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Canadian Environmental Protection Act

Priority Substances List
Assessment Report

Tetrachloroethylene

Government of Canada
Environment Canada
Health Canada

Aussi disponible en français sous le titre de :
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Table of Contents

Synopsis

Tetrachloroethylene is no longer produced in Canada but continues to be imported, primarily for use as a solvent in the dry-cleaning and metal-cleaning industries. Domestic consumption is approximately 14 kilotonnes per year. Since its uses are dispersive and do not result in its transformation or destruction, the majority of the tetrachloroethylene used in Canada is expected to enter the environment, primarily the atmosphere. Tetrachloroethylene has been measured in outdoor air and in the air inside homes within Canada, and has been detected in drinking water across the country and in contaminated surface waters in the Great Lakes and the St. Lawrence River. The substance is present in groundwaters in several provinces, often as a result of its inappropriate disposal and release from dry-cleaning facilities or landfills.

Concentrations of tetrachloroethylene in surface waters in Canada are generally an order of magnitude or more below the effects threshold estimated for the most sensitive aquatic species. Limited data suggest, however, that concentrations in some surface waters replenished by contaminated groundwaters may exceed this threshold. For wild mammals, the estimated effects threshold is more than double the "worst-case" daily intake estimated for mink. The estimated effects threshold for terrestrial plants, notably trees exposed to tetrachloroethylene in the atmosphere, was equivalent to airborne concentrations observed at a rural location, and was exceeded by the mean concentrations reported for various urban locations.

Tetrachloroethylene is present in low concentrations and has a short half-life in the atmosphere. As such, it is not expected to contribute significantly to the formation of ground-level ozone, global warming or depletion of stratospheric ozone.

Based on data on the concentrations of tetrachloroethylene in outdoor ambient air, indoor air, drinking water and food, the total daily average intakes of this substance by various age groups of the general population have been estimated. These average daily intakes are less (by approximately 13 to 28 times) than the tolerable daily intake derived on the basis of 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 concluded that tetrachloroethylene occurs at concentrations that may be harmful to the environment, but that do not constitute a danger to the environment on which human life depends, or 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 the List of Toxic Substances (Schedule I of the Act). Consideration can then be given to developing guidelines, codes of practice or regulations 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 tetrachloroethylene 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 to levels that could cause harmful **effects**.

Data relevant to the assessment of whether tetrachloroethylene is "toxic" to the environment were identified from on-line searches completed in April 1992, of a number of commercial databases (including ENVIROFATE, TOXLINE, BIOSIS, MEDLARS II, CAB Abstracts, ELIAS, MICROLOG, ENVIROLINE, AQUAREF, ASFA, BIOSIS Previews, NTIS, AQUIRE, CESARS, PHYTOTOX, AGRICOLA, SWRA, RTECS, CA SEARCH, Soviet Science and Technology, Pollution Abstracts and Hazardous Substances Databank). Data relevant to assessment of whether tetrachloroethylene is "toxic" to the environment obtained after completion of these sections of the document (October 1992) were not considered for inclusion.

In addition to published scientific literature, the following individuals in universities and government agencies were also contacted to identify relevant data: Mr. A.D. Cameron (Water Resources Branch, Nova Scotia, Environment Canada); Dr. J.A. Cherry (Waterloo Centre For Groundwater Research, Canada); Ms. J. Deschamps (Department of the Environment, United Kingdom); Mr. R. Doyle (Ontario Ministry of the Environment, Canada); Mr. B. Eckert (Ontario Ministry of the Environment, Canada); Dr. K. Figge (NATEC Institute für Naturwissenschaftlich-Technische Dienste GmbH, Germany); Mr. M.H. Laengner (Ontario Ministry of the Environment, Canada); Dr. J.P. Lay (Deutsche Bundesstiftung Umwelt, Germany); Dr. S. Lesage (Canada Centre for Inland Waters, Canada); Mr. J. Rose (Transport Canada, Ottawa); Dr. P. Schröder (Fraunhofer Institute for Atmospheric Environmental Research, Germany); Dr. D. Smyth (Waterloo Centre For Groundwater Research, Canada); Mr. T. Wingrove (UMA Engineering, Canada).

Data relevant to the assessment of whether tetrachloroethylene is "toxic" to human health were identified through evaluation of existing review documents of the Agency for Toxic Substances and Disease Registry (ATSDR, 1990), as well as a more recent update of this report (ATSDR, 1991), the U.S. Environmental Protection Agency Office of Health and Environmental Assessment (U.S. EPA, 1985), the U.S. Environmental Protection Agency Office of Drinking Water Criteria and Standards Division (U.S. EPA, 1990), the International Programme on Chemical Safety/World Health Organisation (WHO, 1984) and the European Chemical Industry Ecology and Toxicology Centre (ECETOC, 1990), as well as a review prepared under contract by Michael Holliday & Associates (Holliday and Park, 1991). On-line databases including HSDB, RTECS, MEDLINE, TOXLINE, TOXLIT, IRIS, CHRIS, DOBIS, AQUAREF, CODOC, FSTA and ELIAS were searched (up to October 1991) in order to identify the relevant literature necessary to assess the environmental exposure and toxicological effects of tetrachloroethylene on human health. Data relevant to assessment of whether tetrachloroethylene is "toxic" to human health obtained after completion of these sections of the document (April 1992), were not considered for inclusion.

Review articles were consulted where appropriate; however, all original studies that form the basis for determining whether tetrachloroethylene is "toxic" under CEPA have been critically evaluated by staff of Health Canada (human exposure and effects on human health) and Environment Canada (entry and environmental exposure and effects). The following officials contributed to the preparation of this report:

R. Arseneault (Environment Canada)
B.M. Braune (Environment Canada)
R.A. Kent (Environment Canada)
R.G. Liteplo (Health Canada)
M.E. Meek (Health Canada)
E.L. Porter (Environment Canada)
U.A. Schneider (Environment Canada)
M. Taché (Environment Canada)
S. Teed (Environment Canada)

In this report, a synopsis that will appear in the *Canada Gazette* is presented. A summary of 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 tetrachloroethylene is "toxic" is presented in Section 3.0.

As part of the review and approvals process established by Environment Canada for its contribution to these reports, sections related to the assessment of effects on the environment were reviewed by Dr. N.J. Bunce (University of Guelph), Dr. H. Frank (Universität Bayreuth, Germany), Dr. J.T. Trevors (University of Guelph) and Dr. V. Zitko (Department of Fisheries and Oceans). Sections related to the assessment of effects on human health were reviewed by Dr. T. Green (ICI Central Toxicology Laboratory, Cheshire, U.K.; Supporting Documentation only), Dr. J. Borzelleca and Dr. J. Egle (Medical College of Virginia), Dr. G. Plaa (Université de Montréal), Dr. R. Bull (Washington State University) and BIBRA Toxicology International (Surrey, U.K.), and subsequently approved by the Standards and Guidelines Rulings Committee of the Bureau of Chemical Hazards. 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:

Environmental Health Centre
Health Canada
Room 104
Tunney's Pasture
Ottawa, Ontario, Canada
K1A 0L2

Commercial Chemicals Branch
Environment Canada
14th Floor
Place Vincent Massey
351 Saint-Joseph Boulevard
Hull, Quebec, Canada
K1A 0H3

2.0 Summary of Information Critical to Assessment of "Toxic"

2.1 Identity, Properties, Production and Uses

The Chemical Abstracts Service (CAS) Registry Number for tetrachloroethylene is 127-18-4 and synonyms include 1,1,2,2-tetrachloroethylene, tetrachloroethene, ethylene tetrachloride, carbon dichloride, carbon bichloride and perchloroethylene. Trade names for tetrachloroethylene include Ankilostin, Antisal 1, Dee-Solv, Didakene, DowPer, ENT 1860, Fedal-Un, Nema, Perk, Perclene, Percosolv, Perklone, PerSec, Tetlen, Tetracap, Tetraleno, Tetravec, Tetroguer and Tetropil (WHO, 1984, 1987).

Tetrachloroethylene [C_2Cl_4; molecular weight = 165.8] is a nonflammable, nonviscous liquid with a density of 1.62 g/mL at 20°C. It is relatively insoluble in water (water solubility ranges from 150 to 484 mg/L at 10° to 25°C) [Schwarzenbach *et al.*, 1979; Banerjee *et al.*, 1980; Verschueren, 1983; Budavari, 1989]. The log K_{ow} is approximately 3, based on measured and calculated values of 2.53 (Banerjee *et al.*, 1980) and 3.40 (Hansch and Leo, 1985), respectively. Tetrachloroethylene absorbs infrared radiation, including wavelengths in the 7 to 13 μm region (Sadtler Research Laboratories, 1982). In air, 1 ppm is equivalent to 6.78 mg/m^3 (at 25°C and 101 kPa) [ATSDR, 1991; U.S. EPA, 1985].

The analytical method most widely reported in the literature for quantifying tetrachloroethylene isolated from water, sediments, biota and air is gas chromatography using an electron capture detector (Singh *et al.*, 1982; Comba and Kaiser, 1983; Ziglio *et al.*, 1983; Dann and Wang, 1992). Reported detection limits are as low as 0.8 ng/L in water (Comba and Kaiser, 1983), 0.2 μg/kg (fresh weight) in fish tissues (Ofstad *et al.* 1981) and 0.1 μg/m^3 in air (Dann and Wang, 1992).

Since the sole Canadian producer ceased production in May 1992 (Chen, 1993), tetrachloroethylene is no longer manufactured in Canada. As a result, tetrachloroethylene is imported into Canada to meet domestic demand. For 1990, total imports and exports of tetrachloroethylene for Canada were 6.5 and 11.5 kilotonnes, respectively, while annual domestic demand totalled 14.0 kilotonnes (CIS, 1990). For the period 1983 to 1988, demand was estimated to be 14.5 kilotonnes per year.

Tetrachloroethylene is the principal solvent used in the dry-cleaning industry across Canada (IPB, 1991). Approximately 10 kilotonnes of tetrachloroethylene were used for this purpose in 1990 (CIS, 1990). Other major industrial uses of tetrachloroethylene in Canada during 1990 included the cleaning and degreasing of metals (1.4 kilotonnes) and the production of chlorofluorocarbons (2.2 kilotonnes). The sole Canadian

manufacturer of chlorofluorocarbons ceased production of these chemicals in December 1992 (Chen, 1993). Tetrachloroethylene is also used in smaller quantities in Canada in the finishing and processing of textiles, the manufacture of paint removers and printing inks, the formulation of adhesives and specialized cleaning fluids, and as aerosols and dye carriers (IARC, 1979; Verschueren, 1983; WHO, 1984; Environment Canada, 1990).

Tetrachloroethylene is present in household products, including automobile cleaners, suede protectors, paint removers and strippers, water repellents, silicone lubricants, belt lubricants and dressings, specialized aerosol cleaners, ignition wire driers, fabric finishes, spot removers, adhesives, and wood cleaners (U.S. EPA, 1982).

2.2 Entry into the Environment

There are no known natural sources of tetrachloroethylene, and therefore entry into the environment results from anthropogenic sources. Quantitative information on releases of this substance into the Canadian environment from these sources is limited to reported spills. In view of its volatility, and because its uses are dispersive and do not result in its transformation or destruction, the majority of the tetrachloroethylene in Canadian commerce is expected to enter the environment, primarily the atmosphere. These releases occur during production and use from process or distillation vents, and fugitive emissions. Releases have also occurred from the discharge of industrial and municipal liquid effluents, and in leachate from some landfill sites.

The release of tetrachloroethylene from wastewater treatment plants in Sarnia, Ontario, and Peace River, Alberta, has been reported. Concentrations in the Sarnia wastewater treatment-plant influent and effluent were 31 and 26 µg/L, respectively (Marsalek, 1986). Since these values were higher than those reported in both urban runoff and in township ditches that convey surface runoff, it can be concluded that the sources of tetrachloroethylene were commercial or industrial operations discharging into municipal sewers. In Peace River, the concentration of tetrachloroethylene in the sewage treatment-plant effluent was 8 µg/L (NAQUADAT/ENVIRODAT, 1991).

A total of 34 spills involving tetrachloroethylene (ranging in volume from < 1 L to 43 652 L) have been voluntarily reported to the National Analysis of Trends in Emergency Spills Database since 1977 (NATES, 1992) and the Dangerous Goods Accident Information System since 1988 (DGAIS, 1992). These spills occurred in 7 Canadian provinces and 1 territory, and totalled 123 074 L. Of this total volume, 86.8% was spilled from industrial plants and storage facilities in the chemical and services industry sector, while the remaining spills occurred during the transport of tetrachloroethylene.

2.3 Exposure-related Information

2.3.1 Fate

The behaviour of tetrachloroethylene in the environment is affected by a number of processes, including atmospheric photooxidation, volatilization and biotransformation. Tetrachloroethylene that is discharged to the terrestrial or aquatic environment and not removed by degradative or evaporative processes can accumulate in groundwater.

The primary environmental receiving compartment for tetrachloroethylene is the troposphere. Reaction of tetrachloroethylene with photochemically-produced hydroxyl radicals is the major mechanism of removal, while wet deposition is considered a minor process (Howard, 1990; Singh *et al.*, 1982). The products of the photooxidation reaction include trichloroacetyl chloride, trichloroacetic acid, carbon monoxide, hydrochloric acid, ozone and phosgene (Gay *et al.*, 1976; U.S. EPA, 1982; Frank *et al.*, 1991). Dimitriades *et al.* (1983) reviewed the photochemical reactivity of tetrachloroethylene in the atmosphere and in smog chambers and suggested that ambient concentrations of tetrachloroethylene generally do not contribute significantly to the formation of ground-level ozone in most urban atmospheres. Based on smog-chamber studies, Frank (1990) reported the photooxidation yield of trichloroacetyl chloride, which was subsequently hydrolysed to trichloroacetic acid, to be approximately 80%. The latter compound has a short half-life in the troposphere, since rainout is an effective removal process (Correia *et al.*, 1977). The estimated half-life for tetrachloroethylene in the atmosphere varies according to the latitude, season and concentration of hydroxyl radicals (Bunce, 1992). For Canada, the tropospheric half-life has been calculated by Bunce (1992) to range from 27 to 58 days in June and July. Limited degradation of tetrachloroethylene takes place in the troposphere during winter months in Canada. Migration of tetrachloroethylene from the troposphere to the stratosphere was estimated to take between 5 and 10 years (Rowland, 1990).

Tetrachloroethylene that is discharged into aquatic systems remains in solution, forms coalesced droplets on the bottom or volatilizes into the atmosphere; however, based on its relatively low water solubility and high vapour pressure, volatilization is considered the dominant fate process (Callahan *et al.*, 1979; Schwarzenbach *et al.*, 1979; Wakeham *et al.*, 1983; Kaiser and Comba, 1986a). For tetrachloroethylene released as a concentrated spill, a large portion will initially coalesce to form dense, non-aqueous phase liquid (DNAPL) puddles on the bottom of water bodies, as occurred in the St. Clair River, Ontario, following a major release in 1986 (Lau and Marsalek, 1986). Subsequently, small droplets will separate, resuspend in the water column, dissolve and ultimately volatilize. As a result, concentrations of tetrachloroethylene are expected to be low in surface waters, except in areas of industrial discharge or

accidental spills. By comparison, tetrachloroethylene is more persistent in groundwater, since the rates of volatilization and biodegradation are greatly reduced (U.S. EPA, 1985; WHO, 1984).

The amount of tetrachloroethylene adsorbed to soils is dependent on the partition coefficient, the organic carbon content of the soil, the type of release (ponding or streaming) and the concentration of tetrachloroethylene in the liquid phase (Seip *et al.*, 1986; Poulsen and Kueper, 1992). Tetrachloroethylene moves through sandy soil at almost the same rate as water; however, there can be considerable retention in soils with a higher organic carbon (2.2 to 3.7%) and clay (9.2 to 10.1%) content (Seip *et al.*, 1986). The permeability and porosity of soil as well as the amount of tetrachloroethylene released will determine the depth to which tetrachloroethylene will migrate into the soil. Tetrachloroethylene is, therefore, expected to be mobile in most soils and able to penetrate to depths where groundwater can be contaminated (Poulsen and Kueper, 1992; Schwille, 1988).

Results of identified laboratory, microcosm and pilot-scale studies indicate that microbial degradation of tetrachloroethylene occurs under anaerobic conditions, but not to any substantial extent under aerobic conditions (Bouwer *et al.*, 1981; Fogel *et al.*, 1986; Barrio-Lage *et al.*, 1986; Freedman and Gossett, 1989). The general pathway of microbial degradation of tetrachloroethylene under anaerobic conditions involves reductive dehalogenation to trichloroethylene, dichloroethylene and vinyl chloride, with mineralization to carbon dioxide or dehalogenation to ethylene as end-products (Freedman and Gossett, 1989). Trichloroacetic acid can also be produced from the oxidative biotransformation of tetrachloroethylene (Frank, 1989). The products of the sequential dechlorination of tetrachloroethylene have been detected in contaminated groundwater (Parsons *et al.*, 1984; Jackson *et al.*, 1988; Lesage *et al.*, 1990).

Tetrachloroethylene likely has a low to moderate potential for bioconcentration, based on its log octanol/water partition coefficient (log $K_{ow} \approx 3$). Barrows *et al.* (1980) examined the bioconcentration of waterborne tetrachloroethylene by bluegill sunfish (*Lepomis macrochirus*) in a 21-day test. A whole-body bioconcentration factor (BCF) of 49 was reported and the half-life for elimination was estimated to be < 1 day. Neely *et al.* (1974) reported a BCF of 39.6 for tetrachloroethylene in muscle of rainbow trout (*Oncorhynchus mykiss*). In a 32-day early life-stage toxicity study with fathead minnows (*Pimephales promelas*), a whole-body BCF of 61.5 was reported (Ahmad *et al.* 1984). Pearson and McConnell (1975) reported that the bioconcentration of tetrachloroethylene in the liver of a marine fish (*Limanda limanda*) [BCF = 200 to 400] was two orders of magnitude greater than in muscle (BCF = 5 to 9). The accumulation of tetrachloroethylene in terrestrial plants can occur following exposure to low ambient concentrations of this substance (Figge, 1990).

