Canadian Environmental Protection Act

Priority Substances List
Assessment Report

Trichloroethylene

Government of Canada
Environment Canada
Health Canada

Aussi disponible en français sous le titre de :
Loi canadienne sur la protection de l'environnement
Liste des substances d'intérêt prioritaire
Rapport d'évaluation : *Trichloroéthylène*

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Table of Contents

List of Figures and Tables

Synopsis

Trichloroethylene is primarily used as a solvent in the vapour-degreasing and cold-cleaning of fabricated metal parts, and in smaller amounts in dry-cleaning operations, paints and paint removers, and various household products. Domestic consumption is approximately 1.4 kilotonnes per year, all of which is supplied by importation. Due to the dispersive and non-destructive nature of its uses, the majority of the trichloroethylene consumed is expected to enter the Canadian environment, primarily the atmosphere. Trichloroethylene has been detected in ambient air and in the air inside homes in Canada, as well as, occasionally, in drinking water and surface waters across the country. It has also been detected in groundwaters in several provinces, often as a result of its inappropriate disposal by consumers and release from metal-degreasing facilities or landfills.

Mean concentrations of trichloroethylene in surface waters in Canada are generally more than 10 times less than the effects threshold estimated for the most sensitive aquatic species. For wild mammals, the estimated worst-case daily intake is 30 times less than the estimated effects threshold. The estimated effects threshold for terrestrial plants, notably trees, exposed to trichloroethylene in the atmosphere is similar to concentrations in air observed at a rural location, is approximately equal to mean concentrations in air in several cities in Canada and is exceeded by the maximum concentrations reported in various urban locations.

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

Based on estimation of the total average daily intake from ambient and indoor air, drinking water and food for various age groups in the general population, indoor air appears to be the most significant source of human exposure to trichloroethylene in Canada. Based on the weight of evidence of carcinogenicity in experimental animals, trichloroethylene is classified as "probably carcinogenic to humans", i.e., as a substance for which there is believed to be some chance of adverse health effects at any level of exposure. For such substances, estimated exposure is compared to quantitative estimates of cancer potency to characterize risk and provide guidance for further action (i.e., analysis of options to reduce exposure). For trichloroethylene, such a comparison suggests that the priority for analysis of options to reduce exposure would be low to moderate.

Based on these considerations, it has been concluded that trichloroethylene occurs at concentrations that may be harmful to the environment, and that may constitute a danger in Canada to human life or health. It has been concluded that trichloroethylene occurs at concentrations that do not constitute a danger to the environment on which human life depends.

1.0 Introduction

The *Canadian Environmental Protection Act* (CEPA) requires the 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, 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 trichloroethylene is "toxic", as defined under CEPA, was based on the determination of whether it **enters** or is likely to enter the Canadian environment in a concentration or quantities or under conditions that could lead to **exposure** of humans or other biota at levels that could cause harmful **effects**.

Data relevant to the assessment of whether trichloroethylene is "toxic" to the environment were identified from on-line searches completed in December 1991, of a number of commercial databases (including AGRICOLA, ASFA, AQUAREF, AQUIRE, Biological Abstracts, BIOSIS Preview, Chemical Abstracts [1987 to 1991], CAB, CESARS, Chemical Exposure, Chemical Name, Chemical Regulations, CHEM INTELL, CIS, CODOC, ELIAS, ENVIROLINE, Environmental Bibliography, FATERATE, Federal Register, GEOREF, IRIS, IRPTC, MEDLINE, MICROLOG, NRTCR, NRC PUBS, NTIS, PHYTOTOX, Pollution Abstracts, RTECS, Water

Resources Abstracts and TOXLINE). Information obtained after completion of the environmental sections of this report (i.e., May 1993), was not considered for inclusion.

