroethane has been demonstrated *in vitro*, as mixed results have been reported for induction of gene mutation and conversions in prokaryotic systems in the presence of metabolic activation, and chromosomal aberrations and cell transformation in mammalian cells. 1,1,2,2-tetrachloroethane is reported to bind to cellular macromolecules, including DNA, RNA and proteins of several organs in rodents following *in vivo* exposure (Colacci *et al.*, 1987; Mitoma *et al.*, 1985; Hanley *et al.*, 1988), although it has been suggested that this results from uptake of carbon atoms during normal biosynthetic pathways (Hanley *et al.*, 1988).

Liver tumors induced by some chemicals in mice appear to be of limited relevance for assessing hazard to humans. However, little information has been identified on the mechanism(s) of liver tumor induction in mice exposed to 1,1,2,2-tetrachloroethane.

Although several of the metabolites of 1,1,2,2-tetrachloroethane, including trichloroethylene, tetrachloroethylene, trichloroacetic acid, and dichloroacetic acid, have been demonstrated to be carcinogenic in experimental animals (e.g., National Toxicology Program, 1986; 1988; 1990; National Cancer Institute, 1977; Maltoni et al., 1986; 1988; Herren-Freund et al., 1987; Bull et al., 1990; DeAngelo et al., 1991), mechanistic studies have been conducted which indicate that some of the tumors induced by these substances may not be relevant to humans, or at least that humans are less susceptible. Paolini et al., (1992) have suggested that the formation of free radicals produced by reductive metabolism of 1,1,2,2-tetrachloroethane observed in mice administered 300 or 600 mg/kg (b.w.) of the compound by intraperitoneal injection, along with marked changes in heme turnover and activities of hepatic microsomal oxygenases, may contribute to hepatotoxicity through lipid peroxidation. The metabolites trichloroacetic acid and dichloroacetic acid have been demonstrated to induce lipid peroxidation to a similar degree in mice and rats, with the latter having greater lipoperoxidative activity (Larson and Bull, 1992). Such damage may play a role in the aetiology of liver tumors observed in mice. Bull (personal communication, 1992) has suggested that the 1,1,2,2-tetrachloroethane-induced liver tumors in mice are likely due to the ability of dichloroacetic acid (the major metabolite of 1,1,2,2-tetrachloroethane) to cause hepatic damage distinct from peroxisome proliferation, such as focal necrosis associated with intense cellular proliferation (Larson and Bull, 1992). It has also been hypothesized that a compensatory increase in hepatic DNA synthesis following hepatic injury or altered homeostasis may act in concert with genetic predisposition in B6C3F₁ mice to enhance the rate of spontaneous tumor formation in this strain (Hanley et al., 1988).

Available data are insufficient to evaluate the effect of exposure to 1,1,2,2-tetrachloroethane on the reproduction or development of experimental animals. Histological changes in the testes have been reported in rats administered 8 mg/[kg b.w.)·day] in peanut oil by gavage (Gohlke *et al.*, 1977), but not consistently in rats exposed to 13.3 mg/m³ (Schmidt *et al.*, 1972; Gohlke and Schmidt, 1972), or a single monkey exposed to 6980 to 27 920 mg/m³ (Horiuchi *et al.*, 1962), although it should be noted that the experimental protocol and results were poorly documented in these studies. Immunological effects, the significance of which is unclear, have been reported in rabbits following inhalation of 10 or 100 mg/m³ of 1,1,2,2-tetrachloroethane for 8 months (Shmuter, 1977; Kulinskaya and Verlinskaya, 1972). Neurotoxic effects have been noted in several species following acute or short-term exposure to 1,1,2,2-tetrachloroethane, e.g., at concentrations as low as 200 ppm (1396 mg/m³) for 6 hours (Horvath and Frantik, 1973).

2.4.2 *Humans*

No significant increase in mortality due to any specific cause was noted in a limited epidemiological investigation in a population of 1099 men exposed to unknown concentrations of tetrachloroethane (probably the 1,1,2,2-isomer), although non-statistically significant increases in mortality due to cancers of the genital organs, leukemia and aleukemia, and other lymphatic cancers were reported (Norman *et al.*, 1981). The prevalence of tremors was reported to increase with airborne concentration

of 1,1,2,2-tetrachloroethane (up to 98 ppm or 684 mg/m³) in a group of 380 workers in India exposed for varying durations, although no information was presented on the prevalence of these signs in an unexposed group (Lobo-Mendonca, 1963).