2.3.2 Concentrations

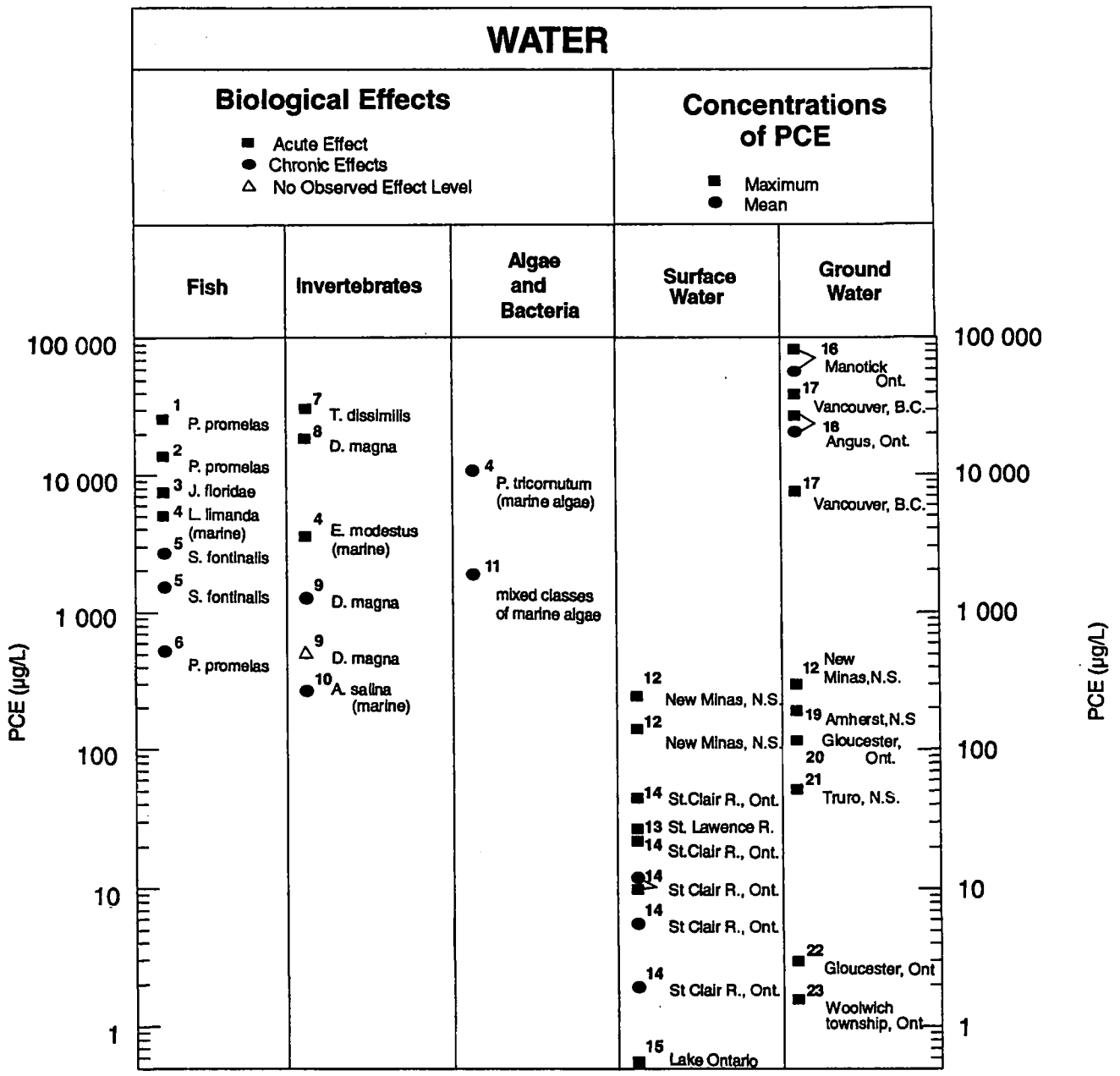
Tetrachloroethylene has been detected in outdoor and indoor air, surface and groundwater, drinking water, sediment, and biota in various regions of Canada. Data on the concentrations of tetrachloroethylene in surface water, groundwater and outdoor air are represented in Figures 1 and 2.

Concentrations of tetrachloroethylene in air in remote regions are generally in the ng/m^3 range, with higher levels occurring in urban areas (e.g., Singh *et al.* 1977). The concentration of tetrachloroethylene in ambient air can fluctuate over relatively short periods of time (changes close to one order of magnitude within hours) depending on the strength of emission sources, variations in wind direction and velocity, and rain scavenging and photodecomposition (Frank, 1991; Figge, 1990; Ohta *et al.*, 1977).

In a recent national survey conducted in 1990 of 22 sites in 11 Canadian cities, mean concentrations of tetrachloroethylene in outdoor urban air ranged from 0.2 μg/m^3 to 5.0 μg/m^3 (detection limit = 0.1 μg/m^3) [Dann and Wang, 1992]. The maximum level recorded was 45.7 μg/m^3, in Hamilton, Ontario (Dann and Wang, 1992). In a limited survey conducted in 1987, tetrachloroethylene was detected in ambient air near 6 homes in Toronto, Ontario; the mean concentration was 1.9 μg/m^3 (Chan *et al.*, 1990). Bell *et al.* (1991) reported mean concentrations of tetrachloroethylene of 1.6 and 0.6 μg/m^3 in samples of air obtained from 5 residential and 16 business district sites in Toronto, Ontario, in 1990. The mean concentration of tetrachloroethylene in 40 samples of air obtained at Walpole Island (a rural location in Ontario) between January and November 1990 was 0.2 μg/m^3; the maximum level was 0.4 μg/m^3 (Dann and Wang, 1992).

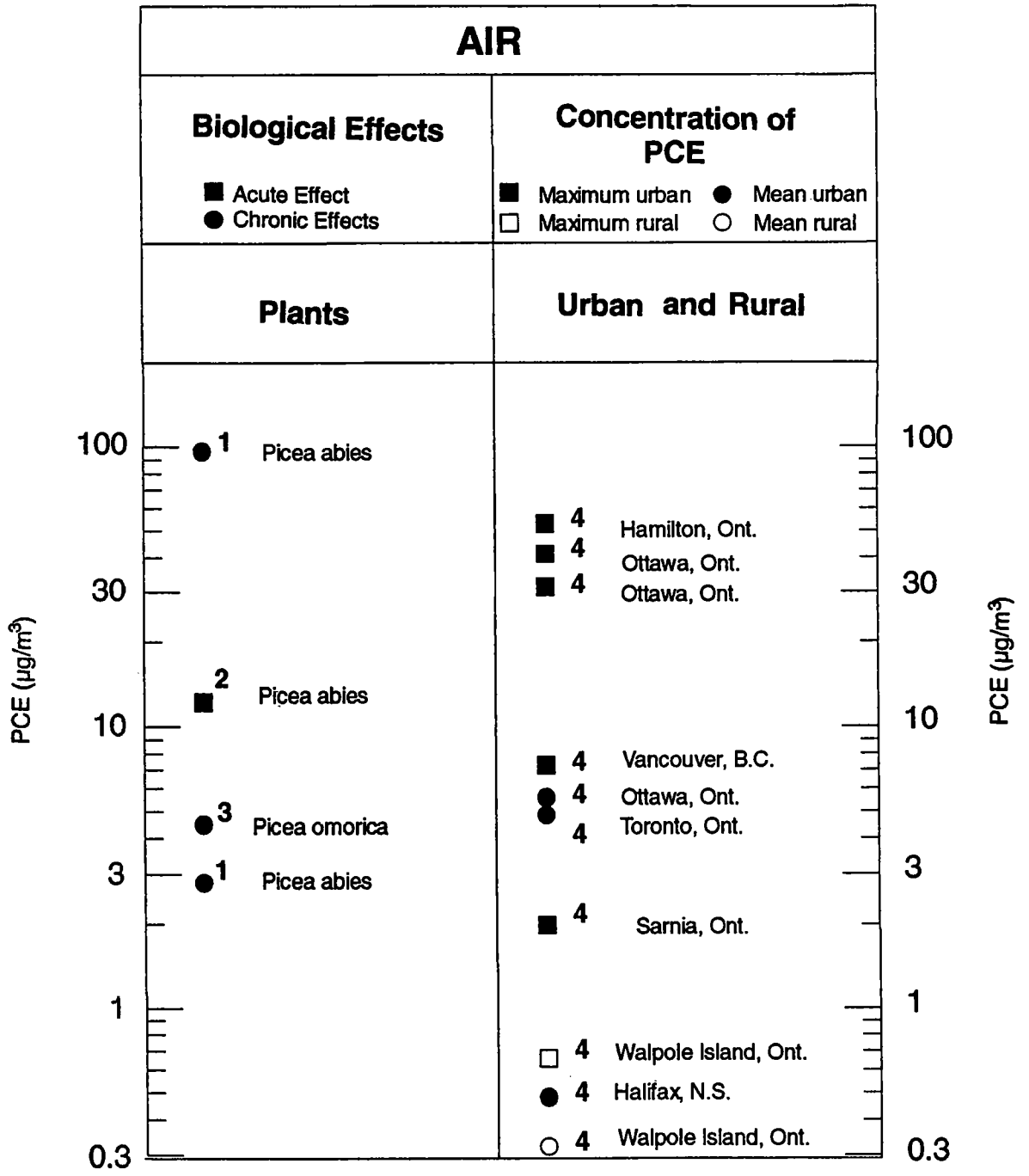
Otson *et al.* (1992) reported, on the basis of preliminary results, that the mean concentration of tetrachloroethylene in the indoor air of 757 randomly selected homes within Canada was approximately 5.1 μg/m^3 (method detection limit = 2 μg/m^3). The concentration of tetrachloroethylene in the indoor air of 12 homes in the Toronto area ranged from 1 to 171 μg/m^3 (Chan *et al.*, 1990). At these locations, the concentration of tetrachloroethylene in the ambient outdoor air ranged from not detectable (detection limit not clearly described) to 4 μg/m^3. Bell *et al.* (1991) reported concentrations of tetrachloroethylene in 3 urban (Toronto-area) homes ranging from 2.8 to 9.0 μg/m^3, while the levels in 8 business offices ranged from trace (i.e., between 1.4 and 7.1 μg/m^3) to 34.9 μg/m^3; the mean concentrations were 5.8 and 13.9 μg/m^3, respectively. The results of the latter 2 studies are limited, owing to the small number of samples analyzed.

Figure 1. Representative tetrachloroethylene (PCE) concentrations in the Canadian aquatic environment and concentrations causing adverse biological effects.



1. Brodorius and Kahl, 1985.
2. Walbridge *et al.*, 1983.
3. Smith *et al.*, 1991.
4. Pearson and McConnell, 1975.
5. ATRG, 1988.
6. Ahmad *et al.*, 1984.
7. Call *et al.*, 1983.
8. LeBlanc, 1980.
9. Richter *et al.*, 1983.
10. Kerster and Schaeffer, 1983.
11. Erickson and Hawkins, 1980.
12. Brodie and McLeod, 1984.
13. Comba *et al.*, 1989.
14. OMOE, 1991a.
15. Kaiser *et al.*, 1983.
16. Doyle, unpublished data, 1992.
17. Golder Associates, 1989.
18. Laengner, unpublished data, 1992.
19. Cameron and McLeod, 1983.
20. Lesage *et al.*, 1990.
21. McLeod *et al.*, 1985.
22. Jackson *et al.*, 1988.
23. Reinhard *et al.*, 1984.

Figure 2. Representative tetrachloroethylene (PCE) concentrations in the Canadian air and concentrations causing adverse effects.



1. Frank, 1990.
2. Frank and Frank, 1986a.
3. Frank and Frank, 1985.
4. Dann and Wang, 1992.

Based on limited data identified for Canadian surface waters, environmental levels of tetrachloroethylene are generally low unless the waters receive direct releases from industrial or other sources. Tetrachloroethylene was measured at several sites in the St. Lawrence River near the Ottawa River confluence, Lac St. Louis and Québec City; concentrations were reported to range from 2 to 12 µg/L (Allan, 1988). In another study in the St. Lawrence River, the mean concentration of tetrachloroethylene in 297 samples was 0.012 µg/L, with a maximum value of 27 µg/L (Comba *et al.*, 1989). Concentrations of tetrachloroethylene in 10 samples of surface water from Crawford Lake (a meromictic lake in Ontario that was isolated from known sources of contamination) ranged up to 0.009 µg/L (detection limit = 0.0008 µg/L); the authors suggested that atmospheric transport could have been the source of the tetrachloroethylene (Comba and Kaiser, 1983).

The transboundary waters of the St. Clair and Niagara Rivers are contaminated by a number of industrial sources in Canada and the United States. Concentrations of tetrachloroethylene in samples of bottom water collected downstream from petroleum products facilities on the St. Clair River near Sarnia, Ontario, ranged from 0.002 µg/L to 34.6 µg/L (Kaiser and Comba, 1986b). Kaiser and Comba (1986b) calculated a mean concentration of tetrachloroethylene of 0.21 µg/L (based on an analysis of 8 samples of water) at the point where the St. Clair River enters Lake St. Clair. These authors also reported concentrations of tetrachloroethylene in an effluent outfall in the St. Clair River as high as 0.28 µg/L (Comba and Kaiser, 1985). As part of an extensive investigation of trace organics in the St. Clair River that was initiated following the discovery of black liquid puddles containing tetrachloroethylene on the river bottom at Sarnia, Marsalek (1986) reported that the mean concentration of tetrachloroethylene at 8 urban runoff sites was 4.4 µg/L (range = 0.05 to 26.0 µg/L; the detection limit was not stated). Furthermore, ambient mean concentrations of tetrachloroethylene at 43 stations from the river headwaters to the St. Clair delta ranged from non-detected to 11.0 µg/L (detection limit = 1 µg/L; distances from shore = 10 m, 30 m, and 100 m; sampling depths = 1 to 16 m; 6 to 14 samples per station) during a monitoring program from May to October 1986. The highest individual value was 44 µg/L in a sample obtained 30 m offshore from a chemical plant outfall in Sarnia, Ontario, at a depth of 7 m (OME, 1991a). Concentrations of tetrachloroethylene in ambient suspended solids ranged from non-detected to 2 800 ng/g in surface waters, and from non-detected to 2 900 ng/g in bottom waters (dry weight; detection limit = 1 ng/g; detected in 18 of 25 samples and in 20 of 23 samples collected, respectively). Concentrations of tetrachloroethylene in surficial sediments that were analyzed during the same study ranged from 0.4 to 1 300 ng/g (dry weight) [detected in 19 of 30 sediment samples collected] (OME, 1991a).

The mean concentration of tetrachloroethylene in 17 samples of surface water collected from the lower Niagara River in 1981 was 0.036 µg/L, with a maximum level of 0.134 µg/L (Kaiser *et al.*, 1983). Except for one sample collected at the heavily industrialized, western end of Lake Ontario (0.59 µg/L), measurable levels of tetrachloroethylene in 82 samples of water from Lake Ontario did not exceed 0.015 µg/L (Kaiser *et al.*, 1983).

Contamination of groundwater with tetrachloroethylene has been observed in several areas in Canada, most often in association with dry-cleaning facilities and waste disposal sites. In a recent investigation of an aquifer under the town of Manotick, Ontario (December 1991 to November 1992), concentrations of tetrachloroethylene ranged from below detection to 80 000 µg/L (detection limit = 2.0 µg/L; more than 220 samples were analyzed); mean concentrations ranged from below the detection limit to 66 000 µg/L. Improper disposal of tetrachloroethylene by a dry-cleaning establishment that closed in 1988 was reported to be the source of contamination (Doyle, 1992; Eckert, 1993). Tetrachloroethylene was also detected in groundwater in Angus, Ontario, in 1992, where concentrations ranged from 8 µg/L to 27 000 µg/L (more than 130 samples were analyzed) [Laengner, 1992] and mean concentrations at individual sites ranged from 61 µg/L to 20 683 µg/L. The source of contamination was not identified, although the affected wells were in close proximity to a dry-cleaning facility.

Groundwater contamination has also been observed in several areas in Nova Scotia, including the towns of New Minas, Truro and Amherst (Cameron and McLeod, 1983; Brodie and McLeod, 1984; McLeod *et al.*, 1985). In New Minas, samples of water were collected in 1983 from both the deep and shallow wells serving the town. Concentrations of tetrachloroethylene ranged from 153 µg/L to 290 µg/L (mean = 228 µg/L; 3 samples, detection limit = 2 µg/L) and from 95 µg/L to 145 µg/L (mean = 114 µg/L; 4 samples) for deep and shallow wells, respectively. The aquifer was contaminated by a dry-cleaning establishment, although other minor sources of tetrachloroethylene were not ruled out. This same aquifer feeds a surface spring and a nearby pond, not connected to the spring. A sample of surface water collected at the point where the spring flowed into a nearby stream contained 244 µg/L tetrachloroethylene, while the sample from the pond contained 177 µg/L tetrachloroethylene (Brodie and McLeod, 1984).

Reports of groundwater contamination with tetrachloroethylene were identified for 3 landfill sites in Canada. Concentrations of tetrachloroethylene in groundwater under the landfill at Ville Mercier, Quebec following a waste oil spill ranged from 1 µg/L to 9 859 µg/L at the 10 sites tested (Pakdel *et al.*, 1989). Lesage *et al.* (1990) reported concentrations of tetrachloroethylene in the outwash aquifer from the landfill site in Gloucester, Ontario ranging from below the detection level to

105 µg/L (detection limit = 1 µg/L). Mean concentrations of tetrachloroethylene in groundwater at depths of 19.6 to 25.6 m near the Woolwich Township landfill in Ontario were 0.79 to 1.7 µg/L (Reinhard *et al.*, 1984).

Tetrachloroethylene was detected in 39 of 90 samples of potable water obtained from 30 water-treatment plants across Canada in 1979; the maximum concentration was 4 µg/L (Otson *et al.*, 1982). In a subsequent study, Otson (1987) detected (detection limit = 0.1 µg/L) tetrachloroethylene in only one of 45 samples of potable water obtained (during 1982 and 1983) from 10 water-purification plants in the Great Lakes region.

During the years 1985, 1987 and 1988, tetrachloroethylene was detected in 2 of 31 samples of (treated) drinking water obtained in Newfoundland. The maximum reported concentration was 0.2 µg/L, which was below the minimum quantitation limit of 0.5 µg/L (Environment Canada, 1989a). During the period between 1986 and 1988, tetrachloroethylene was detected in 14 of 23 samples of drinking water obtained in Prince Edward Island. The maximum reported concentration was 4.2 µg/L, which was well above the minimum quantitation limit of 0.5 µg/L (Environment Canada, 1989b). Tetrachloroethylene was detected in 25 of 43 samples of drinking water obtained in Nova Scotia during the years 1985 to 1987; the maximum reported level was 2.4 µg/L, which was well above the minimum quantitation limit of 0.5 µg/L (Environment Canada, 1989c). Tetrachloroethylene was detected (minimum quantitation limit = 0.5 µg/L) in 14 of 37 samples of drinking water obtained in New Brunswick between 1985 and 1988 (Environment Canada, 1989d); the maximum concentration was 4.2 µg/L.