Data relevant to the assessment of whether trichloroethylene is "toxic" to human health were identified in review documents prepared by the Agency for Toxic Substances and Disease Registry (ATSDR, 1989) and the California Air Resources Board (1990) and a background report prepared under contract by T. Colborn in March 1990. In addition, literature searches were conducted on a number of computerized databases. In November 1990, the databases CHEMID, RTECS, HSDB, Chemical Abstracts and ENVIROLINE were searched for relevant literature published in 1989 and 1990. In October 1991, searches were conducted on HSDB, RTECS, IRIS, CHRIS, TOXLINE and TOXLIT to identify relevant literature published in 1991. More recently, the MEDLINE subfile of the TOXLINE database (1989 to 1992), the EMBASE database (1989 to 1992) and the CCRIS, DART and GENETOX databases of the TOXNET system (all years), were searched. Information obtained after completion of the health-related sections of this report (i.e., October 1992) was not considered for inclusion.

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

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B. Idris (Health Canada) also contributed to the consolidation of the Assessment Report. S. Bartlett and M. Walker of Health Canada provided the quantitative estimates of carcinogenic potency.

This report contains a synopsis that will appear in the *Canada Gazette*, a summary of technical information critical to the assessment (Section 2.0) and the assessment of whether trichloroethylene is "toxic" as defined under CEPA (Section 3.0). Supporting Documentation, in which the technical information is presented in greater detail, is also available upon request.

As part of the review and approvals process established by Environment Canada, 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. K.L.E. Kaiser (National Water Research Institute), Dr. A. Smith (Lakehead University) and Dr. V. Zitko (Fisheries and Oceans Canada). Sections of the Supporting Documentation related to the assessment of effects on human health were reviewed by Dr. T. Green of Imperial Chemical Industries Central Toxicology Laboratory (U.K.). Following peer review of sections of the Supporting Documentation and Assessment Report related to human health by staff of BIBRA Toxicology International (U.K.), Dr. R. Bull of Washington State University and Dr. G. Plaa of the University of Montreal, they were 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:

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2.0 Summary of Information Critical to Assessment of "Toxic"

2.1 Identity, Properties, Production and Uses

Trichloroethylene (1,1,2-trichloroethene; TCE; CAS Registry No. 79-01-6) is an unsaturated, chlorinated, aliphatic compound (chemical formula C_2HCl_3) with a low molecular weight (131.4 g/mol). At room temperature, it is a volatile, nonviscous liquid (boiling point = 86.7°C) with a higher density (1.46 g/mL [20°C/4°C]) and a lower surface tension (0.029 N/m) than water. Under conditions of normal use, trichloroethylene is considered nonflammable and is moderately stable, but requires the addition of stabilizers (up to 2% v/v) in commercial grades. Trichloroethylene is moderately soluble in water (1.1 to 1.4 g/L), and has a low *n*-octanol/water partition coefficient (log K_{ow} 2.29 to 2.42) and a high vapour pressure (8.0 to 9.9 kPa at 20–25°C)[McNeill, 1979; Eisenreich *et al*., 1981; ATSDR, 1989]. In air, 1 ppm is equivalent to 5.41 mg/m^3 (at 20°C and 101.3 kPa) [Verschueren, 1983].

The analytical method most widely reported for quantifying trichloroethylene is gas chromatography with an electron capture detector. Reported detection limits are as low as 0.9 ng/L in water (Comba and Kaiser, 1983), 0.5 µg/kg (fresh material) and 2.5 to 100 µg/kg (extractable fat) in tissues of fish (Ofstad *et al*., 1981) and 0.1 µg/m^3 in air (Dann and Wang, 1992).

Trichloroethylene is generally produced by chlorinating ethylene or ethylene dichloride (WHO, 1985; ATSDR, 1991). Until 1985, it was produced in Canada at two plants, both in Shawinigan, Quebec. Currently, domestic demand is met by importation. Total Canadian imports of trichloroethylene were 1.6 kt during 1989, of which 0.1 kt were re-exported (CIS, 1991). Predicted imports for 1990 and 1993 are 1.5 and 1.4 kt, respectively (CIS, 1991).