2.4.3 Ecotoxicology

Although terrestrial organisms would be the most likely of environmental biota to be exposed to 1,1,2,2-tetrachloroethane, ecotoxicological studies were found only for aquatic organisms.

Toxicity bioassays were conducted by Blum and Speece (1991) on three groups of environmental bacteria: methanogens (anaerobes from an enrichment culture maintained for >10 years); aerobic heterotrophs (seed bacteria obtained from the mixed liquor of an activated sludge wastewater treatment plant); and *Nitrosomonas* (seed bacteria obtained from the mixed liquor of an activated sludge plant that treats meat-packing, rendering, and hide-curing wastewater). Inhibition of gas production (methanogens), oxygen uptake (aerobic heterotrophs), and ammonia consumption (*Nitrosomonas*) were the endpoints used in this study to evaluate toxicity. Varying degrees of sensitivities were exhibited; however, *Nitrosomonas* were more sensitive than methanogens (IC₅₀ value of 4.1 mg/L), and significantly more sensitive than aerobic heterotrophs (IC₅₀ 130 mg/L of 1,1,2,2-tetrachloroethane), having an IC₅₀ value of 1.4 mg/L.

Based on bioluminescence, the five-minute IC_{50} was 5.4 mg/L of 1,1,2,2-tetrachloroethane in a Microtox test using *Photobacterium phosphoreum* (Blum and Speece, 1991).

Only two acute toxicity studies on freshwater invertebrates were identified, both of which used first instar *Daphnia magna* (<24 hours old) under static test conditions. Unfed and fed *D. magna* had similar measured 48-h LC₅₀ values of 62 and 57 mg/L of 1,1,2,2-tetrachloroethane, respectively (Richter *et al.*, 1983). Using complete immobilization as the endpoint, the 48-h EC₅₀ values were 23 and 25 mg/L, for unfed and fed *D. magna*, respectively. LeBlanc (1980) conducted a similar test at 22 °C and reported a nominal 24-h and 48-h LC₅₀ value and corresponding 95% confidence limits of 18 (12 to 24) and 9.3 (6.8 to 13) mg/L, respectively.

Chronic 28-day toxicity tests were conducted on *Daphnia magna* to determine the lowest-observable-effect-concentration (LOEC) and the no-observable-effect-concentration (NOEC) based on reproductive impairment. The measured 28-day LOEC and NOEC values were 14.4 and 6.9 mg/L of 1,1,2,2-tetrachloroethane under flow-through conditions (Richter *et al.*, 1983). Occasionally, the animals were observed in a comatose state, demonstrating the narcotic properties of 1,1,2,2-tetrachloroethane.

Numerous acute toxicity studies have been conducted on a variety of freshwater fish species and, in general, 96-h LC₅₀ values were very similar. The response of 30-day-old fathead minnows (*Pimephales promelas*) to acute exposures of 1,1,2,2-tetrachloroethane was investigated by Veith *et al.* (1983), Walbridge *et al.* (1983), and Geiger *et al.* (1985). Under flow-through conditions, the measured 96-h

LC₅₀s were found to be 20.3, 20.4, and 20.3 mg/L (Veith *et al.*, 1983; Walbridge *et al.*, 1983; Geiger *et al.*, 1985). The acute toxicity of 1,1,2,2-tetrachloroethane to juvenile (2 to 4 month) flagfish (*Jordanella floridae*) was investigated by the Aquatic Toxicity Research Group (ATRG, 1988) and then repeated by Smith *et al.* (1991) using both flow-through and static-renewal test systems. The measured 96-h LC₅₀ for the flow-through toxicity test was 18.5 mg/L of 1,1,2,2-tetrachloroethane; the nominal LC₅₀ value in a static-renewal 96-h toxicity test was 26.8 mg/L.

No valid acute toxicity studies of marine fish were identified.

Chronic toxicity studies under flow-through test conditions were conducted on the early life-stages of flagfish (*Jordanella floridae*) by ATRG (1988) and then later repeated by Smith *et al.* (1991). Egg hatchability was unaffected at a measured 1,1,2,2-tetrachloroethane concentration of 22.0 mg/L, the highest concentration tested in both studies. The measured LOEC for reduced 10-day larval survival was 10.6 and 7.2 mg/L and the LOEC for 28-day juvenile survival was 11.7 and 8.5 mg/L (ATRG, 1988; Smith *et al.*, 1991). The effects of 1,1,2,2-tetrachloroethane on the growth of 1-week-old fry over a 28-day exposure period were not statistically significant, even at the highest concentration tested (11.7 mg/L).