Tetrachloroethylene was detected (detection limit = 0.05 µg/L) in 22 of 93 samples of drinking water obtained from municipalities in the province of Quebec, during the period between 1985 and 1988 (Quebec Ministry of the Environment, 1990); the highest reported concentration was 1.5 µg/L.

Tetrachloroethylene was detected at trace levels (i.e., below the detection limits of 0.2 or 3.0 µg/L) in only 3 of 1 512 samples of water taken from 215 treated and 14 raw water supplies in the province of Alberta between the years 1986 and 1991 (Alberta Environment, 1991). In samples of drinking water obtained from 106 sites in the province of Ontario during the period 1988 to 1991, the levels of tetrachloroethylene ranged from not detectable (detection limit = 0.05 µg/L) to 5.25 µg/L (OME, 1991b).

Little information was identified with respect to the concentration of tetrachloroethylene in Canadian soil, although it has been detected (at concentrations ranging from 0.006 to greater than 10 mg/kg dry matter) in samples obtained from an industrial site in Vancouver (Golder Associates, 1989).

Only limited information was identified on the concentrations of tetrachloroethylene in biota in Canada. Levels ranged from 220 to 380 ng/g (mean = 307 ng/g; 3 samples; wet weight; detection limit was not stated) in juvenile emerald shiners (*Notropis atherinoides*) in 3 locations in the St. Clair River, Ontario, in 1985. Levels ranged from 4 to 31 ng/g (mean = 16 ng/g) in 3 samples obtained from the same locations in 1986 (OME, 1991a). Tetrachloroethylene was also identified (but not quantified) in whole body lipid extracts from adult herring gulls collected in 1973 from Pigeon Island near Kingston Harbour, Lake Ontario, and in whole body lipid extracts from adult herring gulls found feeding in the Kingston garbage dump during 1976 (Hallett *et al.*, 1982).

No information on the concentration of tetrachloroethylene in terrestrial plants in Canada was identified; however, Diezel *et al.* (1988) reported that the mean concentration of tetrachloroethylene in spruce needles downwind from a heavily industrialized area in Germany was 5.5 ng/g (detection limit = 3 ng/g; dry or wet weight not specified; number of samples unknown).

Information on the concentration of tetrachloroethylene in foodstuffs in Canada is extremely limited. Based on market-basket surveys in the United States reported by Daft (1988) [231 samples] and Heikes (1987), the average concentrations of tetrachloroethylene in dairy, meat, cereal, fruit, vegetable, fats and oil, and sugar composites (Environmental Health Directorate, 1992) were estimated to be approximately 6.6, 12.3, 14.7, 0.8, 0.4, 12.9 and 2.9 ng/g, respectively.

2.4 Toxicokinetics

The major metabolites of tetrachloroethylene in the urine of laboratory animals (rodents) are trichloroacetic acid and oxalic acid. Minor metabolites, which have been detected in some but not all studies, include trichloroethanol, dichloroacetic acid and N-oxalylaminoethanol (U.S. EPA, 1985; Dekant *et al.*, 1986). Minor amounts (from 1 to 2%) of CO_2 (which is eliminated in the expired air) may also be produced from the metabolism of tetrachloroethylene (Pegg *et al.*, 1979). The results of a number of studies have indicated that the oxidative metabolism of tetrachloroethylene in laboratory animals (i.e., rodents) is limited at elevated levels of exposure. In mice, the hepatotoxic effect of tetrachloroethylene appears to be related to the extent of its oxidative metabolism (Buben and O'Flaherty, 1985).

Trichloroacetic acid has been identified as the principal metabolite of tetrachloroethylene in humans (ATSDR, 1990; U.S. EPA, 1985); however, only a very small amount (from 1 to 2%) of the tetrachloroethylene absorbed by humans is metabolized and subsequently excreted in the urine as trichloroacetic acid—most of the absorbed material is eliminated unchanged in expired air (Monster, 1979; Monster *et al.*, 1979; Ohtsuki *et al.*, 1983; Koppel *et al.*, 1985; Riihimaki, 1985; Fernandez *et al.*, 1976;

Ogata *et al.*, 1971). The liver is regarded as the primary site of the oxidative metabolism of tetrachloroethylene to trichloroacetic acid. Trichloroethanol has also been identified in the urine of individuals exposed to tetrachloroethylene, although it is a relatively minor metabolite (U.S. EPA, 1985; ATSDR, 1990). The oxidative metabolism of tetrachloroethylene to trichloroacetic acid appears to be limited at levels of exposure greater than 50 ppm to 100 ppm (339 to 678 mg/m^3) [Ikeda *et al.*, 1972; Ikeda, 1977; Ohtsuki *et al.*, 1983]. The available data indicate that the metabolism of tetrachloroethylene to trichloroacetic acid is greater in mice than in either rats (Pegg *et al.*, 1979; Schumann *et al.*, 1980; Odum *et al.*, 1988; Bolt, 1987) or humans (Ikeda and Ohtsuji, 1972).

In rodents, tetrachloroethylene may also be conjugated with cellular glutathione, followed by loss of glutamine and glycine, producing S-(1,2,2-trichlorovinyl)-L-cysteine, which may be either metabolized via the mercapturic acid pathway, producing N-acetyl-S-(1,2,2-trichlorovinyl)-L-cysteine (which is excreted in the urine), or activated by the renal β-lyase enzyme producing the (putative) highly reactive intermediate, trichlorovinylthiol, which upon rearrangement may be capable of forming covalent links with proteins or nucleic acids. Formation of the tetrachloroethylene-glutathione conjugate takes place in the liver, with subsequent metabolism occurring primarily in the kidney (Green, 1990a). The conjugation of tetrachloroethylene with glutathione and activation of S-(1,2,2-trichlorovinyl)-L-cysteine by the renal β-lyase occurs to a greater extent in rats than in mice (Dekant *et al.*, 1986; Green, 1990a). Based on the results of dose-response studies, Green *et al.* (1990) concluded that the glutathione-conjugation pathway of tetrachloroethylene metabolism only becomes quantitatively important, once the oxidative pathway is saturated.

The results of *in vitro* enzymatic assays have indicated that humans appear to lack the hepatic enzyme required to synthesize the tetrachloroethylene-glutathione conjugate, and that the metabolism of S-(1,2,2-trichlorovinyl)-L-cysteine in male rats is approximately 2-fold greater than in females and 30-fold higher than in mice or humans (of either sex) [Green *et al.*, 1990]. Thus, although conjugation of tetrachloroethylene with glutathione and activation of S-(1,2,2-trichlorovinyl)-L-cysteine by the renal β-lyase does take place in rats and (to some extent) in mice, it may not be relevant to humans (or the enzymatic activities in humans may be much less) [Green, 1990a].

2.5 Effects-related Information

2.5.1 *Experimental Animals and* In Vitro

The acute toxicity of tetrachloroethylene is relatively low. LC_{50}s for the 4-hour exposure of mice to tetrachloroethylene range from 2 613 ppm to 5 200 ppm (17 716 to 35 256 mg/m^3) [NTP, 1986; Friberg *et al.*, 1953]. The LD_{50} for the oral administration of tetrachloroethylene to these animals is approximately 8.1 g/kg bw (Wenzel and Gibson, 1951). LC_{50}s for the 4-hour exposure of rats to tetrachloroethylene between 2 445 ppm and 5 163 ppm (16 577 to 35 005 mg/m^3) have been reported (NTP, 1986; Bonnet *et al.*, 1980). The LD_{50} for the oral administration of tetrachloroethylene to these animals ranges from 3.0 to 12.96 g/kg bw (Hayes *et al.*, 1986; Withey and Hall, 1975; Smyth *et al.*, 1969). The acute exposure of laboratory animals to tetrachloroethylene produces hypoactivity, ataxia, anaesthesia, tremors and central nervous system (CNS) depression. Liver and kidney dysfunction have also been observed at near-lethal doses.

Dose-dependent adverse effects in the liver, kidney, hematopoetic, reproductive and central nervous systems are associated with the repeated exposure of experimental animals to tetrachloroethylene, with mice being more sensitive than rats to the hepatotoxic effects. In short-term studies, exposure (7 hours/day, 5 days/week over a period of 18 days) of rats to high concentrations (2 500 ppm; 16 950 mg/m^3) of tetrachloroethylene reduced survival by 90% (Rowe *et al.*, 1952). The continuous exposure of mice to 9 ppm (61 mg/m^3) tetrachloroethylene for 30 days produced small increases in plasma butyrylcholinesterase activity and liver weight (lowest-observed-effect-level (LOEL) = 9 ppm; 61 mg/m^3) [Kjellstrand *et al.*, 1984]. The exposure of mice to 50 ppm (339 mg/m^3) tetrachloroethylene for 4 weeks produced minor changes in the levels of hepatic and renal microsomal proteins (LOEL = 50 ppm; 339 mg/m^3) [Soni *et al.*, 1990]. A LOEL of 100 mg/kg bw/day in B6C3F$_1$ mice, and a no-observed-effect-level (NOEL) of 500 mg/kg bw/day in Sprague-Dawley rats was derived on the basis of the results from a study in which this substance was administered (orally) to these animals for 11 consecutive days; effects observed at the LOEL were an increased liver/body weight ratio and hepatocellular hypertrophy and swelling (Schumann *et al.*, 1980).

A NOEL of 100 ppm (678 mg/m^3) was derived from a study in which the exposure of F344/N rats and B6C3F$_1$ mice to tetrachloroethylene for 6 hours/day, 5 days/week for 13 weeks produced effects including diminished survival and reduced weight gain (in both species) and lung and liver congestion (in rats), as well as hypoactivity, poor coordination, unconsciousness, hepatic (centrilobular necrosis, bile stasis, leucocyte infiltration) and renal (karyomegaly) toxicity in mice (NTP, 1986). The LOEL was considered to be 20 mg/kg bw/day based on hepatic damage (degeneration, karyorrhexis, necrosis, polyploidy) observed in a study in which tetrachloroethylene

was administered orally to Swiss-Cox mice for 5 days/week over a period of 6 weeks (Buben and O'Flaherty, 1985). A NOEL of 14 mg/kg bw/day was derived from a study in which the administration of drinking water containing tetrachloroethylene to Sprague-Dawley rats over a period of 90 days produced effects at the next highest concentration, which included reduced weight gain and altered liver or kidney to body weight ratios (Hayes *et al.*, 1986). Marth (1987) reported reversible erythropoietic damage in mice receiving low concentrations of tetrachloroethylene in drinking water (equivalent to 50 µg/kg bw/day) over a period of 49 days; however, these results have not been confirmed in other studies.

The toxicological effects produced by the chronic exposure of laboratory animals to tetrachloroethylene have been examined only in studies primarily designed to assess the carcinogenic potential of this substance (NTP, 1986). Toxic effects produced by chronic exposure (6 hours/day, 5 days/week over a period of 103 weeks) of F344/N rats to tetrachloroethylene included a significant reduction in their survival, an increased incidence of renal karyomegaly in both males and females, renal tubular cell hyperplasia in the males, an increased incidence of nasal cavity thrombosis and nasal squamous metaplasia, and an increased incidence of adrenal medullary (males) and cortical (females) hyperplasia (lowest-observed-adverse-effect-level [LOAEL] = 200 ppm; 1 356 mg/m^3) [NTP, 1986].

Compared to unexposed controls, the exposure (6 hours/day, 5 days/week for 103 weeks) of F344/N rats to 200 or 400 ppm (1 356 or 2 712 mg/m^3) tetrachloroethylene produced a small (but not statistically significant) increase in the incidence of renal tubular cell adenomas and adenocarcinomas in the male, but not in female animals (NTP, 1986). The incidence of renal tubular cell adenomas or adenocarcinomas in groups of male rats exposed to 0, 200 or 400 ppm (0, 1 356 or 2 712 mg/m^3) tetrachloroethylene was 1/49, 3/49 and 2/50, and 0/49, 0/49 and 2/50, respectively. The incidence of testicular interstitial tumours (39/49 and 41/50 in males exposed to 200 or 400 ppm (1 356 or 2 712 mg/m^3) tetrachloroethylene was slightly (but significantly) increased compared to controls (35/50), although the increase was not considered to be substance related, since the incidence in both exposed groups was similar to the overall incidence (89%) observed in historical controls (NTP, 1986). In male and female rats exposed to 0, 200 and 400 ppm (0, 1 356 or 2 712 mg/m^3) tetrachloroethylene, the incidence of mononuclear cell leukemia was 28/50, 37/50, 37/50, and 18/50, 30/50, 29/50, respectively. It should be noted, however, that in this particular study the incidence of this type of tumour (56% and 36%) in the male and female non-exposed controls was higher than in historical controls.

Enhanced cellular proliferation resulting from cell damage produced by the renal accumulation of α_{2u}-globulin (i.e., hyaline droplet formation resulting in hyaline droplet nephropathy), and the formation of genotoxic metabolites of tetrachloroethylene within the kidney, have been proposed as mechanisms by which tetrachloroethylene induces the formation of kidney tumours in male rats exposed to this substance. The mechanism by which structurally diverse hydrocarbons (including tetrachloroethylene) induce hyaline droplet nephropathy in male rats has been well documented (Goldsworthy *et al.*, 1988; Swenberg *et al.*, 1989; Olson et al., 1990). It is believed that the substance (or one of its metabolites) binds to α_{2u}-globulin, which is normally reabsorbed in the kidney by endothelial cells within the P2 segment of the proximal tubule. Binding of the substance reduces the catabolism of α_{2u}-globulin, resulting in its accumulation within the lysosomes of these cells (i.e., protein droplet accumulation). Protein droplet accumulation leads to lysosomal overload, resulting in cell necrosis and subsequent cellular regeneration, characteristic of hyaline protein nephropathy. Resulting excessive renal cell proliferation may ultimately lead, in a few cases, to the development of renal tubular adenocarcinomas. Importantly, α_{2u}-globulin is produced in large amounts in the male F344 rat, but not in female F344 rats, mice or humans (Olson *et al.*, 1990).

Hyaline droplet formation has been observed in the kidneys of male F344 rats exposed for short periods to concentrations of tetrachloroethylene higher than those administered in the NTP bioassay (e.g., following exposure [by inhalation for up to 10 days] to 1 000 ppm [6 780 mg/m^3] tetrachloroethylene [Green *et al.*, 1990]). While hyaline droplet formation has been observed in the kidneys of male F344 rats receiving (orally) 1 g/kg bw/day tetrachloroethylene for 10 days (Goldsworthy *et al.*, 1988) or 1.5 g/kg bw/day tetrachloroethylene for 42 days (Green *et al.*, 1990), a similar effect was not observed in female F344 rats (Goldsworthy *et al.*, 1988).

It has also been proposed that covalent binding to nucleic acids or proteins of a reactive metabolite produced in the kidney by the glutathione-conjugation pathway of tetrachloroethylene metabolism (which may become quantitatively important upon saturation of the oxidative pathway [Green *et al.*, 1990]), may also play a role in the induction of renal tumours in male rats (Green, 1990a, 1990b; Green *et al.*, 1990; Dekant *et al.*, 1990a, 1990b; Vamvakas *et al.*, 1989).

Toxic effects produced by the chronic exposure (6 hours/day, 5 days/week over a period of 103 weeks) of B6C3F$_1$ mice to tetrachloroethylene included diminished survival, an increased incidence of renal nephrosis and tubular cell karyomegaly and an increased number of renal casts, as well as increased lung congestion, hepatic degeneration and necrosis (LOAEL = 100 ppm; 678 mg/m^3) [NTP, 1986]. The exposure (6 hours/day, 5 days/week for 103 weeks) of B6C3F$_1$ mice to 0, 100 or 200 ppm (0, 678 or 1 356 mg/m^3) tetrachloroethylene produced an increase in the incidence of hepatocellular carcinomas in both males and females (7/49, 25/49 and

26/50 in males and 1/48, 13/50 and 36/50 in females, respectively) [NTP, 1986]. The incidence of hepatocellular adenomas (12/49, 8/49 and 19/50 in male mice exposed to 0, 100 and 200 ppm (0, 678 and 1 356 mg/m^3) tetrachloroethylene was only increased at the highest concentration (NTP, 1986).

The exposure of male and female Sprague-Dawley rats to 300 or 600 ppm (2 034 or 4 068 mg/m^3) tetrachloroethylene for 6 hours/day, 5 days/week for 52 weeks did not significantly increase the incidence of tumours, compared to unexposed controls (Rampy *et al.*, 1978, cited in ATSDR, 1990; ECETOC, 1990; U.S. EPA, 1985); however, these results are inconclusive, due to the relatively short period of exposure. In a carcinogenesis bioassay in which tetrachloroethylene (dissolved in corn oil) was administered by gavage (NCI, 1977), there was an increase in the incidence of hepatocellular carcinomas in both male and female B6C3F$_1$ mice, but no increase in tumour incidence in Osborne-Mendel rats; however, reduced survival in both species, due, in part, to respiratory disease and pneumonia, the presence of impurities in the administered tetrachloroethylene, and the large volume of vehicle used, limit the usefulness of these results.

The incidence of lung tumours in A-strain mice was not increased following the intraperitoneal administration of tetrachloroethylene (Theiss *et al.*, 1977; Maronpot *et al.*, 1986). Tetrachloroethylene was not significantly carcinogenic in "skin tumour" assays (Van Duuren *et al.*, 1979), and evidence concerning the potential of tetrachloroethylene to act as a tumour "promoter" in a liver-tumour induction assay system is equivocal (Milman *et al.*, 1988; Lundberg *et al.*, 1987).

Based on examination of a range of genetic end-points in both *in vitro* and *in vivo* bioassays, the weight of evidence indicates that tetrachloroethylene is not genotoxic (see Supporting Documentation).

Following the exposure of pregnant mice to tetrachloroethylene, the substance was found within embryonic and fetal tissues (Ghantous *et al.*, 1986). On the basis of limited available data, tetrachloroethylene has not been teratogenic and has induced minor embryotoxic and foetotoxic effects, but only at doses or concentrations toxic to the mothers (see Supporting Documentation).