The major use of trichloroethylene in Canada (1.3 kt in 1989) is for the vapour-degreasing and cold-cleaning of fabricated metal parts in the automotive and metals industries (CIS, 1991). Trichloroethylene is also used in the production of adhesives and copolymers, household and industrial dry-cleaning, textile manufacturing, the cleaning of electronic components, petroleum industry processes involving refining catalysts, paint removers coatings and vinyl resins, and in laboratory reagent/solvent applications. Household or consumer products that may contain trichloroethylene include typewriter correction fluids, paint removers/strippers, adhesives, spot removers and rug-cleaning fluids (WHO, 1985; Frankenberry *et al*., 1987; ATSDR, 1989; Bruckner *et al.*, 1989; ATSDR, 1991).

Although the use of trichloroethylene in Canada has declined recently, demand could increase in the future as global production and use of 1,1,1-trichloroethane is reduced and eliminated. 1,1,1-Trichloroethane is also used for metal cleaning in significantly larger quantities (14.5 kt in 1989) than trichloroethylene (1.3 kt in 1989) [CCB, 1990; CIS, 1991].

2.2   Entry into the Environment

There are no known natural sources of trichloroethylene in the environment. Limited data are available regarding releases of trichloroethylene to the Canadian environment from anthropogenic sources. Since nearly all uses of trichloroethylene are dispersive, however, total annual releases to the Canadian environment are expected to be close to the net quantity of trichloroethylene consumed in Canada annually (i.e., 1.5 kt in 1989) [CIS, 1991].

Pandullo *et al.* (1985) reported that metal-degreasing operations are the major industrial source of trichloroethylene emissions to the atmosphere in the United States. Since Canadian metal-degreasing operations consume approximately 85% of the domestic supply of trichloroethylene each year (CIS, 1991), it is likely that they are also an important source of emissions in Canada. Based on information on releases in the United States, other likely emission sources in Canada include discharges from dry-cleaning operations, sewage treatment plants, textile mills and other industries, releases from landfills, incinerators, septic tanks and storage tanks, and use and disposal of trichloroethylene-containing products (e.g., glues, paints) [Pandullo *et al.,* 1985; ATSDR, 1991]. Trichloroethylene can also be formed in groundwater as a biodegradation product of tetrachloroethylene (Major *et al.*, 1991).

Between 1981 and 1988, 6 accidental discharges and spills of trichloroethylene were voluntarily reported in Canada (NATES, 1992; DGAIS, 1992). The causes of these releases included material failure, equipment damage and transportation accidents. Release volumes ranged from less than 1 L to 5.3 tonnes.

2.3   Exposure-related Information

2.3.1   *Fate*

The fate of trichloroethylene released to the environment is influenced by transport processes, including volatilization, diffusion and advection, and by transformation processes, including photooxidation and biodegradation.

The majority of trichloroethylene is released to the atmosphere, where it may react with photochemically produced hydroxyl radicals (Singh *et al*., 1982; Bunce, 1992) to produce phosgene, dichloroacetyl chloride, formyl chloride and other degradation

products (Atkinson, 1985; Bunce, 1992). Trichloroethylene does not readily undergo chemical oxidation or hydrolysis in the atmosphere, and direct photolysis is a minor transformation process (Jensen and Rosenberg, 1975; Bunce, 1992). The estimated half-life for trichloroethylene in the atmosphere varies with latitude, season and concentration of hydroxyl radicals. In Canada, the calculated half-lives range from 1 day in the south to 3 days in the north during the summer months, and from approximately 2