No studies were identified on the effects on wild birds or mammals. The limited number of toxicity studies involving laboratory mammals were not used to extrapolate to wildlife as the endpoints chosen were considered insufficient to assess potential risks to wildlife populations.

3.0 Assessment of "Toxic" Under CEPA

3.1 CEPA 11(a) Environment

There is no current commercial activity involving 1,1,2,2-tetrachloroethane in Canada. However, 1,1,2,2-tetrachloroethane enters the Canadian environment through air emissions from the incineration of wastes generated during production of vinyl chloride monomer and ethylene dichloride; air emissions and leachates from existing waste disposal sites; or long-range atmospheric transport from other countries.

Low concentrations of 1,1,2,2-tetrachloroethane have been detected in Canadian ambient air; it is not frequently detected in groundwater or surface waters. Although no data were identified on levels of 1,1,2,2-tetrachloroethane in sediments, soil, or biota in Canada, it is not likely to be present in these media, based on its physical and chemical properties and the results of laboratory studies on the fate of 1,1,2,2-tetrachloroethane in various environmental media. Since 1,1,2,2-tetrachloroethane is no longer used or manufactured in Canada, the levels currently found are not likely to increase, and in fact may decrease over time.

The freshwater organism most sensitive to long-term exposure of 1,1,2,2-tetrachloroethane was the flagfish (*Jordanella floridae*), the 10-day larval survival of which was affected at 7.2 mg/L (LOEC). Using a factor of 0.1 to convert the LOEC to a chronic no-observed-effect-concentration (NOEC) for a non-persistent, non-bioaccumulative substance and to account for differences in species sensitivity and extrapolation from laboratory to field conditions, the estimated effects threshold is 720 μ g/L for long-term exposure. The estimated effects threshold concentration for long-term exposure is 180 times greater than the maximum concentration found in Canadian surface waters (4.0 μ g/L). Given the large difference between the estimated effects threshold and ambient water concentrations, no adverse effects are expected to result from exposure of freshwater organisms to 1,1,2,2-tetrachloroethane at current levels.

Most 1,1,2,2-tetrachloroethane is released to the atmosphere. Reliable effects data on terrestrial organisms are unavailable. As a result, it is not possible to assess whether current 1,1,2,2-tetrachloroethane concentrations in air will adversely effect terrestrial biota.

Therefore, on the basis of available data, it is not possible to conclude whether 1,1,2,2-tetrachloroethane is "toxic" as defined under Paragraph 11(a) of the *Canadian Environmental Protection Act*.

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

1,1,2,2-Tetrachloroethane is released to the atmosphere in relatively low amounts in Canada. Furthermore, because of its high volatility, rapid photo-oxidation in the

atmosphere, and an atmospheric ozone-depleting potential of less than 0.001 relative to CFC-l 1, 1,1,2,2-tetrachloroethane is not expected to contribute significantly to either the depletion of the stratospheric ozone layer or global warming.

Therefore, on the basis of available data, 1,1,2,2-tetrachloroethane is not considered to be "toxic" as defined under Paragraph 11(b) of the *Canadian Environmental Protection Act*.

3.3 CEPA 11(c) - Human Life or Health

3.3.1 Population Exposure

Estimated average daily intakes (on a body weight basis) of 1,1,2,2tetrachloroethane from environmental media for various age groups of the general population in Canada and the assumptions upon which they are based are presented in Table 1. Indoor air is the main source of exposure to 1,1,2,2-tetrachloroethane, with estimated intakes ranging from 0.43 to 0.67 µg/[kg (b.w.)·day]. Intake from ambient air is estimated to range from <0.005 to 0.02 µg/[kg (b.w.)·day]. Drinking water is estimated to contribute from 0.001 to 0.11 μ g/[kg (b.w.) day] to the daily intake of 1,1,2,2tetrachloroethane, although it should be noted that these values very likely overestimate exposure via drinking water, since 1,1,2,2-tetrachloroethane has only rarely been detected in treated drinking water in Canada. 1,1,2,2-Tetrachloroethane was not detected in two surveys of foodstuffs in Canada and one survey conducted in the United States. Food probably does not represent a significant source of 1,1,2,2-tetrachloroethane for the general population in Canada, based on its volatility and low potential for bioconcentration. Inadequate data were available to estimate exposure to 1,1,2,2-tetrachloroethane via breast milk in infants, or through use of consumer products (including cigarettes) in all age groups. Total average daily intake of 1,1,2,2-tetrachloroethane by the general population in Canada is estimated to range from <0.44 to $0.72 \mu g/[kg (b.w.) \cdot day]$.