The neurotoxicological effects produced by the exposure of laboratory animals to tetrachloroethylene are dose dependent. The exposure of rodents to 1 600 to 5 163 ppm (10 848 to 35 005 mg/m^3) tetrachloroethylene produced restlessness, tremors, CNS depression, ataxia and loss of equilibrium and coordination (Rowe *et al.*, 1952; NTP, 1986). The administration (oral) of tetrachloroethylene (in doses ranging from 2 200 to 8 850 mg/kg bw) to Sprague-Dawley rats resulted in tremors, ataxia and CNS depression being observed prior to death of the animals (Hayes *et al.*, 1986). Exposure of Mongolian gerbils to concentrations of tetrachloroethylene as low as

60 ppm (407 mg/m^3) produced small alterations in the DNA content in the brain (Rosengren *et al.*, 1986); however, no relationship was established between this biochemical change and any other neurotoxicological or neurobehavioral effects. Alterations in the levels of DNA, lipid, protein and amino acids in the brain of Mongolian gerbils or rats exposed to concentrations of tetrachloroethylene ranging from 120 to 320 ppm (814 to 2 170 mg/m^3) have also been observed (Rosengren *et al.*, 1986; Kyrklund *et al.*, 1990; Briving *et al.*, 1986); however, the biological significance of these changes is not clear. The short-term (4-day) exposure of male Sprague-Dawley rats to 200 ppm (1 356 mg/m^3) tetrachloroethylene had no significant effect on the protein or RNA content of the brain, but ambulatory (open-field) behaviour was transiently increased immediately after exposure (Savolainen *et al.*, 1977).

Aranyi *et al.* (1986) reported that exposure (3 hours) of female CD1 mice to 50 ppm (339 mg/m^3) tetrachloroethylene resulted in a diminished resistance to streptococcal pneumonia and reduced pulmonary bactericidal activity, compared to unexposed controls. Effects in mice exposed to 25 ppm (170 mg/m^3) tetrachloroethylene were not significantly different from those of the controls.

2.5.2 Humans

The accidental (acute) exposure of humans to elevated concentrations of tetrachloroethylene produces hepatotoxic and nephrotoxic effects, and death (Stewart, 1969; Koppel *et al.*, 1985; Levine *et al.*, 1981; Hake and Stewart, 1977; U.S. EPA, 1985; ATSDR, 1990). In clinical studies, following short-term exposure of volunteers to concentrations of tetrachloroethylene ranging from 106 to 2 000 ppm (719 to 13 560 mg/m^3), symptoms ranging from mild eye and nasal irritation to dizziness and anaesthesia were observed (LOAEL = 106 ppm; 719 mg/m^3) [Carpenter, 1937; Rowe *et al.*, 1952]; with increasing concentrations of tetrachloroethylene, the severity of the effects increased, while the time of onset became shorter. Light-headedness, speech difficulties, nausea, and eye and throat irritation were observed in male and female volunteers exposed to 100 ppm (678 mg/m^3) tetrachloroethylene for 7 hours/day (for 5 consecutive days) [Stewart *et al.*, 1970].

In a clinical study, Altmann *et al.* (1990) reported that exposure to 50 ppm (339 mg/m^3) tetrachloroethylene can lead to mild visual system dysfunction, manifested as delayed neuronal processing time and altered contrast perception; however, exposure to 10 ppm (67.8 mg/m^3) tetrachloroethylene had no significant effect upon peripheral hearing ability. Neurobehavioral changes produced by long-term occupational exposure to tetrachloroethylene may include deficits in visual/spatial function and cognitive flexibility, changes in mood (Echeverria *et al.*, 1991), and clinical and preclinical effects upon frontal lobe and limbic functions (White and Echeverria, 1992).

The incidence of, or mortality due to, cancer associated with occupational exposure to tetrachloroethylene has been examined in case-control studies of laundry and dry-cleaning workers with liver (Stemhagen *et al.*, 1983) or bladder (Smith *et al.*, 1985) cancer, and in cohort studies of populations employed in the dry-cleaning and laundry industry (Blair *et al.*, 1979, 1990; Katz and Jowett, 1981; Duh and Asal, 1984; McLaughlin *et al.*, 1987; Brown and Kaplan, 1987; Lynge and Thygesen, 1990), or workers at an aircraft maintenance facility (Spirtas *et al.*, 1991).

In individual studies, increased risks of liver cancer (Stemhagen *et al.*, 1983), increased mortality due to cancer of the cervix (Blair *et al.*, 1979, 1990; Katz and Jowett, 1981), bladder (Brown and Kaplan, 1987; Katz and Jowett, 1981), kidney (Brown and Kaplan, 1987; Katz and Jowett, 1981; Duh and Asal, 1984), lung and respiratory system, (Duh and Asal, 1984), skin (Katz and Jowett, 1981), genitals, (Katz and Jowett, 1981), oesophagus (Blair *et al.*, 1990), lymphosarcoma (Katz and Jowett, 1981), multiple myeloma and non-Hodgkin's lymphoma (Spirtas *et al.*, 1991), and an increased incidence of liver and pancreatic cancer (Lynge and Thygesen, 1990) have been reported. There is little consistent evidence, therefore, for increases in cancer of a specific type in these occupationally exposed populations. Moreover, workers in these industrial settings were probably exposed to other solvents in addition to tetrachloroethylene, and in virtually all of these epidemiological investigations little or no quantitative information concerning the level of exposure to tetrachloroethylene was presented. Notably, in a study of dry-cleaning workers, Brown and Kaplan (1987) reported no increase in mortality due to cancer in a subcohort of 615 individuals exposed only to tetrachloroethylene. In addition, in many of the available studies, individuals who were employed in the dry-cleaning and laundry industries were analyzed as a single group, although their exposure to tetrachloroethylene is likely to be quite different, and the impact of potential confounding factors (such as smoking) on the morbidity or mortality due to cancer was not taken into account.

The potential effects of occupational exposure to tetrachloroethylene on reproduction and development have been examined in a number of case-control (Rachootin and Olsen, 1983; Taskinen *et al.*, 1989; Kyyronen *et al.*, 1989; Lindbohm *et al.*, 1990; Ahlborg, 1990), cross-sectional (Hemminki *et al.*, 1980a, 1980b; Bosco *et al.*, 1987; Eskenazi *et al.*, 1991a, 1991b) and cohort (McDonald *et al.*, 1986, 1987) studies. An increased risk of spontaneous abortion was reported in some (Hemminki *et al.*, 1980a, 1980b; Kyyronen *et al.*, 1989) but not all (Ahlborg, 1990; Bosco *et al.*, 1987; Lindbohm *et al.*, 1990; Taskinen *et al.*, 1989; Eskenazi *et al.*, 1991b; McDonald *et al.*, 1986, 1987) studies. Occupational exposure to tetrachloroethylene was not associated with an increased risk of birth defects (McDonald *et al.*, 1986, 1987; Bosco *et al.*, 1987; Kyyronen *et al.*, 1989; Ahlborg, 1990), or significant alterations in the quality of sperm (Eskenazi *et al.*, 1991a); however, Rachootin and Olsen (1983) reported a positive association between idiopathic infertility in females and exposure to

dry-cleaning chemicals. These occupationally exposed workers were likely exposed to other solvents, and quantitative information on exposure to tetrachloroethylene was usually not presented.

The effects of chronic exposure to tetrachloroethylene on renal function have been examined in a limited number of cross-sectional studies of workers employed in the dry-cleaning industry (Franchini *et al.*, 1983; Lauwerys *et al.*, 1983; Vyskocil *et al.*, 1990; Solet and Robins, 1991). Other than a slight increase in the level of lysozyme in the urine of workers exposed to tetrachloroethylene (Franchini *et al.*, 1983; Vyskocil *et al.*, 1990), there has been no evidence of renal dysfunction.

Seeber (1989) assessed the potential neurobehavioral effects in workers employed in dry-cleaning facilities exposed to 83.4 ± 53.3 mg/m^3 (7 males and 50 females; "low exposure") and 363.8 ± 114.2 mg/m^3 tetrachloroethylene (5 males and 39 females; "high exposure") and in a group of 84 non-exposed "controls". Some small psychological differences were noted between the control and exposed groups (based upon a number of psychological tests on personality and attention, as well as perceptual, sensorimotor, intellectual, mnestic and coordination functions); however, differences between the "low"- and "high"-exposure groups were not significant.

Ikeda *et al.* (1980) found no significant difference in the frequency of chromosomal aberrations or sister-chromatid exchange in lymphocytes from 10 workers exposed to 10 to 220 ppm (67.8 to 1 492 mg/m^3) tetrachloroethylene compared to 11 unexposed individuals. Seiji *et al.* (1990) reported that the frequency of sister-chromatid exchange in lymphocytes obtained from 27 smoking or non-smoking workers (of either sex) employed in dry-cleaning establishments (and exposed to a geometric mean [time-weighted-average] concentration of 10 ppm [67.8 mg/m^3] for 41 months) was not significantly different from that in 26 controls; however, the frequency of sister-chromatid exchange in 12 male smokers exposed to tetrachloroethylene was significantly ($p < 0.05$) greater (18%) than in 3 male (control) nonsmokers.

2.5.3 Ecotoxicology

Numerous studies concerning the acute and chronic toxicity of tetrachloroethylene to aquatic biota at various trophic levels were identified; however, only a limited number of studies on the effects of tetrachloroethylene to terrestrial plants, and no studies on the effects to terrestrial wildlife, were identified. Data from the critical studies are also summarized in Figures 1 and 2.

Brook trout (*Salvelinus fontinalis*) at the embryo/alevin stages and rainbow trout (*Oncorhynchus mykiss*) fingerlings were considered by ATRG (1988) and Call *et al.* (1983) to be among the aquatic species most sensitive to the effects of tetrachloroethylene. The lowest-observed-effect-concentration (LOEC) for the survival of brook trout alevins to swim-up (mortality = 37%) and fry (mortality = 39%) following exposure to tetrachloroethylene for 120 days was 2.66 mg/L (ATRG, 1988). The LOEC associated with a 61% decrease in growth in brook trout surviving over 120 days was 1.52 mg/L (ATRG, 1988). The 24-hour LC_{50} for rainbow trout was 4.99 mg/L (Call *et al.*, 1983). Smith *et al.* (1991) evaluated the toxicity of tetrachloroethylene to embryo/larval flagfish (*Jordanella floridae*). Hatchability of flagfish eggs was not affected at any of the concentrations tested (0.79 to 7.81 mg/L); however, the survival of larvae after 10 days was reduced to 55% at a concentration of 4.85 mg/L (the reported LOEC) and to 20% at 7.81 mg/L tetrachloroethylene. The survival over 28 days of 1-week-old flagfish exposed simultaneously to tetrachloroethylene in the same test system as the flagfish embryo/larvae was reduced to 63% at a concentration of 5.82 mg/L; no fish survived exposure to 9.3 mg/L tetrachloroethylene.

Fathead minnow larvae (*Pimephales promelas*) [24 to 35 days old] were exposed to 6 different concentrations of tetrachloroethylene in several tests. Values for the 96-hour LC_{50}s were similar, ranging from 13.4 to 23.8 mg/L (Veith *et al.* 1983a, 1983b; Walbridge *et al.*, 1983; Broderius and Kahl, 1985; Geiger *et al.* 1985). During acute toxicity testing with the fathead minnow, Geiger *et al.* (1985) observed a number of sublethal effects (including loss of schooling behaviour, swimming near the surface, hypoactivity, darkened colouration, increased respiratory rate and loss of equilibrium) that occurred prior to death. The calculated 96-hour EC_{50} for these effects was 8.45 mg/L. Alexander *et al.* (1978) observed a loss of equilibrium, narcosis, melanization and swollen, haemorrhaged gills in fathead minnows exposed to tetrachloroethylene, and estimated a 96-hour TE_m (median tolerance effect; equivalent to an EC_{50}) of 14.4 mg/L.

Only one toxicity study of acceptable quality was identified for marine fish. Pearson and McConnell (1975) reported a 96-hour LC_{50} of 5 mg/L tetrachloroethylene for the dab (*Limanda limanda*).

For aquatic invertebrates, both Call *et al.* (1983) and Richter *et al.* (1983) published data from the same study with first instar *Daphnia magna*. Based on 2 exposure regimens (fed and unfed), 48-hour LC_{50}s of 18.1 and 9.1 mg/L, respectively, were reported. The EC_{50}s (for complete immobilization) were 8.5 and 7.5 mg/L for fed and unfed *Daphnia*, respectively. Call *et al.* (1983) conducted static acute-toxicity tests using 3rd or 4th instar midge larvae (*Tanytarsus dissimilis*). The midge appeared to be less sensitive to the effects of tetrachloroethylene than *Daphnia magna*, based on a 48-hour LC_{50} of 30.8 mg/L. LeBlanc (1980) reported a 48-hour LC_{50} of 18 mg/L

tetrachloroethylene for *Daphnia magna* that were less than 24 hours old. Richter *et al.* (1983) reported a 28-day LOEC of 1.1 mg/L for *Daphnia magna*, where growth and reproduction (numbers of young) were reduced by 7.7% and 62%, respectively. The 28-day no-observed-effect-concentration (NOEC) for effects on growth and reproduction was 0.51 mg/L tetrachloroethylene.

Lay *et al.* (1984) investigated field effects on endemic populations of *Daphnia magna* in several compartments of outdoor ponds containing 0.44 or 1.2 mg/L tetrachloroethylene. Complete mortality was observed within 3 and 4 days at 0.44 mg/L, and within 3 hours and 2 days at 1.2 mg/L tetrachloroethylene. In ponds containing 0.44 and 1.2 mg/L tetrachloroethylene, the concentration decreased below the detection limit (0.1 mg/L) within 5 and 36 days, respectively.

Pearson and McConnell (1975) reported a 48-hour LC_{50} of 3.5 mg/L tetrachloroethylene for barnacle nauplii (*Elminius modestus*), based on static tests in Atlantic seawater. Kerster and Schaeffer (1983) monitored the effect of tetrachloroethylene on the growth of brine shrimp nauplii (*Artemia salina*) over 48 hours, and, based on the results, estimated an EC_{50} of 0.25 mg/L.

Data on the toxicity of tetrachloroethylene to marine plants were only identified for unicellular algae. For *Phaeodactylum tricornutum* cultured in Atlantic seawater, the EC_{50} for the uptake of carbon dioxide during photosynthesis was estimated to be 10.5 mg/L tetrachloroethylene (Pearson and McConnell, 1975). Erickson and Hawkins (1980) exposed mixtures of various classes of marine algae (*Chlorophyceae, Cyanophyceae, Bacillariophyceae*) to tetrachloroethylene and monitored the uptake of [^{14}C]sodium bicarbonate. A 13% decrease in the uptake of radioactivity was observed at a concentration of 2.0 mg/L tetrachloroethylene; however, no effect was found at lower concentrations (0.5 or 1.0 mg/L).

The adverse effects of chloroethylenes (particularly tetrachloroethylene and trichloroethylene) on forests has been studied in Germany and Finland. It has been reported that in Fir (*Abies alba*), Norway spruce (*Picea abies*), Beech (*Fagus silvatica*) and other trees in these areas, there was an increased incidence of chlorosis (bleaching of needles), necrosis (death of needles) and premature needle loss over the last 2 decades (Frank and Frank, 1986a, 1986b; Frank, 1989). These effects were attributed to exposure to chloroethylenes under photo-activated conditions (Frank and Frank, 1985, 1986a, 1986b; Frank, 1991). The principal photodegradation product of chloroethylenes, trichloroacetic acid (a known herbicide), is also likely involved (Frank, 1990; Frank *et al.*, 1990, 1992).

In laboratory investigations, Frank and Frank (1986a) observed the effects on Norway spruce needles (*Picea abies*) exposed simultaneously to tetrachloroethylene and ultraviolet radiation. Needles that were irradiated and exposed to 14 $\mu g/m^3$ (2 ppbv) tetrachloroethylene for 5 hours had reduced concentrations of photosynthetic pigments, compared to controls. The photosynthetic pigments most affected were chlorophyll-a (reduced by 52% compared to controls) and β-carotene (reduced by 58% compared to controls). In another laboratory study, several 3- to 7-year-old Norway spruce trees were exposed (in a smog chamber) to various concentrations of tetrachloroethylene over a period of several weeks (Frank, 1990). The spruce trees were irradiated with artificial light closely matching wavelengths found in the natural environment. Chlorosis (bleaching of needles) and necrosis were observed following exposure to 3 to 6 $\mu g/m^3$ and 40 $\mu g/m^3$ tetrachloroethylene, respectively, over a period of 1 to 2 weeks. Trees died following exposure to 100 to 130 $\mu g/m^3$ tetrachloroethylene for 1 to 2 months. The observed damage was dependent upon the duration of exposure and concentration of tetrachloroethylene.

Frank and Frank (1985) reported similar effects in a field experiment in which a 10-year-old Serbian spruce (*Picea omorica*) was continuously exposed to tetrachloroethylene and trichloroethylene for 7 months. The effects observed included chlorosis and necrosis, particularly on the sun-exposed faces of the needles. Along several of the sun-exposed twigs, a total loss of chlorophyll was observed. Similar effects were observed on the sun-exposed leaves of a hornbeam shrub (*Carpinus betulus*) located 2 m downwind of the spruce tree. Concentrations of tetrachloroethylene among the branches of the spruce were monitored during the study and were as high as 12 $\mu g/m^3$ (1.7 ppbv).

General damage to trees has been reported for years in Finland, but conifers growing in Lapland are considered particularly vulnerable. Frank *et al.* (1992), who studied the new to 2-year-old needles from damaged conifers (*Pinus sylvestris* and *Picea abies*) and leaves from birch trees (*Betula pubescens*) [sampled from August 1991 to July 1992], reported that trichloroacetic acid levels ranged from 3 ng/g to 126 ng/g (wet weight). They also positively correlated these concentrations with the observed extent of needle loss. Trichloroacetic acid is the major tropospheric metabolite of tetrachloroethylene (Frank, 1990).

3.0 Assessment of "Toxic" under CEPA

3.1 CEPA 11(*a*): Environment

Tetrachloroethylene is used in Canada primarily as a cleaning and degreasing solvent associated with the dry-cleaning and metal-cleaning industries. Due to its volatility, releases of tetrachloroethylene to the Canadian environment are most often in the form of emissions to the atmosphere, although discharge in liquid effluents occurs. Furthermore, tetrachloroethylene has been released in numerous spills, some of which have been in substantial volumes. Tetrachloroethylene has been measured in air across Canada and in contaminated surface waters in the Great Lakes and St. Lawrence River regions. It has also been found in groundwaters and surface waters in several provinces of Canada, often as result of its inappropriate disposal or release from dry-cleaning facilities or landfills.