Trichloroethylene does not partition to aquatic sediments to any appreciable degree (Pearson and McConnell, 1975), except in sediments with a high organic content (McConnell *et al.*, 1975; Lay *et al.*, 1984; Smith *et al.*, 1990). Trichloroethylene may biodegrade to carbon dioxide in sediment. In one study, methane-utilizing bacteria isolated from sediment reduced the concentration of trichloroethylene from 630 μg/L to 200 μg/L in 4 days at 20°C (Fogel *et al.*, 1986).
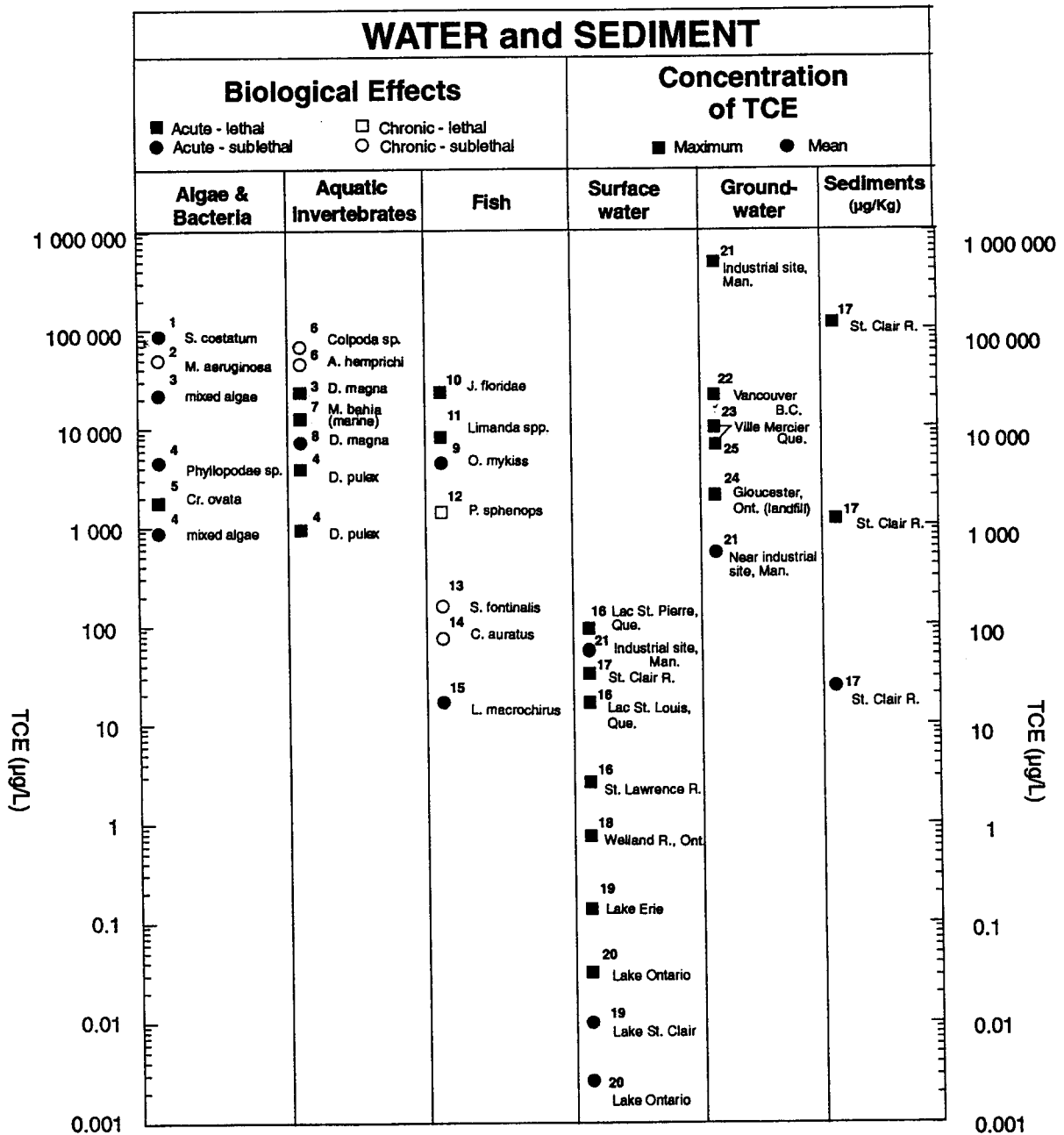
The majority of trichloroethylene released onto soil surfaces will volatilize to the atmosphere. Trichloroethylene present in subsurface soil may be transported by diffusion, advection or dispersion of the pure liquid, as a solute in water, or by gaseous diffusion throughout the spaces within porous soils (Schwille, 1988). As a result, trichloroethylene can penetrate the soil and contaminate groundwater (Schwille, 1988). Trichloroethylene partitions to soil particles of high organic content (Garbarini and Lion, 1986; Seip *et al.*, 1986; Stauffer and MacIntyre, 1986). Information on the importance of biodegradation in removing trichloroethylene from subsurface soil is limited. In one study, no degradation of trichloroethylene by anaerobic soil microorganisms was detected after 16 weeks (Wilson *et al.*, 1981); however, aerobic biodegradation has been demonstrated following artificial nutrient enrichment and induction (Wilson and Wilson, 1985; Walton and Anderson, 1990). In some subsurface soils, sorption and desorption of trichloroethylene is slow. Thus, subsurface liquid trichloroethylene may continue to contaminate groundwater aquifers and soils long after sources have been eliminated (Smith *et al.*, 1990).