3.3.2 Effects

Based on the available data, carcinogenicity is potentially the most sensitive endpoint for determination of "toxic" under Paragraph 11(c) of CEPA. The weight of evidence for carcinogenicity, therefore, has been considered, based on the criteria developed for this purpose for the "Determination of 'Toxic' under Paragraph 11(c) of the *Canadian Environmental Protection Act*" (Environmental Health Directorate, 1992).

No adequate epidemiological studies have been identified in which the carcinogenicity of 1,1,2,2-tetrachloroethane in humans has been investigated.

The incidence of hepatocellular carcinomas was significantly increased in both male and female B6C3F₁ mice administered 1,1,2,2-tetrachloroethane by gavage for 78 weeks. These tumors also appeared earlier in mice administered the higher dose

Table 1 Estimated Average Total Daily Intake of 1,1,2,2-Tetrachloroethane by the General Population in Canada

Madan	Estimated Intake [μg/(kg b.w.·day)]					
Medium	*0 to 6 mo ^a	7 rno to 4yr ^b	5 to 11 yr ^c	12 to 19 yr ^d	20 to 70 yr ^e	
Ambient Air ^f	<0.005 to 0.01	<0.006 to 0.02	<0.007 to 0.02	<0.006 to 0.02	< 0.005 to 0.01	
Indoor Air ^g	0.43	0.58	0.67	0.55	0.49	
Drinking Waterh	0.005 to 0.11	0.003 to 0.06	0.002 to 0.03	0.001 to 0.02	0.001 to 0.02	
Total Intake	<0.44 to 0.55	<0.59 to 0.66	<0.68 to 0.72	<0.56 to 0.59	<0.50 to 0.52	

^{*} Age

- Assumed to weigh 7 kg, breathe 2 m³ of air per day, and drink 0.75 L of water per day (Environmental Health Directorate, 1992).
- Assumed to weigh 13 kg, breathe 5 m³ of air per day, and drink 0.8 L of water per day (Environmental Health Directorate, 1992).
- Assumed to weigh 27 kg, breathe 12 m³ of air per day, and drink 0.9 L of water per day (Environmental Health Directorate, 1992).
- d Assumed to weigh 57 kg, breathe 21 m³ of air per day, and drink 1.3 L of water per day (Environmental Health Directorate, 1992).
- e Assumed to weigh 70 kg, breathe 23 m³ of air per day, and drink 1.5 L of water per day (Environmental Health Directorate, 1992).
- Based on the range of mean concentrations of 1,1,2,2-tetrachloroethane in ambient air in ten Canadian cities (1988 to 1990) of <0.1 to $0.25 \,\mu\text{g/m}^3$ (Environment Canada, 1992), and an average of 4 hours per day spent outdoors (Environmental Health Directorate, 1992).
- Based on a mean concentration of 1,1,2,2-tetrachloroethane in indoor air from approximately 750 homes in ten Canadian provinces of 1.8 µg/m³ (Otson *et al.*, 1992) and an average of 20 hours per day spent indoors (Environmental Health Directorate, 1992).
- Based on range of detection limits in survey of 30 water treatment facilities across Canada (Otson *et al.*, 1982) and monitoring programs in Ontario (Lachmaniuk, 1991) and New Brunswick (Ecobichon and Allen, 1990) of 0.05 to 1.0 μg/L; since 1,1,2,2-tetrachloroethane has only rarely been detected in treated drinking water in Canada, these estimates likely overestimate exposure in this medium.

(National Cancer Institute, 1978). In a similar bioassay in Osborne-Mendel rats, no statistically significant increases in the incidence of any type of tumor were reported. However, there were two hepatocellular carcinomas (a rare tumor in this strain of rat) and one hepatic neoplastic nodule in male rats in the high-dose group, while none was noted in male controls (National Cancer Institute, 1978). The number of pulmonary adenomas per animal was not increased in a limited bioassay in which mice were administered 1,1,2,2-tetrachloroethane intraperitoneally for 24 weeks, although this study is inadequate even for screening of the carcinogenic potential of 1,1,2,2-tetrachloroethane due to poor survival of mice and the lack of histopathological confirmation of all tumors (Theiss *et al.*, 1977).

1,1,2,2-Tetrachloroethane acted as a potent promoter in an initiation/promotion assay in Osborne-Mendel rats initiated with diethylnitrosamine (Milman *et al*, 1988; Story *et al.*, 1986). Although not adequately tested *in vivo* (negative and equivocal results have been reported), 1,1,2,2-tetrachloroethane may have some genotoxic potential *in vitro*.