Brook trout (*Salvelinus fontinalis*) and rainbow trout (*Oncorhynchus mykiss*) have been identified to be among aquatic species most sensitive to the effects of acute and chronic exposure to tetrachloroethylene, based on a 24-hour LC_{50} of 4.99 mg/L and a 120-day LOEC for decreased growth of 1.52 mg/L, respectively. Dividing the chronic LOEC by a factor of 10, to account for differences in species sensitivity and to extrapolate laboratory findings to the field, yields an estimated effects threshold for aquatic species of 152 µg/L. Concentrations of tetrachloroethylene in surface waters in Canada are generally 10 times lower than this effects threshold.

Concentrations of tetrachloroethylene in Canadian groundwater that are considerably higher than those in surface waters have been found in several locations in 3 Canadian provinces. Since the sources of contamination involve dry-cleaning facilities or landfills, for which similar sites exist across Canada, the extent of groundwater contamination with tetrachloroethylene is likely widespread. Groundwater is part of an integrated hydrological cycle that enables surface waters to recharge, serving as sources of water to aquatic ecosystems and wildlife. The concentrations of tetrachloroethylene in a surface spring and a nearby, non-connected pond, both originating from a contaminated aquifer near New Minas, Nova Scotia, were compared to the effects threshold of 152 µg/L. Their respective levels of 244 µg/L and 177 µg/L exceed the effects threshold, suggesting that adverse effects could occur in aquatic biota at these sites, or at similar sites that may exist elsewhere in Canada.

The major route of exposure of wildlife to tetrachloroethylene is ingestion of contaminated food, based on the total daily intake estimated for the piscivorous mammal, mink (*Mustela vision*), in the St. Clair River area of southern Ontario (see Table 1). The St. Clair River area was chosen because it is the only region in Canada for which levels in surface water and fish were available. It is also considered representative of a worst-case exposure scenario, since the estimated intake is based on the maximum concentration of tetrachloroethylene in water and fish and these were higher than in other regions of the Great Lakes, and most areas in Canada.

Table 1
Estimated Total Daily Exposure to Tetrachloroethylene of a Piscivorous Mammal Around Lake St. Clair

Exposure Route	Environmental Levels[a]	Daily Rate of Consumption (per kg bw)[b]	Estimated Daily Intake (µg/kg bw/day)
Surface water	44 µg/L	0.1 L/day	4.4
Air	1.9 µg/m^3	0.55 m^3/day	1
Biota	380 ng/g (ww)	155 g/day	58.9
Total	–	–	64.3

a. The level in air is the mean level measured in an urban environment in Ontario in 1987 (Chan *et al.*, 1990); the level in surface water is the maximum level measured in the St. Clair area in 1986 (OME, 1991a); the level in fish is the maximum value measured in juvenile shiners in Lake St. Clair (OME, 1987).

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.

In the absence of toxicological data for wildlife, the results of a 90-day, sub-chronic ingestion study with laboratory rats were used as a basis for estimating an effects threshold for mammals. The NOEL from this study was 14 mg/kg bw/day (Hayes *et al.*, 1986). Dividing the NOEL by a factor of 10 to account for interspecies variability in sensitivity to tetrachloroethylene, and by another factor of 10 to account for extrapolation of a sub-chronic laboratory result to a chronic field situation, yields an effects threshold for wild mammals of 140 µg/kg bw/day. The estimated daily intake of tetrachloroethylene by mink is 2-fold lower than the effects threshold.

In Germany and Finland, phytotoxic effects of chloroethylenes, including tetrachloroethylene, on forests under circumstances where there is simultaneous exposure to radiation from natural sunlight occurring at mountain elevations, have been reported. Effects include chlorosis, necrosis, and premature needle loss. The concentrations of tetrachloroethylene at which these effects occur were not established, and there is some suggestion that the principal photodegradation product of tetrachloroethylene, trichloroacetic acid, is involved. In the laboratory, spruce (*Picea abies*) were identified to be among the most sensitive tree species to tetrachloroethylene, with chlorosis and premature needle loss being observed following exposure to concentrations of tetrachloroethylene as low as 3 $\mu g/m^3$ under irradiated conditions at natural-light wavelengths. Dividing this value by a factor of 10 to account for interspecies variations in sensitivity and to extrapolate the results of a laboratory study to the field yields an estimated effects threshold of 0.3 $\mu g/m^3$. This threshold is equivalent to mean airborne concentrations observed at a rural site, and is exceeded by mean atmospheric concentrations of tetrachloroethylene measured in various cities across Canada.

Therefore, on the basis of available information, tetrachloroethylene is entering the Canadian environment in significant quantities but does not result in concentrations that, in general, would be expected to cause adverse effects to aquatic biota or terrestrial wildlife; however, limited data suggest that atmospheric concentrations of tetrachloroethylene may be sufficient to cause adverse effects to some terrestrial plants, notably trees, in Canada. Furthermore, contamination of groundwater and groundwater-recharged surface water in Canada with tetrachloroethylene could be significant, particularly in areas where there has been inappropriate disposal of this substance from dry-cleaning facilities and landfills. It has been concluded, therefore, that tetrachloroethylene has the potential to cause harm to the environment.

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

The tropospheric half-life of tetrachloroethylene in Canada is less than 2 months, and its halogenated degradation products are short-lived. These degradation products are also water-soluble and will, therefore, be washed out quickly. The migration time of tetrachloroethylene to the stratosphere is estimated to be over 5 years, and, consequently, only minute amounts of tetrachloroethylene may reach the stratosphere. It is not, therefore, thought to be involved in the destruction of stratospheric ozone. Tetrachloroethylene absorbs in the infrared region but is generally present at low concentrations in the atmosphere and has a relatively short half-life. It is, therefore, thought to make a minor contribution to both ground-level ozone formation and to global warming.

On the basis of available information, tetrachloroethylene is not involved in the depletion of stratospheric ozone, nor is it significantly involved in the formation of ground-level ozone and global warming. It has been concluded that tetrachloroethylene is 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

Population Exposure

Estimates of the average daily intake of tetrachloroethylene by the Canadian population are summarized in Table 2. The total daily intake of tetrachloroethylene was estimated to range from approximately 1.2 to 2.7 µg/kg bw/day in various age groups of the general population. It is evident that the time spent indoors makes the greatest contribution to the overall exposure to tetrachloroethylene, while the ingestion of drinking water (generally) makes a minor contribution. The use of household products containing this substance, as well as residual tetrachloroethylene present on recently dry-cleaned clothes, are likely to be predominantly responsible for the greater levels of tetrachloroethylene observed in indoor air compared to the general ambient environment (Wallace *et al.*, 1987, 1989; Kawauchi and Nishiyama, 1989).

Table 2
Estimated Daily Intake of Tetrachloroethylene by the Canadian Population

Route of Exposure	Estimated intake of tetrachloroethylene (μg/kg bw/day) by various age groups				
	0 – 6 mo[a]	7 mo – 4 yr[b]	5 – 11 yr[c]	12 – 19 yr[d]	20+ yr[e]
Ambient Air[f]	0.01 – 0.24	0.01 – 0.32	0.01 – 0.37	0.01 – 0.31	0.01 – 0.27
Indoor Air[g]	1.21	1.63	1.88	1.56	1.40
Total Air	1.22 – 1.45	1.64 – 1.95	1.89 – 2.25	1.57 – 1.87	1.41 – 1.67
Drinking Water[h]	–	0.006 – 0.06	0.003 – 0.03	0.002 – 0.02	0.002 – 0.02
Food[i]	–	0.65	0.39	0.20	0.12
Total Intake[j]	1.22 – 1.45	2.30 – 2.66	2.28 – 2.67	1.77 – 2.09	1.53 – 1.81

a. Assumed to weigh 7 kg, breathe 2 m^3 air and drink 0 L of water per day (Environmental Health Directorate, 1992).
b. Assumed to weigh 13 kg, breathe 5 m^3 air and drink 0.8 L of water per day (Environmental Health Directorate, 1992).
c. Assumed to weigh 27 kg, breathe 12 m^3 air and drink 0.9 L of water per day (Environmental Health Directorate, 1992).
d. Assumed to weigh 57 kg, breathe 21 m^3 air and drink 1.3 L of water per day (Environmental Health Directorate, 1992).
e. Assumed to weigh 70 kg, breathe 23 m^3 air and drink 1.5 L of water per day (Environmental Health Directorate, 1992).
f. Assumed to spend 4 hours/day outdoors (Environmental Health Directorate, 1992); based on a range of mean concentrations of tetrachloroethylene (0.2 to 5.0 μg/m^3) from a national survey of sites across Canada (Dann and Wang, 1992).
g. Assumed to spend 20 hours/day indoors (Environmental Health Directorate, 1992); based on a mean concentration of tetrachloroethylene in the indoor air of 757 randomly selected homes within Canada of approximately 5.1 μg/m^3 (Otson *et al.*, 1992)
h. Based on a range of mean concentrations of tetrachloroethylene (0.1 to 0.9 μg/L) in drinking water from national (Otson *et al.*, 1982) and provincial (Environment Canada, 1989a, 1989b, 1989c, 1989d; Quebec Ministry of the Environment, 1990; Alberta Environment, 1991; OME, 1991b) surveys.
i. Based on the average levels of tetrachloroethylene in the various composite food groups and the daily Canadian intake of these food groups (Environmental Health Directorate, 1992). The average concentrations of tetrachloroethylene in the dairy, meat, cereal, fruit, vegetable and sugar composite food groups were considered to be 6.6, 12.3, 14.7, 0.8, 0.4 and 2.9 ng/g, respectively; these values were derived from the information reported by Daft (1988), which represents the only single comprehensive source. The average concentration of tetrachloroethylene in the fat and oil composite group was calculated as 12.9 ng/g, based on the results reported by Daft (1988) and Heikes (1987).
j. Available data were insufficient to estimate intake from soil.

Effects

Epidemiological studies concerning the carcinogenicity of tetrachloroethylene in humans are limited principally to investigations of workers employed in the dry-cleaning and laundry industries (usually combined), who were likely exposed to several substances in addition to tetrachloroethylene, and for whom quantitative data on cumulative exposure were not available. Although increased mortality and morbidity due to various types of cancer have been observed in workers employed in this occupational setting, owing to the lack of consistency of reported results and to possible confounding by concomitant exposure to other substances that may have contributed to the observed effects, the available information is considered inadequate to assess the carcinogenicity of tetrachloroethylene in humans.

An increased incidence of renal tubular cell adenomas and adenocarcinomas (although not statistically significant) in male rats, mononuclear cell leukemias in male and female rats, and hepatocellular adenomas (males) and carcinomas (male and female) in mice exposed by inhalation to tetrachloroethylene, have been observed in an NTP carcinogenesis bioassay (NTP, 1986). On the basis of these results, it was concluded (NTP, 1986) that there was *clear evidence* of carcinogenicity of tetrachloroethylene in male F344/N rats (although several members of the review panel believed that the results supported a designation of only "some evidence" of carcinogenicity in male rats), *some evidence* of carcinogenicity in female F344/N rats, and *clear evidence* of carcinogenicity in (male and female) $B6C3F_1$ mice. Owing to the limitations of other bioassays (NCI, 1977; Rampy *et al.*, 1978 cited in ATSDR, 1990; ECETOC, 1990, and U.S. EPA, 1985; Theiss *et al.*, 1977; Maronpot *et al.*, 1986; Van Duuren *et al.*, 1979; Milman *et al.*, 1988; Lundberg *et al.*, 1987), the results of these investigations are not useful in assessing the weight of evidence of carcinogenicity.

Generally, a substance for which there is adequate evidence of carcinogenicity in 2 species of laboratory animals (as observed in the NTP carcinogenesis bioassay for tetrachloroethylene) would be categorized in Group II (probably carcinogenic to humans) of the classification scheme developed for use in the derivation of the "Guidelines for Canadian Drinking Water Quality" (Environmental Health Directorate, 1989); however, consideration of data on possible mechanisms of action reduces the relevance of several of the increases in tumour incidence observed in the NTP bioassay in assessing the weight of evidence for the carcinogenicity of tetrachloroethylene to humans.

The increase in renal tumour cell adenomas and adenocarcinomas in male rats in the NTP bioassay was small and not statistically significant. Moreover, it is probable that the small increase in the incidence of these relatively rare tumours in male F344/N rats exposed to tetrachloroethylene is a species- and gender-specific response. The induction by tetrachloroethylene of kidney tumours in the male rat has been proposed

to be the result of enhanced cellular proliferation resulting from cell damage produced by the renal accumulation of α_{2u}-globulin (i.e., hyaline droplet formation resulting in hyaline droplet nephropathy), as well as the formation of genotoxic metabolites of tetrachloroethylene within the kidney of these animals.[1] (The weight of available data indicates that tetrachloroethylene itself is not genotoxic in either *in vivo* or *in vitro* bioassays.) Since α_{2u}-globulin is not produced in humans (Olson *et al.*, 1990), and on the basis of the results of *in vitro* enzymatic analysis of hepatic and renal extracts, there appear to be significant differences with respect to formation of the tetrachloroethylene-glutathione conjugate (the precursor of the reactive metabolite) and its subsequent metabolism in rats and humans (Green *et al.*, 1990), the induction of renal tumors in (specifically) male rats exposed to tetrachloroethylene may not be relevant to humans (or at least, humans may be much less sensitive to such effects) [Green, 1990b].

Available data indicate that the hepatotoxic effects of tetrachloroethylene in mice are due principally to trichloroacetic acid, a metabolite of tetrachloroethylene, and that the metabolism of tetrachloroethylene to trichloroacetic acid is greater in mice than in either rats (Pegg *et al.*, 1979; Schumann *et al.*, 1980; Odum *et al.*, 1988; Bolt, 1987) or humans (Ikeda and Ohtsuji, 1972). Mice appear to be more sensitive than rats to the hepatotoxic effects produced by trichloroacetic acid (Bull *et al.*, 1990; DeAngelo *et al.*, 1989). Whereas the administration of trichloroacetic acid to mice increases the incidence of hepatocellular tumors (Herren-Freund *et al.*, 1987; Bull *et al.*, 1990), DeAngelo and Daniel (1992) have reported (in abstract form) that trichloroacetic acid was not (hepato)carcinogenic in male F344 rats, based on a study in which this compound was administered (in drinking water at [mean time-weighted] doses of 3.6, 36 and 378 mg/kg bw/day) to these animals over a period of 100 to 104 weeks.

Available data indicate (although it has not been unequivocally proven) that peroxisomal proliferation may play an important role in the development of hepatic tumours in rodents. Trichloroacetic acid is a potent inducer of peroxisomal proliferation in the liver of rodents, and in some (DeAngelo *et al.*, 1989; Goldsworthy and Popp, 1987) but not all (Elcombe, 1985) studies, the effect of trichloroacetic acid on hepatic peroxisomal proliferation was greater in mice than in rats. Moreover, trichloroacetic acid inhibits gap-junction mediated intercellular communication in hepatocytes from mice but not rats (Klaunig *et al.*, 1989). Thus, the increased incidence of hepatic tumours in mice but (apparently) not rats exposed to tetrachloroethylene is consistent with the greater sensitivity of mice than rats to increases in hepatic peroxisomal proliferation and disruptions of intercellular

1. It is not possible to draw unequivocal conclusions concerning likely mechanisms by which renal tumours were induced in male rats in the NTP bioassay owing to the lack of information on relevant renal pathological effects and metabolism in these animals.

communication induced by trichloroacetic acid. If increased peroxisomal proliferation plays a critical role in the development of hepatic tumours in rodents exposed to specific substances, the observation (based on limited available data) that trichloroacetic acid stimulates such proliferation in rodent but not human hepatocytes (Elcombe, 1985) suggests that these tumours are unlikely to be relevant to humans or, at least, humans are likely to be much less sensitive to the induction of hepatic tumours by tetrachloroethylene.

Dichloroacetic acid, which has been identified as a minor urinary metabolite in mice and rats administered (orally) tetrachloroethylene (U.S. EPA, 1985; Dekant *et al.*, 1986), is hepatocarcinogenic in mice (Herren-Freund *et al.*, 1987; Bull *et al.*, 1990; DeAngelo *et al.*, 1991) and (apparently) in rats (DeAngelo and Daniel, 1992). Although the route by which tetrachloroethylene is metabolized to dichloroacetic acid has not been unequivocally defined, Dekant *et al.* (1986) have indicated that dichloroacetic acid may arise from trichlorovinylthiol, the (putative) reactive metabolite of tetrachloroethylene formed from the conjugation of tetrachloroethylene with glutathione; however, as discussed above, this metabolic pathway likely makes only a very minor (if indeed any) contribution to the overall metabolism of tetrachloroethylene in humans (Green *et al.*, 1990).

Since the observed increase in the incidence of renal tumours in male rats and hepatic tumours in male and female mice exposed to tetrachloroethylene are likely species-specific responses, both of which appear to be induced by mechanisms that are not relevant to humans or, at least, for which humans are likely to be much less sensitive, the results considered most pertinent in assessing the weight of evidence for carcinogenicity are the small increases in the incidence of spontaneously occurring mononuclear cell leukemias in a single species (i.e., male and female F344 rats) in the NTP bioassay, in which the incidence of this tumour in the non-exposed (control) rats was higher than that observed in historical controls (NTP, 1986). The proportion of animals with this tumour in the high-dose group of males and females was 74% and 58%, respectively, compared to 56% and 36% in the concurrent control groups and 29% and 19% in historical controls (NTP, 1986).

On the basis of these observations, tetrachloroethylene has been classified in Group III (possibly carcinogenic to humans) of the classification scheme developed for use in the derivation of the "Guidelines for Canadian Drinking Water Quality" (Environmental Health Directorate, 1989). Generally, for compounds classified in Group III, a tolerable-daily-intake (TDI) is derived on the basis of a no- or lowest-observed-(adverse)-effect-level (NOAEL or LOAEL) in humans or animal species (by the most relevant route of exposure) divided by an uncertainty factor, which, when considered appropriate, takes into account the limited evidence of carcinogenicity.