Based on its low *n*-octanol/water partition coefficient (log K_{ow} 2.29 to 2.42) and the results of field studies, trichloroethylene is unlikely to bioaccumulate significantly in aquatic biota and piscivorous birds (Pearson and McConnell, 1975; Dickson and Riley, 1976; Kawasaki, 1980; Barrows *et al.*, 1980; Ofstad *et al.*, 1981; Wang *et al.*, 1985; Freitag *et al.*, 1985; Smets and Rittmann, 1990). Measured bioaccumulation factors ranged from < 3 for muscle tissues of marine and freshwater birds to approximately 100 for fish livers (Pearson and McConnell, 1975). No studies on the bioaccumulation of trichloroethylene in terrestrial plants or mammals were identified.

2.3.2   *Concentrations*

Trichloroethylene has been detected in all environmental media in Canada. Critical data on concentrations of trichloroethylene in surface water, groundwater and outdoor air are presented in Figures 1 and 2.

Figure 1. Representative trichloroethylene (TCE) concentrations in Canadian water and sediment and concentrations causing adverse effects to biota.

WATER and SEDIMENT

Biological Effects

■ Acute - lethal   □ Chronic - lethal
● Acute - sublethal   ○ Chronic - sublethal

Concentration of TCE

■ Maximum   ● Mean

Algae & Bacteria	Aquatic Invertebrates	Fish	Surface water	Ground-water	Sediments (µg/Kg)

TCE (µg/L)

1 000 000

100 000
- ● 1 S. costatum
- ○ 2 M. aeruginosa
- 3
- ● mixed algae

100 000
- ○ 6 Colpoda sp.
- ○ 6 A. hemprichi
- ■ 3 D. magna
- ■ 7 M. bahia (marine)
- ● 8 D. magna

- ■ 10 J. floridae

- ■ 21 Industrial site, Man.

- ■ 17 St. Clair R.

10 000
- ● 4 Phyllopodae sp.
- ■ 5 Cr. ovata
- ● 4 mixed algae

- ■ 4 D. pulex
- ■ 4 D. pulex

- ■ 11 Limanda spp.
- ● 9 O. mykiss
- □ 12 P. sphenops

- ■ 22 Vancouver
- 23 B.C.
- ■ Ville Mercier Que.
- ■ 25
- ■ 24 Gloucester, Ont. (landfill)
- ● 21 Near industrial site, Man.

- ■ 17 St. Clair R.

1 000

100
- ○ 13 S. fontinalis
- ○ 14 C. auratus
- ● 15 L. macrochirus

- ■ 16 Lac St. Pierre, Que.
- ● 21 Industrial site, Man.
- ■ 17 St. Clair R.
- ■ 16 Lac St. Louis, Que.

- ● 17 St. Clair R.

100

10

- ■ 16 St. Lawrence R.