Due to the lack of sufficient data on the mechanism of 1,1,2,2-tetrachloroethane-induced cancer in mice, it is not possible to assess, with any degree of confidence, the relevance to humans of the hepatocellular carcinomas observed in the bioassay conducted by the National Cancer Institute (1978). Therefore, on the basis of the observed increase in liver tumors in mice, the non-significant increase in hepatocellular tumors in rats, and the genotoxic potential demonstrated in some *in vitro* studies, 1,1,2,2-tetrachloroethane is classified in Group III ("Possibly Carcinogenic to Humans") of the classification scheme developed for the determination of "toxic" under Paragraph 11(c) of CEPA (Environmental Health Directorate, 1992).

For substances classified in Group III, a tolerable daily intake (TDI) is generally developed by division of a relevant No-Observed-(Adverse)-Effect Level [NO(A)EL] or Lowest-Observed-(Adverse)-Effect Level [LO(A)EL] in animal species by an uncertainty factor, which takes into account, where appropriate, the limited evidence of carcinogenicity.

Available data are considered inadequate, however, to develop a TDI for 1,1,2,2-tetrachloroethane, as none of the studies identified was of sufficient quality to determine a NO(A)EL or LO(A)EL for non-neoplastic endpoints. Consequently, it is not possible to evaluate whether current concentrations of 1,1,2,2-tetrachloroethane present in the environment constitute a danger in Canada to human life or health.

For compounds classified in Group III, if the weight of evidence of carcinogenicity is considered sufficient, estimates of exposure are sometimes compared to quantitative estimates of cancer potency to provide guidance in establishing priorities for additional research. For 1,1,2,2-tetrachloroethane, this approach was considered inappropriate owing to the minimal weight of evidence for carcinogenicity and the suspicion that the observed tumors may not be relevant to humans.

Therefore, on the basis of available data, it is not possible to conclude whether 1,1,2,2-tetrachloroethane is "toxic" as defined under Paragraph 11(c) of the Canadian Environmental Protection Act.

3.4 Conclusion

Therefore, on the basis of available data, 1,1,2,2-tetrachloroethane is not considered to be "toxic" as defined under Paragraph 11 (b) of CEPA. It has also been concluded that available data are insufficient to conclude whether 1,1,2,2-tetrachloroethane is "toxic" as defined under Paragraphs 11 (a) and (c) of the *Canadian Environmental Protection Act*.

4.0 Recommendations for Research and Evaluation

1,1,2,2-Tetrachloroethane is no longer produced or imported into Canada; therefore, exposure of biota and humans is currently low and is expected to decrease over time. Since available data are too limited to determine trends in concentrations in air, which is the primary source of exposure in Canada, continued monitoring of this substance is recommended. If exposure continues to decrease, the priority for the following research is considered to be low. However, if exposure to 1,1,2,2-tetrachloroethane increases, then the priority for obtaining the additional data outlined below should be reassessed.

- 1) It would be desirable to obtain monitoring data on levels of 1,1,2,2-tetrachloroethane in food (using more sensitive analytical methodology than that in currently available surveys), drinking water, and human breast milk in Canada, to more accurately determine the exposure of the general population to 1,1,2,2-tetrachloroethane in these media.
- To investigate the potential effects of exposure to 1,1,2,2-tetrachloroethane on health, more complete subchronic studies are required. In these studies, a range of endpoints should be examined in experimental animals exposed to several dose levels of 1,1,2,2-tetrachloroethane by inhalation (the route of exposure most relevant to humans).
- A carcinogenicity bioassay is desirable in which non-neoplastic endpoints, such as organ weight changes, and biochemical and hematological effects, are also examined in two species of experimental animals exposed to 1,1,2,2-tetrachloroethane by inhalation (the route of exposure most relevant to humans) in order to more completely assess the potential effects of this compound in humans.
- 4) It would be desirable to conduct additional investigations into the mechanism of liver tumor induction by 1,1,2,2-tetrachloroethane in mice, to interpret the relevance of these tumors to humans.
- 5) Additional data are desirable on the developmental toxicity, reproductive toxicity, neurotoxicity and immunotoxicity, and the *in vivo* genotoxicity of 1,1,2,2-tetrachloroethane to determine the potential for these effects on health.
- To investigate the potential effects of exposure to 1,1,2,2-tetrachloroethane on terrestrial biota, toxicity studies on terrestrial plants, and oral and inhalation subchronic studies on wild mammals and birds are desirable.

5.0 References

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