The available epidemiological data are considered inadequate to serve as a basis for development of a TDI. The effects of occupational exposure to tetrachloroethylene on reproduction and development, the nervous system or renal function were examined in a number of epidemiological studies; however, there were numerous shortcomings in these investigations, such as small population sizes, little or no information concerning the level or duration of exposure to tetrachloroethylene, possible concomitant exposure to other chemicals and the possible contribution to observed effects by other confounding factors. In clinical studies of volunteers exposed to tetrachloroethylene, neurological and neurobehavioral effects have been observed, but these studies are considered to be inadequate to serve as a basis for development of a TDI, since they are limited to short-term investigations of neurological effects in very small numbers of subjects.

Inhalation is considered to be the most important route of exposure to tetrachloroethylene for the general population. A TDI has been derived, therefore, on the basis of results from the longest-term study of adequate design in which tetrachloroethylene was administered by inhalation to laboratory animals (NTP, 1986). In this study, the lowest concentration of tetrachloroethylene at which adverse effects (reduced survival [in males] hepatotoxicity [males]; lung congestion and nephrotoxicity [males and females]) were observed (LOAEL) was 100 ppm (678 mg/m^3), administered to mice. It should be noted, however, that biochemical or hematological effects were not assessed in the NTP bioassay. In general, in shorter-term studies in which these end-points were examined, adverse effects have not been observed following inhalation of tetrachloroethylene at concentrations less than the LOAEL in mice observed from the NTP bioassay. In a sub-chronic study, increases in serum enzymes were reported in NMRI mice exposed to 150 ppm (1 017 mg/m^3) [Kjellstrand *et al.*, 1984]. Small (10% to 20%) increases in liver weight in male and female NMRI mice were observed following 30 days exposure to 9 ppm (61 mg/m^3) tetrachloroethylene (Kjellstrand *et al.*, 1984); however, this effect was not confirmed in another strain of mice (B6C3F$_1$) exposed to a higher concentration (200 ppm; 2 712 mg/m^3) for 14, 21 or 28 days (Odum *et al.*, 1988).

In the few studies in which the potential neurotoxicity of tetrachloroethylene has been examined in laboratory animals, meaningful effects have been observed only at concentrations higher than the LOAEL in mice observed in the NTP bioassay. The lowest concentration at which behavioral effects have been observed is 200 ppm (1 356 mg/m^3) tetrachloroethylene, in a study in which rats were exposed to this substance for 4 days (Savolainen *et al.*, 1977). Only minor biochemical effects on the brain, the significance of which is unclear, have been observed at lower concentrations (as low as 60 ppm [407 mg/m^3] following exposure of Mongolian gerbils for 90 days [Rosengren *et al.*, 1986]). In the only identified study of potential immunological effects produced by tetrachloroethylene, diminished resistance to streptococcal

pneumonia and reduced pulmonary bactericidal activity were observed in mice exposed for 3 hours to a concentration (50 ppm; 339 mg/m^3) slightly less than the LOAEL in mice in the NTP bioassay (Aranyi *et al.*, 1986).

Therefore, on the basis of the LOAEL of 100 ppm (678 mg/m^3) observed in the NTP bioassay, a TDI has been derived as follows:

$$\text{TDI} = \frac{[(678\ \text{mg/m}^3) \times (0.043\ \text{m}^3\text{/day}) \times (6/24) \times (5/7)]}{(0.0305\ \text{kg}) \times 5\ 000}$$

$$= 34\ \mu\text{g/kg bw/day}$$

where:

- 678 mg/m^3 is the LOAEL (reduced survival and hepatotoxic effects in males, lung congestion and nephrotoxic effects [in males and females]) in mice, in the longest-term study of adequate design in which tetrachloroethylene was administered by inhalation (NTP, 1986);
- 0.043 m^3/day is the assumed volume of air inhaled by mice (NIOSH, 1985);
- 6/24 and 5/7 is the conversion of 6 hours/day, 5 days/week to continuous exposure;
- 0.0305 kg is the average body weight of the mice in the NTP (1986) study; and
- 5 000 is the uncertainty factor (10 × for intraspecies variation, 10 × for interspecies variation, 10 × for use of a LOAEL rather than a NOAEL, 5 × for limited evidence of carcinogenicity); an additional factor for limitations of the study (i.e., lack of assessment of biochemical and hematological effects) was not incorporated since, in general, in shorter-term studies in which these end-points were examined, adverse effects have not been observed at concentrations less than the value used here as the basis for development of the TDI.[2]

In order to ensure that the TDI derived on the basis of inhalation studies is sufficiently protective, it is also possible to derive a TDI on the basis of studies in which tetrachloroethylene was administered by ingestion. With the exception of one investigation in which reversible erythropoietic damage was reported at low concentrations (50 µg/kg bw/day) [Marth, 1987] but not confirmed in other studies, the lowest NOEL (based on a "theoretical daily dose" estimated by the authors) in the longest-term (90-day) study conducted to date in which tetrachloroethylene was administered orally (in 4% Emulphor in drinking water) to rats is 14 mg/kg bw/day, based on effects on body weight gain, the ratio of liver or kidney weight to body weight, and serum 5'-nucleotidase activity at the next highest dose (Hayes *et al.*,

2. Owing to the paucity of available information on interspecies variation in the concentrations at which the oxidative metabolism of tetrachloroethylene is limited and to the role of dichloroacetic acid in the aetiology of toxic effects in various species, it was also not possible to take interspecies variation in metabolism into account in derivation of the TDI.

1986). Similarly, a LOEL of 20 mg/kg bw/day for a slight increase in liver weight was reported by Buben and O'Flaherty (1985) in a 6-week study in mice. Values for the TDI, which would be derived on the basis of the results of these 2 studies, are within the same order of magnitude as that calculated above on the basis of results of bioassays in which animals were exposed by inhalation.

The estimated total daily intake of tetrachloroethylene for various age groups in the general population in Canada ranges from approximately 1.2 to 2.7 µg/kg bw/day, based on currently available information. It is possible that exposure may be increased somewhat (although available information is insufficient for quantitation) for populations residing in the vicinity of dry-cleaning establishments. The estimated average daily intakes of tetrachloroethylene for the general population in Canada are approximately 13- to 28-fold lower than the TDI derived above from inhalation studies in laboratory animals. Although the difference between the TDI and estimated intake at the lower end of this range is small in comparison to that for most other Priority Substances (i.e., 13-fold), the TDI is considered to be conservative, since, on the basis of available metabolic data, it seems likely that humans are less sensitive to the toxic effects of tetrachloroethylene than mice, and the commonly used additional factor of 10 × for interspecies variation has been incorporated.

Therefore, on the basis of the available data, it has been concluded that tetrachloroethylene 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

Therefore, based upon the available data, it has been concluded that tetrachloroethylene is entering the environment in quantities or under conditions that may be harmful to the environment; however, this substance is not entering the environment in quantities or under conditions that may constitute a danger to the environment on which human life depends, or to human life or health.

4.0 Recommendations

In view of the small difference between the estimated total daily intake and the TDI of tetrachloroethylene, it is important that exposure of the Canadian population to this substance continue to be monitored, to ensure that it does not increase to any significant extent.

In addition, generation of additional data in the following areas is desirable:

(i) characterization of the extent of contamination of Canadian groundwater by tetrachloroethylene, and the movement of this substance in this medium as well as in hydrologically connected surface waters in Canada;

(ii) investigations of the mechanisms by which tetrachloroethylene induces tumours in laboratory animals and their relevance to humans;

(iii) studies of the effects on terrestrial plants, especially trees and Canadian commercial crops, due to atmospheric exposure to tetrachloroethylene, under conditions found in the Canadian environment;

(iv) sediment bioassays to enable interpretation of effects of high sediment concentrations on benthic organisms in contaminated areas;

(v) soil bioassays to enable interpretation of effects of high soil concentrations on soil-dwelling biota; and

(vi) toxicity tests involving the various environmental routes of exposure to representative wildlife species (mammals, birds, reptiles and invertebrates).

5.0 References

Ahlborg, G. 1990. Pregnancy outcome among women working in laundries and dry-cleaning shops using tetrachloroethylene. Am. J. Ind. Med. 17: 567–575.

Ahmad, N., D. Benoit, L. Brooke, D. Call, A. Carlson, D. DeFoe, J. Huot, A. Moriarty, J. Richter, P. Shubat, G. Veith, and C. Walbridge. 1984. Aquatic toxicity tests to characterize the hazard of volatile organic chemicals in water: a toxicity data summary (EPA-600/S3-84-009). 4 pp.

Alberta Environment. 1991. Personal communication. Environmental Protection Services, Municipal Branch.

Alexander, H.C., W.M. McCarty, and E.A. Bartlett. 1978. Toxicity of perchloroethylene, trichloroethylene, 1,1,1-trichloroethane, and methylene chloride to fathead minnows. Bull. Environ. Contam. Toxicol. 20: 344–352.

Allan, R.J. 1988. Toxic chemical pollution of the St. Lawrence River (Canada) and its upper estuary. Water Sci. Technol. 20: 77–88.

Altmann, L., A. Botterger, and H. Wiegand. 1990. Neurophysiological and psychophysical measurements reveal effects of acute low-level organic solvent exposure in humans. Int. Arch. Occup. Environ. Health 62: 493–499.

Aranyi, C., W.J. O'Shea, J.A. Graham, and F.J. Miller, 1986. The effects of inhalation of organic chemical air contaminants on murine lung host defences. Fund. Appl. Toxicol. 6: 713–720.

ATRG (Aquatic Toxicity Research Group). 1988. Aquatic Toxicity of Multiple Organic Compounds, Part II: Chlorinated Ethanes and Chlorinated Ethylenes. Summary Report-Interim prepared for the Ontario Ministry of the Environment, ATRG, Lakehead University, Thunder Bay, Ontario. 96 pp.

ATSDR (Agency for Toxic Substances and Disease Registry). 1990. Toxicological Profile for Tetrachloroethylene. United States Public Health Service. 102 pp.

ATSDR (Agency for Toxic Substances and Disease Registry). 1991. Toxicological Profile for Tetrachloroethylene. (Draft Update). United States Public Health Service. 141 pp.

Banerjee, S., S.H. Yalkowsky, and S.C. Valvani. 1980. Water solubility and octanol/water partition coefficients of organics. Limitations of the solubility-partition coefficient correlation. Environ. Sci. Technol. 14: 1227–1229.

Barrio-Lage, G., F.Z. Parsons, R.S. Nassar, and P.A. Lorrenzo. 1986. Sequential dehalogenation of chlorinated ethenes. Environ. Sci. Technol. 20: 96–99.

Barrows, M.E., S.R. Petrocelli, K.J. Macek, and J.J. Carroll. 1980. Bioconcentration and elimination of selected water pollutants by the bluegill sunfish (*Lepomis macrochirus*). In: R. Haque, ed. Dynamics, Exposure, and Hazard Assessment of Toxic Chemicals. Ann Arbor Science, Ann Arbor, Michigan. pp. 379–392.

Bell, R.W., R.E. Chapman, B.D. Kruschel, M.J. Spencer, K.V. Smith, and M.A. Lusis. 1991. The 1990 Toronto Personal Exposure Pilot (PEP) Study. Draft Report. Air Resources Branch, Ontario Ministry of the Environment. ARB-207-90.

Blair, A., P. Decoufle, and D. Grauman. 1979. Causes of death among laundry and dry-cleaning workers. Am. J. Public Health 69: 508–511.

Blair, A., P.A. Stewart, P.E. Tolbert, D. Grauman, F.X. Moran, J. Vaught, and J. Rayner. 1990. Cancer and other causes of death among a cohort of dry-cleaners. Br. J. Ind. Med. 47: 162–168.

Bolt, H.M. 1987. Pharmacokinetic factors and their implication in the induction of mouse liver tumors by halogenated hydrocarbons. Arch. Toxicol. Suppl. 10: 190–203.

Bonnet, P., J.M. Francin, D. Gradinski, G. Raoult, and D. Zissu. 1980. Détermination de la concentration léthale$_{50}$ des principaux hydrocarbures aliphatiques chlorés chez le rat. Arch. Mal. Prof. 41: 317–321.

Bosco, M.G., I. Figa-Talamanca, and S. Salerno. 1987. Health and reproductive status of female workers in dry-cleaning shops. Int. Arch. Occup. Environ. Health 59: 295–301.

Bouwer, E.J., B.E. Rittmann, and P.L. McCarty. 1981. Anaerobic degradation of halogenated 1- and 2-carbon organic compounds. Environ. Sci. Technol. 15: 596–599.

Briving, C., I. Jacobsen, A. Hamberger, P. Kjellstrand, K.G. Haglid, and L.E. Rosengren. 1986. Chronic effects of perchloroethylene and trichloroethylene in the gerbil brain amino acids and glutathione. Neurotoxicol. 7: 101–108.

Broderius, S., and M. Kahl. 1985. Acute toxicity of organic chemical mixtures to the fathead minnow. Aquat. Toxicol. 6: 307–322.

Brodie, N., and N. McLeod. 1984. Tetrachloroethylene Well Contamination in New Minas. Nova Scotia Dept. of the Environment, January 16, 1984.

Brown, D.P., and S.D. Kaplan. 1987. Retrospective cohort mortality study of dry-cleaner workers using perchloroethylene. J. Occup. Med. 29: 535–541.

Buben, J.A., and E.J. O'Flaherty. 1985. Delineation of the role of metabolism in the hepatotoxicity of trichloroethylene and perchloroethylene: a dose-effect study. Toxicol. Appl. Pharmacol. 78: 105–122.

Budavari, S. 1989. The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals. 11th Edition. Merck & Co., Inc., Rahway, New Jersey. 951 pp.

Bull, R.J., I.M. Sanchez, M.A. Nelson, J.L. Larson, and A.J. Lansing. 1990. Liver tumor induction in B6C3F$_1$ mice by dichloroacetate and trichloroacetate. Toxicol. 63: 341–359.

Bunce, N.J. 1992. Rates of Tropospheric Transformation of Certain Chlorinated Aliphatic Pollutants in the Troposphere. Unpublished report. Prepared for Environment Canada.

Calder, W.A., and E.J. Braun. 1983. Scaling of osmotic regulation in mammals and birds. Am. J. Physiol. 244: R601–R606.

Call, D.J., L.T. Brooke, N. Ahmad, and J.E. Richter. 1983. Toxicity and Metabolism Studies with EPA Priority Pollutants and Related Chemicals in Freshwater Organisms. Office of the United States Environmental Protection Agency, Duluth, Minnesota. (EPA 600/3-83-095). 120 pp.

Callahan, M.A., M.W. Slimak, N.W. Gabel, I.P. May, C.F. Fowler, J.R. Freed, P. Jennings, R.L. Durfee, F.C. Whitmore, B. Maestri, W.R. Mabey, B.R. Hold, and C. Gould. 1979. Water Related Environmental Fate of 129 Priority Pollutants, Volume II. Office of Toxic Substances, United States Environmental Protection Agency, Washington, D. C. (EPA 4404/4-79-0296).

Cameron, A., and N. McLeod. 1983. The Occurrence of Trichloroethylene and Tetrachloroethylene in Well Water in Amherst, N.S. Nova Scotia Dept. of Environment. 1575-CUM-A2.

Carpenter, C.P. 1937. The chronic toxicity of tetrachloroethylene. J. Ind. Hyg. Toxicol. 19: 323–326.

Chan, C.C., L. Valner, J.W. Martin, and D.T. Williams. 1990. Determination of organic contaminants in residential indoor air using an adsorption-thermal desorption technique. J. Air Waste Manage. Assoc. 40: 62–67.

Chen, E.C. 1993. Tetrachloroethylene: Background Document for "The Strategic Options Report." Draft. March 1993, Chemicals Industries Division, Industrial Programs Branch, Environment Canada. 23 pp.

CIS (Corpus Information Services). 1990. CPI Product Profile, Perchloroethylene. Corpus Information Services, Don Mills, Ontario. 3 pp.

Comba, M.E., and K.L.E. Kaiser. 1983. Determination of volatile contaminants at the ng/L level in water by capillary gas chromatography with electron capture detection. Intern. J. Environ. Anal. Chem. 16: 17–31.

Comba, M.E., and K.L.E. Kaiser. 1985. Volatile hydrocarbons in the Detroit River and their relationship with contaminant sources. J. Great Lakes Res. 11: 404–418.

Comba, M.E., V.S. Palabrica, J. Wasslen, G.A. Bengert, and K.L.E. Kaiser. 1989. St. Lawrence River trace organic contaminants study (Part II), 1986. National Water Research Institute, Contribution No. 89-51. 95 pp.

Correia, Y., G.J. Martens, F.H. Van Mensch, and B.P. Wim. 1977. The occurrence of Trichloroethylene, Tetrachloroethylene, and 1,1,1-Trichloroethane in Western Europe in Air and Water. Atmospheric Environment. 11: 1113–1116.

Daft, J.L. 1988. Rapid determination of fumigant and industrial chemical residues in food. J. Assoc. Off. Anal. Chem. 71: 748–760.

Dann, T., and D. Wang. 1992. Measurement of Volatile Organic Compounds in Canada 1987-1990. Conservation and Protection, River Road Environmental Technology Centre (in preparation).

DeAngelo, A.B., F.B. Daniel, L. McMillan, P. Wernsing, and R.E. Savage. 1989. Species and strain sensitivity to the induction of peroxisome proliferation by chloroacetic acids. Toxicol. Appl. Pharmacol. 101: 285–298.

DeAngelo, A.B., F.B. Daniel, J.A. Stober, and G.R. Olson. 1991. The carcinogenicity of dichloroacetic acid in the male $B6C3F_1$ mouse. Fund. Appl. Toxicol. 16: 337–347.

DeAngelo, A.B., and F.B. Daniel. 1992. An evaluation of the carcinogenicity of the chloroacetic acids in the male F344 rat. The Toxicologist. 12: 206 (abstract).

Dekant, W., M. Metzler, and D. Henschler. 1986. Identification of S-1,2,2,-trichlorovinyl-N-acetylcysteine as a urinary metabolite of tetrachloroethylene: bioactivation through glutathionine conjugation as a possible explanation of its nephrocarcinogenicity. J. Biochem. Toxicol. 1: 57–72.

Dekant, W., S. Vamvakas, M. Koob, A. Kochling, W. Kanhai, D. Muller, and D. Henschler. 1990a. A mechanism of haloalkene-induced renal carcinogenesis. Environ. Health Perspec. 88: 107–110.

Dekant, W., S. Vamvakas, and M.W. Anders. 1990b. Biosynthesis, bioactivation and mutagenicity of S-conjugates. Toxicol. Lett. 53: 53–58.