10

1

- ■ 18 Welland R., Ont.

1

0.1

- ■ 19 Lake Erie

0.1

0.01

- ■ 20 Lake Ontario
- ● 19 Lake St. Clair

0.01

0.001

- ● 20 Lake Ontario

0.001

TCE (µg/L)

1. Ward *et al.*, 1986.
2. Slooff *et al.*, 1983.
3. Lay *et al.*, 1984.
4. Lay and Herrmann, 1991.
5. Herrmann, 1985.
6. Inamori *et al.*, 1989.
7. Ward *et al.*, 1986.
8. Abernethy *et al.*, 1986.
9. Slooff, 1979.
10. Smith et al., 1991

11. Pearson and McConnell, 1975.
12. Loekle *et al.*, 1983.
13. ATRG, 1988.
14. Loekle, 1987.
15. Diamond *et al.*, 1990.
16. Lum and Kaiser, 1986.
17. COARGLWQ, 1986.
18. Kaiser and Comba, 1983.
19. Kaiser and Comba,1986b.
20. Kaiser *et al.*, 1983.

21. U.M.A. Engineering Ltd., 1992.
22. Golder Associates, 1989.
23. Pakdel et al., 1989.
24. Lesage *et al.*, 1990.
25. Lesage *et al.*, 1989.

Note: All of the studies are reported in detail in the supporting document.

Figure 2. Representative trichloroethylene (TCE) concentrations in the Canadian atmosphere and concentrations causing adverse effects to plants.
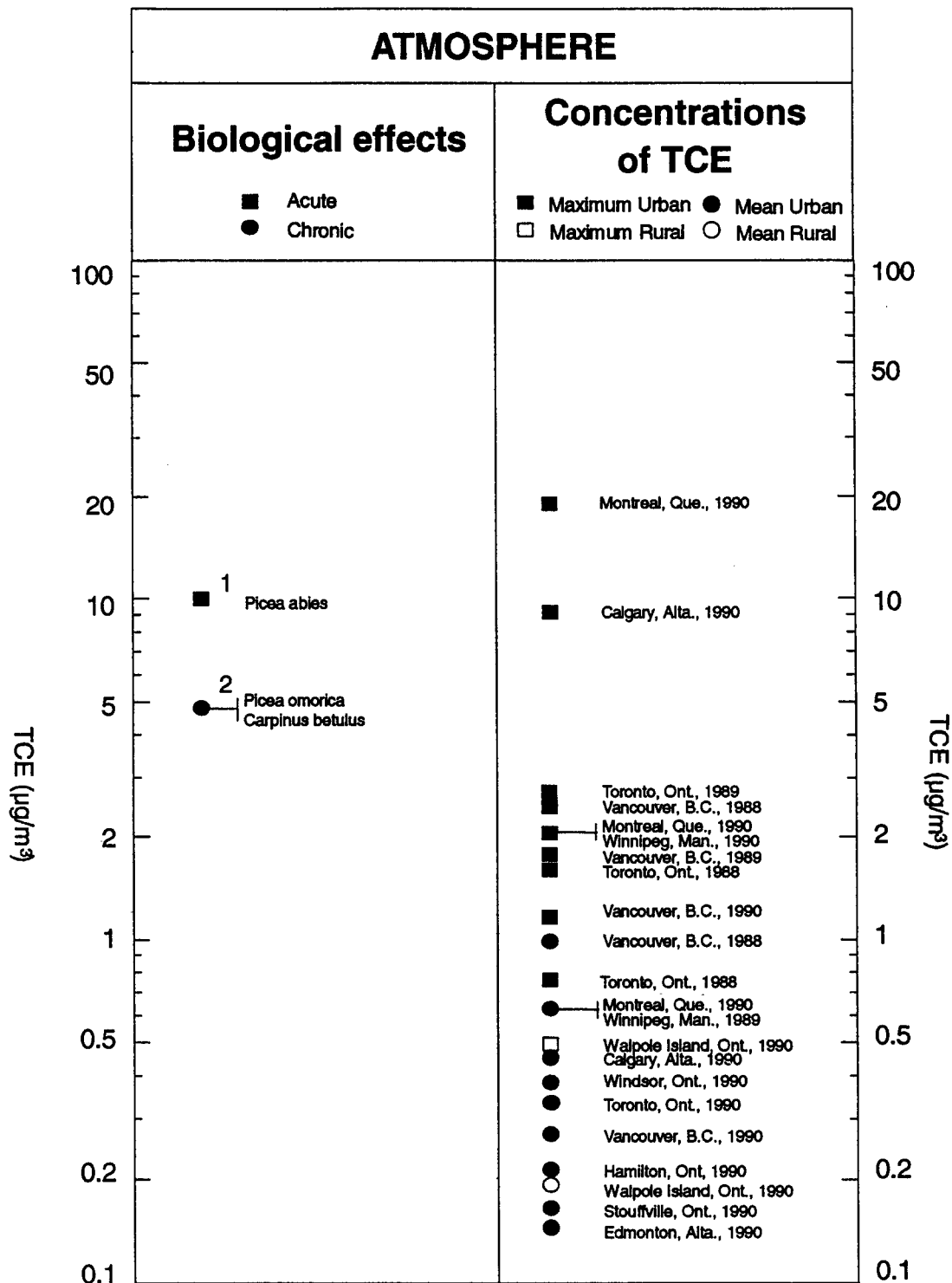
ATMOSPHERE