Diezel, T., H.J. Schreiber, L. Rohrschneider, and G. Wünsch. 1988. Determination of easily volatile halogenated hydrocarbons in spruce needles. Fresenius Z. Anal. Chem. 330: 640–645

Dimitriades, B., B.W. Gay, Jr., R.R. Arnts, and R.S. Seila. 1983. Photochemical reactivity of perchloroethylene: a new appraisal. J. Air. Pollut. Control Assoc. 33: 575–585.

DGAIS (Dangerous Goods Accident Information System). 1992. Tetrachloroethylene Accidents 1988–1992. Transport of Dangerous Good Directorate, Transport Canada.

Doyle, R. 1992. Unpublished data. Senior Environmental Officer, Ontario Ministry of the Environment Ottawa, Ontario. February 27, 1992.

Duh, R-Y., and N.R. Asal. 1984. Mortality among laundry and dry-cleaning workers in Oklahoma. Am. J. Public Health 74: 1278–1280.

ECETOC (European Chemical Industry Ecology and Toxicology Centre). 1990. Tetrachloroethylene: Assessment of Human Carcinogenic Hazard. Technical Report No. 37.

Echeverria, D., R. White, and C. Sampiao. 1991. A neurobehavioral evaluation of PCE exposure in patients and dry-cleaners: possible relationship between clinical and pre-clinical effects. Neurotoxicol. 12: 134–135 (abstract).

Eckert, B. 1993. Unpublished data. Senior Environmental Officer, Ontario Ministry of the Environment, Ottawa, Ontario. March 24, 1993.

Elcombe, C.R. 1985. Species differences in carcinogenicity and peroxisome proliferation due to trichloroethylene: a biochemical human hazard assessment. Arch. Toxicol. Suppl. 8: 6–17.

Environment Canada. 1989a. Atlantic Region Federal-Provincial Toxic Chemical Survey of Municipal Drinking Water Sources. Data Summary Report 1985-1988, Province of Newfoundland. Inland Waters Directorate, Moncton, New Brunswick. IWD-AR-WQB-89-157.

Environment Canada. 1989b. Atlantic Region Federal-Provincial Toxic Chemical Survey of Municipal Drinking Water Sources. Data Summary Report 1985-1988, Province of Prince Edward Island. Inland Waters Directorate, Moncton, New Brunswick. IWD-AR-WQB-89-156.

Environment Canada. 1989c. Atlantic Region Federal-Provincial Toxic Chemical Survey of Municipal Drinking Water Sources. Data Summary Report 1985-1988, Province of Nova Scotia. Inland Waters Directorate, Moncton, New Brunswick. IWD-AR-WQB-89-154.

Environment Canada. 1989d. Atlantic Region Federal-Provincial Toxic Chemical Survey of Municipal Drinking Water Sources. Data Summary Report 1985-1988, Province of New Brunswick. Inland Waters Directorate, Moncton, New Brunswick. IWD-AR-WQB-89-155.

Environment Canada. 1990. Chlorinated hydrocarbons use pattern update 1989. Commercial Chemicals Branch, Environment Canada.

Environmental Health Directorate. 1989. Derivation of maximum acceptable concentrations and aesthetic objectives for chemicals in drinking water. In: Guidelines for Canadian Drinking Water Quality – Supporting Documentation. Health and Welfare Canada, Bureau of Chemical Hazards.

Environmental Health Directorate. 1992. Unpublished. Draft internal report on recommended approach and reference values for exposure assessments for CEPA Priority Substances. Bureau of Chemical Hazards, January 21, 1992.

Erickson, S.J., and C.E. Hawkins. 1980. Effects of halogenated organic compounds on photosynthesis in estuarine phytoplankton. Bull. Environ. Contam. Toxicol. 24: 910–915.

Eskenazi, B., A.J. Wyrobek, L. Fenster, D.F. Katz, M. Sadler, J. Lee, M. Hudes, and D.M. Rempel. 1991a. A study of the effect of perchloroethylene exposure on semen quality in dry-cleaning workers. Am. J. Ind. Med. 20: 575–591.

Eskenazi, B., L. Fenster, M. Hudes, A.J. Wyrobek, D.F. Katz, J. Gerson, and D.M. Rempel. 1991b. A study of the effect of perchloroethylene exposure on the reproductive outcomes of wives of dry-cleaning workers. Am. J. Ind. Med. 20: 593–600.

Fernandez, J., E. Guberan, and J. Caperos. 1976. Experimental human exposures to tetrachlorethylene vapor and elimination in breath after inhalation. Am. Ind. Hyg. Assoc. J. 37: 143–150.

Figge, K. 1990. Luftgetragene, organische Stoffe in Blattorganen [Airborne organic compounds in leave tissues]. Umweltchem. Ökotox. 2: 200–207 (in German).

Fogel, M.M., A.R. Taddeo, and S. Fogel. 1986. Biodegradation of chlorinated ethenes by a methane utilizing mixed culture. Appl. Environ. Microbiol. 51: 720–724.

Franchini, I., A. Cavatorta, M. Falzoi, S. Lucertini, and A. Mutti. 1983. Early indicators of renal damage in workers exposed to organic solvents. Int. Arch. Occup. Environ. Health 52: 1–9.

Frank, H., and W. Frank. 1985. Chlorophyll-bleaching by atmospheric pollutants and sunlight. Naturwissenschaften 72: 139–141.

Frank, H., and W. Frank. 1986a. Photochemical activation of chloroethenes leading to destruction of photosynthetic pigments. Experientia 42: 1267–1269.

Frank, H., and W. Frank. 1986b. Photoaktivierung luftgetragener Chlorkohlenwasserstoffe [Photoactivation of airborne chlorinated hydrocarbons]. Nachr. Chem. Tech. Lab. 34(1): 15–20 (in German).

Frank, H. 1989. Neuartige Waldschäden und luftgetragene Chlorkohlenwasserstoffe [A new kind of forest damage and airborne chlorinated hydrocarbons]. UWSF - Z. Umweltchem. Ökotox. 4: 7–11 (in German).

Frank, H., 1990. Phytotoxizität flüchtiger Halogenkohlenwasserstoffe [Phytotoxicity of volatile halogenated hydrocarbons]. Materialien - 72, Bayerisches Staatsministerium für Landesentwicklung und Umweltfragen: 43 (in German).

Frank, H., A. Vincon, J. Reiss, and H. Scholl. 1990. Trichloroacetic acid in the foliage of forest trees. J. High Resol. Chromatogr. 13: 733–736.

Frank, H. 1991. Airborne chlorocarbons, photooxidants, and forest decline. Ambio 20(1): 13–18.

Frank, H., W. Frank, H.J.C. Neves, and R. Englert. 1991. Automated trace analysis of airborne C_1- and C_2-halocarbons. Fresenius Z. Anal. Chem. 340: 678–683.

Frank, H., H. Scholl, S. Sutinen, and Y. Norokorpi, 1992. Trichloroacetic acid in conifer needles in Finland. Ann. Bot. Fenn. (in press).

Freedman, D.L., and J.M. Gossett. 1989. Biological reductive dechlorination of tetrachloroethylene and trichloroethylene to ethylene under methanogenic conditions. Appl. Environ. Microbiol. 55: 2144–2151.

Friberg, L., B. Kylin, and A. Nystrom. 1953. Toxicities of trichloroethylene and tetrachloroethylene and Fujiwara's pyridine-alkali reactions. Acta Pharmacol. Toxicol. 9: 303–312.

Gay, Bw, P.L. Hanst, J.J. Bufalini, and R.C. Noonan. 1976. Atmospheric oxidation of chlorinated ethylenes. Environ. Sci. Technol. 10: 58–67.

Geiger, D.L., C.E. Northcott, D.J. Call, and L.T. Brooke. 1985. Acute toxicities of organic chemicals to fathead minnows (*Pimephales promelas*), Volume 2. Center for Lake Superior Environmental Studies, University of Wisconsin-Superior. 326 pp.

Ghantous, H., B.R.G. Danielsson, L. Dencker, J. Gorczak, and O. Vesterberg. 1986. Trichloroacetic acid accumulates in the murine amniotic fluid after tri- and tetrachloroethylene inhalation. Acta Pharmacol. Toxicol. 58: 105–114.

Golder Associates. 1989. Interim report on supplementary hydrogeological investigations. Golder Associates Ltd., Vancouver, British Columbia.

Goldsworthy, T.L., and J.A. Popp. 1987. Chlorinated hydrocarbon-induced peroxisomal enzyme activity in relation to species and organ carcinogenicity. Toxicol. Appl. Pharmacol. 88: 225–233.

Goldsworthy, T.L., O. Lyght, V.L. Burnett, and J.A. Popp. 1988. Potential role of α-2μ-globulin, protein droplet accumulation and cell replication in the renal carcinogenicity of rats exposed to trichloroethylene, perchloroethylene and pentachloroethane. Toxicol. Appl. Pharmacol. 96: 367–379.

Green, T. 1990a. Species differences in carcinogenicity. The role of metabolism in human risk evaluation. Teratogen. Carcinogen. Mutagen. 10: 103–113.

Green, T. 1990b. Chloroethylenes: a mechanistic approach to human risk evaluation. Annu. Rev. Pharmacol. Toxicol. 30: 73–89.

Green, T., J. Odum, J.A. Nash, and J.R. Foster. 1990. Perchloroethylene-induced rat kidney tumors: an investigation of the mechanisms involved and their relevance to humans. Toxicol. Appl. Pharmacol. 103: 77–89.

Hake, C.L., and R.D. Stewart. 1977. Human exposure to tetrachloroethylene: inhalation and skin contact. Environ. Health Perspec. 21: 231–238.

Hallett, D.J., R.J. Norstrom, F.I. Onuska, and M.E. Comba. 1982. Incidence of chlorinated benzene and chlorinated ethylenes in Lake Ontario Herring gulls. Chemosphere 11: 277–285.

Hansch, C., and A. Leo. 1985. Medchem Project Issue No. 26. Pomona College, Claremont, California. (cited in U.S. EPA, 1988).

Hayes, J.R., L.W. Condie, and J.F. Borzelleca. 1986. The subchronic toxicity of tetrachloroethylene (perchloroethylene) administered in the drinking water of rats. Fund. Appl. Toxicol. 7: 119–125.

Heikes, D.L. 1987. Purge and trap method for determination of volatile halocarbons and carbon disulfide in table-ready food. J. Assoc. Off. Anal. Chem. 70: 215–226.

Hemminki, K., I. Saloniemi, K. Luoma, T. Salonen, T. Partanen, H. Vainio, and E. Hemminki. 1980a. Transplacental carcinogens and mutagens: childhood cancer, malformations, and abortions as risk indicators. J. Toxicol. Environ. Health 6: 1115–1126.

Hemminki, K., E. Franssila, and H. Vainio. 1980b. Spontaneous abortions among female chemical workers in Finland. Int. Arch. Occup. Environ. Health 45: 123–126.

Herren-Freund, S.L., M.A. Pereira, M.D. Khoury, and G. Olson. 1987. The carcinogenicity of trichloroethylene and its metabolites trichloroacetic acid and dichloroacetic acid in mouse liver. Toxicol. Appl. Pharmacol. 90: 183–189.

Holliday, M.G., and J.M. Park. 1991. Tetrachloroethylene: An Environmental Health Effects Review. Prepared for Priority Substances Section, Health Protection Branch, Health and Welfare Canada, Ottawa, Ontario.

Howard, P.H. 1990. Tetrachloroethylene. In: Handbook of Environmental Fate and Exposure Data for Organic Chemicals. Volume II. Lewis Publishers. pp. 418–429.

IARC (International Agency for Research on Cancer). 1979. Some halogenated hydrocarbons. In: Monographs on the evaluation of carcinogenic risk of chemicals to man, Volume 20. 491–514.

Ikeda, M. 1977. Metabolism of trichloroethylene and tetrachloroethylene in human subjects. Environ. Health Perspec. 21: 239–245.

Ikeda, M., and Ohtsuji, H. 1972. A comparative study of the excretion of Fujiwara reaction-positive substances in urine of humans and rodents given trichloro- or tetrachloro-derivatives of ethane and ethylene. Br. J. Ind. Med. 29: 99–104.

Ikeda, M., A. Koizumi, T. Watanabe, A. Endo, and K. Sato. 1980. Cytogenetic and cytokinetic investigations on lymphocytes from workers occupationally exposed to tetrachloroethylene. Toxicol. Lett. 5: 251–256.

IPB (Industrial Programs Branch). 1991. Background Information for an Environmental Code of Practice for Dry Cleaning Facilities. Industrial Programs Branch, Environment Canada.

Jackson, R.E., A.S. Crowe, S. Lesage, and M.W. Priddle. 1988. Aquifer contamination and restoration at the Gloucester Landfill, Ontario, Canada. In: Proceedings of the IAHS Third Scientific Assembly, NWRI Contribution #88–96. 8 pp.

Kaiser, K.L.E., M.E. Comba, and H. Huneault. 1983. Volatile halocarbon contaminants in the Niagara River and in Lake Ontario. J. Great Lakes Res. 9: 212–223.

Kaiser, K.L.E., and M.E. Comba. 1986a. Tracking river plumes with volatile halocarbon contaminants: the St. Clair River-Lake St. Clair example. Environ. Toxicol. Chem. 5: 965–976.

Kaiser, K.L.E., and M.E. Comba. 1986b. Volatile halocarbon contaminant survey of the St. Clair River. Water Pollut. Res. J. Can. 21: 323–331.

Kaiser, K.L.E., and V.S. Palabrica. 1991. *Photobacterium phosphoreum* toxicity data index. Water Poll. Res. J. Canada 26(3): 361–431.

Katz, R.M., and D. Jowett. 1981. Female laundry and dry-cleaning workers in Wisconsin: a mortality analysis. Am. J. Public Health 71: 305–307.

Kawauchi, T., and K. Nishiyama. 1989. Residual tetrachloroethylene in dry-cleaned clothes. Environ. Res. 48: 296–301.

Kerster, H.W., and D.J. Schaeffer. 1983. Brine shrimp (*Artemia salina*) nauplii as a teratogen test system. Ecotoxicol. Environ. Saf. 7: 342–349.

Kjellstrand, P., B. Holmquist, M. Kanje, P. Alm, S. Romare, I. Jonsson, L. Mansson, and M. Bjerkemo. 1984. Perchloroethylene: effects on body and organ weights and plasma butyrylcholinesterase activity in mice. Acta Pharmacol. Toxicol. 54: 414–424.

Klaunig, J.E., R.J. Ruch, and E.L.C. Lin. 1989. Effects of trichloroethylene and its metabolites on rodent hepatocyte intercellular communication. Toxicol. Appl. Pharmacol. 99: 454–465.

Koppel, C., I. Arndt, U. Arendt, and P. Koeppe. 1985. Acute tetrachloroethylene poisoning-blood elimination kinetics during hyperventilation therapy. Clin. Toxicol. 23: 103–115.

Kyrklund, T., P. Kjellstrand, and K. G. Haglid. 1990. Long-term exposure of rats to perchloroethylene with and without a post-exposure solvent-free recovery period: effects on brain lipids. Toxicol. Lett. 52: 279–285.

Kyyronen, P., H. Taskinen, M-L. Lindbohm, K. Hemminki, and O. Heinonen. 1989. Spontaneous abortions and congenital malformations among women exposed to tetrachloroethylene in dry-cleaning. J. Epidemiol. Comm. Health 43: 346–351.

Laengner, M. 1992. Unpublished data. Area Supervisor, Ontario Ministry of the Environment, Barrie, Ontario.

Lau, Y.L., and J. Marsalek. 1986. Movement of perchloroethylene in flowing water. Water Pollut. Res. J. Can. 21: 303–308.

Lauwerys, R., J. Herbrand, J.P. Buchet, A. Bernard, and J. Gaussin. 1983. Health surveillance of workers exposed to tetrachloroethylene in dry-cleaning shops. Int. Arch. Occup. Environ. Health 52: 69–77.

Lay, J.P., W. Schauerte, W. Klein, and F. Korte. 1984. Influence of tetrachloroethylene on the biota of aquatic systems: toxicity to phyto- and zooplankton species in compartments of a natural pond. Arch. Environ. Contam. Toxicol. 13: 135–142.

LeBlanc, G.A. 1980. Acute toxicity of priority pollutants to water flea (*Daphnia magna*). Bull. Environ. Contam. Toxicol. 24: 684–691.

Lesage, S., R.E. Jackson, M.W. Priddle, and P. Riemann. 1990. Occurrence and fate of organic solvent residues in anoxic groundwater at the Gloucester Landfill, Canada. Environ. Sci. Technol. 24: 559–566.

Levine, B., M.F. Fierro, S.W. Goza, and J.C. Valentour. 1981. A tetrachloroethylene fatality. J. Forensic. Sci. 26: 206–209.

Lindbohm, M-L., H. Taskinen, M. Sallmen, and K. Hemminki. 1990. Spontaneous abortions among women exposed to organic solvents. Am. J. Ind. Med. 17: 449–463.

Lundberg, I., J. Hogberg, T. Kronevi, and B. Holmberg. 1987. Three industrial solvents investigated for tumor promoting activity in the rat liver. Cancer Lett. 36: 29–33.

Lynge, E., and L. Thygesen. 1990. Primary liver cancer among women in laundry and dry-cleaning work in Denmark. Scand. J. Work Environ. Health 16: 108–112.

Maronpot, R.R., M.B. Shimkin, H.P. Witschi, L.H. Smith, and J.M. Cline. 1986. Strain A mouse pulmonary tumor test results for chemicals previously tested in the National Cancer Institute carcinogenicity tests. JNCI 76: 1101–1112.

Marsalek, J. 1986. Municipal sources of selected trace organics in Sarnia. Water Pollut. Res. J. Canada 21: 422–432.

Marth, E. 1987. Metabolic changes following oral exposure to tetrachloroethylene in subtoxic concentrations. Arch. Toxicol. 60: 293–299.

McDonald, A.D., B. Armstrong, N.M. Cherry, C. Delorme, A. Diodati-Nilon, J.C. McDonald, and D. Robert. 1986. Spontaneous abortion and occupation. J. Occup. Med. 28: 1232–1238.

McDonald, A.D., J.C. McDonald, B. Armstrong, N.M. Cherry, C. Delorme, A. Diodati-Nilon, and D. Robert. 1987. Occupation and pregnancy outcome. Br. J. Ind. Med. 44: 512–526.

McLaughlin, J.K., H.S.R. Malker, B.J. Stone, J.A. Weiner, B.K. Malker, J.L.E. Ericsson, W.J. Blot, and J.F. Fraumeni. 1987. Occupational risks for renal cancer in Sweden. Br. J. Ind. Med. 44: 119–123.

McLeod, N., A. Cameron, and D. Gates. 1985. Tetrachloroethylene Contamination in Truro Wells. Progress Reports 3/23/84, 6/21/84 and 4/9/85. Nova Scotia Dept. of the Environment.

Milman, H.A., D.A. Story, E.S. Riccio, A. Sivak, A.S. Tu, G.M. Williams, C. Tong, and C.A. Tyson. 1988. Rat liver foci and *in vitro* assays to detect initiating and promoting effects of chlorinated ethanes and ethylenes. Annal. N.Y. Acad. Sci. 534: 521–530.

Monster, A.C. 1979. Difference in uptake, elimination and metabolism in exposure to trichloroethylene, 1,1,1-trichloroethane and tetrachloroethylene. Int. Arch. Occup. Environ. Health 42: 311–317.

Monster, A.C., G. Boersma, and H. Steenweg. 1979. Kinetics of tetrachloroethylene in volunteers: Influence of exposure concentration and work load. Int. Arch. Occup. Environ. Health 42: 303–309.

Nagy, K.A. 1987. Field metabolic rate and food requirement scaling in mammals and birds. Ecol. Monogr. 57: 111–128.

NAQUADAT/ENVIRODAT. 1991. National water quality database, searched from 1988 to 1991. Eco-health Branch, Ecosystems Science Evaluation Directorate, Environment Canada.

NATES (National Analysis of Trends in Emergencies System Database). 1992. Tetrachloroethylene spills for the years 1974–1992. Environmental Emergency Program Division, Management and Emergencies Branch, Environment Canada.

NCI (National Cancer Institute). 1977. Bioassay of Tetrachloroethylene for Possible Carcinogenicity. Department of Health, Education and Welfare, United States Public Health Service, National Institutes of Health, Bethesda, Maryland (NIH 77-813).

Neely, W.B., D.R. Branson, and G.E. Blau. 1974. Partition coefficient to measure bioconcentration potential of organic chemicals in fish. Environ. Sci. Technol. 8: 1113–1115.

NIOSH. 1985. Registry of Toxic Effects of Chemical Substances (1983–1984). Cumulative supplement to the 1981–1982 edition. U.S. Department of Health and Human Services.

NTP (National Toxicology Program). 1986. Toxicology and Carcinogenesis Studies of Tetrachloroethylene (Perchloroethylene) (CAS No. 127-18-4) in F344/N rats and B6C3F_1 Mice (Inhalation Studies). United States Department of Health and Human Services, Public Health Service, National Institutes of Health, Research Triangle Park, North Carolina (NTP TR 311).

Odum, J., T. Green, J.R. Foster, and P.M. Hext. 1988. The role of trichloroacetic acid and peroxisome proliferation in the differences in carcinogenicity of perchloroethylene in the mouse and rat. Toxicol. Appl. Pharmacol. 92: 103–112.

Ofstad, E.B., H. Drangsholt, and G.E. Carlberg. 1981. Analysis of volatile halogenated organic compounds in fish. Sci. Total Environ. 20: 205–215.

Ogata, M., Y. Takasuka, and K. Tomokuni. 1971. Excretion of organic chlorine compounds in the urine of persons exposed to vapours of trichloroethylene and tetrachloroethylene. Brit. J. Ind. Med. 28: 386–391.

Ohta, T., M. Morita, I. Mizoguchi, and T. Tada. 1977. Washout effect and diurnal variation for chlorinated hydrocarbons in ambient air. Atmos. Environ. 11: 985–987.

Ohtsuki, T., K. Sato, A. Koizumi, M. Kumai, and M. Ikeda. 1983. Limited capacity of humans to metabolize tetrachloroethylene. Int. Arch. Occup. Environ. Health 51: 381–390.

Olson, M.J., J.T. Johnson, and C.A. Reidy. 1990. A comparison of male rat and human urinary droplet proteins: implications for human resistance to hyaline droplet nephropathy. Toxicol. Appl. Pharmacol. 102: 524–536.

OME (Ontario Ministry of the Environment). 1987. R.L. Clark water treatment plant drinking water surveillance program. Water Resources Branch, Ontario Ministry of the Environment, Annual Report 1987 (cited in Health and Welfare Canada, 1990).

OME (Ontario Ministry of the Environment). 1991a. St. Clair River MISA Pilot Site Investigation, Volume II. Part II—Detailed Technical Findings; Part III—Appendices. Prepared by the St. Clair River MISA Pilot Site Team, Water Resources Branch, Ontario Ministry of the Environment.

OME (Ontario Ministry of the Environment). 1991b. Information provided under The Drinking Water Surveillance Program.

Otson, R. 1987. Purgeable organics in Great Lakes raw and treated water. Intern. J. Environ. Anal. Chem. 31: 41–53.

Otson, R., D.T. Williams, and P.D. Bothwell. 1982. Volatile organic compounds in water at thirty Canadian potable water treatment facilities. J. Assoc. Off. Anal. Chem. 65: 1370–1374.

Otson, R., P. Fellin, and R. Whitmore. 1992. A national pilot study on occurrence of airborne VOCs in residences. Proc. EPA/A & WMA Symposium on Measurement of Toxic and Related Air Pollutants, May, 1992, Durham, North Carolina (in press).

Pakdel, H., S. Lesage, P. Gélinas, and C. Roy. 1989. Toxic chemicals in soil and groundwater at the contaminated site of Ville Mercier, Quebec. In: 39th Canadian Chemical Engineering Conference Book of Abstracts. Hamilton, Ontario. p. 167.

Parsons, F.Z., P.R. Wood, and J. DeMarco. 1984. Transformations of tetrachloroethene and trichloroethene in microcosms and groundwater. J. Am. Water Works Assoc. 76: 56–59.

Pearson, C.R., and G. McConnell. 1975. Chlorinated C_1 and C_2 hydrocarbons in the marine environment. Proc. R. Soc. London. 189: 305–332.

Pegg, D.G., J.A. Zempel, W.H. Braun, and P.G. Watanabe. 1979. Disposition of tetrachloro(^{14}C)ethylene following oral and inhalation exposure in rats. Toxicol. Appl. Pharmacol. 51: 465–474.

Poulsen, M.M., and B.H. Kueper. 1992. A field experiment to study the behaviour of tetrachloroethylene in unsaturated porous media. Environ. Sci. Technol. 26: 889–895.

Quebec Ministry of the Environment. 1990. Data collected under the Programme de Surveillance des Micro-polluants.

Rachootin, P., and J. Olsen. 1983. The risk of infertility and delayed conception associated with exposures in the Danish work place. J. Occup. Med. 25: 394–402.

Reinhard, M., N.L. Goodman, and J.F. Barker. 1984. Occurrence and distribution of organic chemicals in two landfill leachate plumes. Environ. Sci. Technol. 18: 953–961.

Richter, J.E., S.F. Peterson, and C.F. Kleiner. 1983. Acute toxicity of some chlorinated benzenes, chlorinated ethanes, and tetrachloroethylene to *Daphnia magna*. Arch. Environ. Contam. Toxicol. 12: 679–684.

Riihimaki, V. 1985. Metabolism and excretion of organic solvents. In V. Riihimaki and U. Uflvarson, eds. Safety and Health Aspects of Organic Solvents. Alan R. Liss, New York, pp. 61–71.

Riihimaki, V., and P. Pfaffli. 1978. Percutaneous absorption of solvent vapors in man. Scand. J. Work Environ. Health. 4: 73–85.

Rosengren, L.E., P. Kjellstrand, and K.G. Haglid. 1986. Tetrachloroethylene: levels of DNA and S-100 in the gerbil CNS after chronic exposure. Neurobehav. Toxicol. Teratol. 8: 201–206.

Rowe, V.K., D.D. McCollister, H.C. Spencer, E.M. Adams, and D.D. Irish. 1952. Vapor toxicity of tetrachloroethylene for laboratory animals and human subjects. Arch. Ind. Hyg. Occup. Health 5: 566–579.

Rowland, F.S. 1990. Stratospheric ozone depletion by chlorofluorocarbons. Ambio 19: 281–292.

Sadtler Research Laboratories. 1982. Infrared Spectra of Priority Pollutants and Toxic Chemicals. Sadtler Research Laboratories, Philadelphia, Pennsylvania.

Savolainen, H., P. Pfaffli, M. Tengen, and H. Vainio. 1977. Biochemical and behavioural effects of inhalation exposure to tetrachloroethylene and dichloromethane. J. Neuropathol. Expt. Neurol. 36: 941–949.

Schumann, A.M., J.F. Quast, and P.G. Watanabe. 1980. The pharmacokinetics and macromolecular interactions of perchloroethylene in mice and rats as related to oncogenicity. Toxicol. Appl. Pharmacol. 55: 207–219.

Schwarzenbach, R.P., E. Molnar-Kubica, W. Giger, and S.G. Wakeham. 1979. Distribution, residence time and fluxes of tetrachloroethylene and 1,4-dichlorobenzene in Lake Zürich, Switzerland. Environ. Sci. Technol. 9: 1367–1373.

Schwille, F. 1988. Dense chlorinated solvents in porous and fractured media. Lewis Publishers, New York. p. 161.

Seeber, A. 1989. Neurobehavioral toxicology of long-term exposure to tetrachloroethylene. Neurotoxicol. and Teratol. 11: 579–583.

Seiji, K., C. Jin, T. Watanabe, H. Nakatsuka, and M. Ikeda. 1990. Sister chromatid exchanges in peripheral lymphocytes of workers exposed to benzene, trichloroethylene, or tetrachloroethylene, with reference to smoking habits. Int. Arch. Occup. Environ. Health 62: 171–176.

Seip, H.M., J. Alstad, G.E. Carlberg, K. Martinsen, and R. Skaane. 1986. Measurement of mobility of organic compounds in soils. Sci. Total Environ. 50: 87–101.

Singh, H.B., L. Salas, H. Shigeishi, and A. Crawford. 1977. Urban-nonurban relationships of halocarbons, SF_6, N_20 and other atmospheric trace constituents. Atmos. Environ. 11: 819–828.

Singh, H.B., L.J. Salas, and R.E. Stiles. 1982. Distribution of selected gaseous organic mutagens and suspect carcinogens in ambient air. Environ. Sci. Technol. 16: 872–880.

Smith, A.D., A. Bharath, C. Mallard, D. Orr, K. Smith, J.A. Sutton, J. Vukmanich, L.S. McCarty, and G.W. Ozburn. 1991. The acute and chronic toxicity of ten chlorinated organic compounds to the American flagfish (*Jordanella floridae*). Arch. Environ. Contam. Toxicol. 20: 94–102.

Smith, E.M., E.R. Miller, W.F. Woolson, and C.K. Brown. 1985. Bladder cancer risk among laundry workers, dry-cleaners and others in chemically-related occupations. J. Occup. Med. 27: 295–297.

Smyth, H.F., C.S. Weil, J.S. West, and C.P. Carpenter. 1969. An exploration of joint action: twenty-seven industrial chemicals intubated in rats in all possible pairs. Toxicol. Appl. Pharmacol. 14: 340–347.

Solet, D., and T.G. Robins. 1991. Renal function in dry cleaning workers exposed to perchloroethylene. Am. J. Ind. Med. 20: 601–614.

Soni, M., H. Nomiyama, and K. Nomiyama. 1990. Chronic inhalation effects of tetrachloroethylene on hepatic and renal microsomal electron transport components and δ-aminolevulinic acid dehydratase in rats. Toxicol. Lett. 54: 207–213.

Spirtas, R., P.A. Stewart, J.S. Lee, D.E. Marano, C.D. Forbes, D.J. Grauman, H.M. Pettigrew, A. Blair, R.N. Hoover, and J.L. Cohen. 1991. Retrospective cohort mortality study of workers at an aircraft maintenance facility, I. Epidemiological results. Br. J. Ind. Med. 48: 515–530.

Stahl, W.R. 1967. Scaling of respiratory variables in mammals. J. Appl. Physiol. 22: 453–460.

Stemhagen, A., J. Slade, R. Altman, and J. Bill. 1983. Occupational risk factors and liver cancer. Am. J. Epidemiol. 117: 443–454.

Stewart, R.D. 1969. Acute tetrachloroethylene intoxication. JAMA 208: 1490–1492.

Stewart, R.D., E.D. Baretta, H.C. Dodd, and T.R. Torkelson. 1970. Experimental human exposure to tetrachloroethylene. Arch. Environ. Health 20: 224–229.

Swenberg, J.A., B. Short, S. Borghoff, J. Strasser, and M. Charboneau. 1989. The comparative pathobiology of α_{2u}-globulin nephropathy. Toxicol. Appl. Pharmacol. 97: 35–46.

Taskinen, H., A. Anttilla, M-L. Lindbohm, M. Sallmen, and K. Hemminki. 1989. Spontaneous abortions and congenital malformations among the wives of men occupationally exposed to organic solvents. Scand. J. Environ. Health 15: 345–352.

Theiss, J.C., G.D. Stoner, M.B. Shimkin, and E.K. Weisberger. 1977. Test for carcinogenicity of organic contaminants of United States drinking waters by pulmonary tumor response in strain A mice. Cancer. Res. 37: 2717–2720.

U.S. EPA (U.S. Environmental Protection Agency). 1978. Ambient Water Quality Criteria for Tetrachloroethylene. Criteria and Standards Division, United States Environmental Protection Agency, Washington, D.C. (EPA PB-292-445/9). 60 pp.

U.S. EPA (U.S. Environmental Protection Agency). 1982. An exposure and risk assessment for tetrachloroethylene. Office of Water, Regulations and Standards, United States Environmental Protection Agency, Washington, D.C. (EPA-4404-85-015). 137 pp.

U.S. EPA (U.S. Environmental Protection Agency). 1985. Health Assessment Report for Tetrachloroethylene (Perchloroethylene). Final Report. Office of Environmental Health and Assessment, U.S. Environmental Protection Agency, Washington, D.C. (PB85-249707).

U.S. EPA (U.S. Environmental Protection Agency). 1990. Quantification of Toxicological Effects of Tetrachloroethylene. Office of Drinking Water Criteria & Standards Division, U.S. Environmental Protection Agency, Washington, D.C. (PB91-143479).

U.S. EPA (U.S. Environmental Protection Agency). 1991. Integrated Risk Information System (IRIS). Information search for tetrachloroethylene.

Vamvakas, S., M. Herkenoff, W. Dekant, and D. Henschler. 1989. Mutagenicity of tetrachloroethylene in the Ames test-Metabolic activation by conjugation with glutathione. J. Biochem. Toxicol. 4: 21–27.

Van Duuren, B.L., B.M. Goldschmidt, G. Loewengart, A.C. Smith, S. Melchionne, I. Seldman, and D. Roth. 1979. Carcinogenicity of halogenated olefinic and aliphatic hydrocarbons in mice. JNCI 63: 1433–1439.

Veith, G.D., D.J. Call, and L.T. Brooke. 1983a. Structure-toxicity relationships for the fathead minnow, *Pimephales promelas*: narcotic industrial chemicals. Can. J. Fish. Aquat. Sci. 40: 743–748.

Veith, G.D., D.J. Call, and L.T. Brooke. 1983b. Estimating the acute toxicity of narcotic industrial chemicals to fathead minnows. In: W.E. Bishop, R.D. Cardwell, and B.B. Heidolph, eds. Aquatic Toxicology and Hazard Assessment: Sixth Symposium, American Society for Testing and Materials. Philadelphia, Pennsylvania. ASTM STP 802.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd edition. Van Nostrand Reinhold Co., New York. 1076–1080.

Vyskocil, A., S. Emminger, J. Tejral, Z. Fiala, E. Ettlerova, and A. Cermanova. 1990. Study on kidney function in female workers exposed to perchloroethylene. Human Exptl. Toxicol. 9: 377–380.

Wakeham, S.G., A.C. Davis, and J.L. Karas. 1983. Mesocosm experiments to determine the fate and persistence of volatile organic compounds in coastal seawater. Environ. Sci. Technol. 17: 611–617.

Walbridge, C.T., J.T. Fiandt, G.L. Phipps, and G.W. Holcombe. 1983. Acute toxicity of ten chlorinated aliphatic hydrocarbons to the fathead minnow (*Pimephales promelas*). Arch. Environ. Contam. Toxicol. 12: 661–666.

Wallace, L.A., E.D. Pellizzari, T.D. Hartwell, R. Whitmore, C. Sparacino, and H. Zelon. 1986. Total exposure assessment methodology (TEAM) study: personal exposures, indoor-outdoor relationships, and breath levels of volatile compounds in New Jersey. Environ. Int. 12: 369–387.

Wallace, L.A., E.D. Pellizzari, T.D. Hartwell, C. Sparacino, R.D. Whitmore, L. Sheldon, H. Zelon, and R. Perritt. 1987. The TEAM study: personal exposures to toxic substances in air, drinking water, and breath of 400 residents of New Jersey, North Carolina, and North Dakota. Environ. Res. 43: 290–307.

Wallace, L.A., E.D. Pellizzari, T.D. Hartwell, V. Davis, L.C. Micheal, and R.W. Whitmore. 1989. The influence of personal activities on exposure to volatile organic compounds. Environ. Res. 50: 37–55.

Wang, D.K.W. 1984. Development of sampling and analytical techniques for measuring trace volatile organic compounds in Canadian urban areas, Part II. Field measurement and data interpretation. Final Report. Environment Canada (cited in Health and Welfare Canada, 1990).

Wenzel, D.G., and R.D. Gibson. 1951. A study of the toxicity and antihelminthic activity of n-butylidene chloride. J. Pharm. Pharmacol. 3: 169–176.

White, R., and D. Echeverria. 1992. A neurobehavioral evaluation of perchloroethylene exposure in patients and dry cleaners: a possible relationship between clinical and pre-clinical effects. The Toxicologist 12: 276 (abstract).

WHO (World Health Organization). 1984. Tetrachloroethylene. Environmental Health Criteria 31, World Health Organization, Geneva. 48 pp.

WHO (World Health Organization). 1987. Tetrachloroethylene Health and Safety Guide. World Health Organization, Geneva. 44 pp.

Withey, R.J., and J.W. Hall. 1975. The joint action of perchloroethylene with benzene or toluene in rats. Toxicol. 4: 5–15.

Ziglio, G., G.M. Fara, G. Beltramelli, and F. Pregliasco. 1983. Human environmental exposure to trichloro- and tetrachloroethylene from water and air in Milan, Italy. Arch. Environ. Contam. Toxicol. 12: 57–64.

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