Biological effects

■ Acute
● Chronic

Concentrations of TCE

■ Maximum Urban ● Mean Urban
□ Maximum Rural ○ Mean Rural

TCE (μg/m³)

100
50
20
10
5
2
1
0.5
0.2
0.1

■ ¹ Picea abies

● ² Picea omorica
  Carpinus betulus

■ Montreal, Que., 1990

■ Calgary, Alta., 1990

■ Toronto, Ont., 1989
  Vancouver, B.C., 1988
■ Montreal, Que., 1990
  Winnipeg, Man., 1990
■ Vancouver, B.C., 1989
  Toronto, Ont., 1988

■ Vancouver, B.C., 1990

● Vancouver, B.C., 1988

■ Toronto, Ont., 1988
● Montreal, Que., 1990
  Winnipeg, Man., 1989
□ Walpole Island, Ont., 1990
● Calgary, Alta., 1990
● Windsor, Ont., 1990
● Toronto, Ont., 1990
● Vancouver, B.C., 1990
● Hamilton, Ont., 1990
○ Walpole Island, Ont., 1990
● Stouffville, Ont., 1990
● Edmonton, Alta., 1990

TCE (μg/m³)

100
50
20
10
5
2
1
0.5
0.2
0.1

1. Frank and Frank, 1986
2. Frank and Frank, 1985

Note: all air levels are based on a 24 h sampling period (Dann and Wang, 1992).

9

Concentrations of trichloroethylene in ambient air may fluctuate widely 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). Concentrations in air over remote regions in Canada and elsewhere are generally in the ng/m^3 range, while higher levels occur over urban areas. Mean concentrations (24-h composite samples averaged over periods varying from 1 month to 1 year) in air sampled from 11 Canadian cities between 1988 and 1990 ranged from 0.07 to 0.96 μg/m^3 (Dann and Wang, 1992). Mean concentrations at these sites averaged over the 3-year period ranged from 0.07 to 0.45 μg/m^3 (Dann and Wang, 1992). The maximum concentration of 19.98 μg/m^3 was measured in Pointe-aux-Trembles in Montréal, Quebec, in 1990 (Dann and Wang, 1992). At the only rural site monitored in Canada (Walpole Island, Ontario), the mean concentration of trichloroethylene in 1990 was 0.18 μg/m^3, with a maximum level of 0.46 μg/m^3 (Dann and Wang, 1992).

Data on levels of trichloroethylene in air at Canadian landfill or hazardous-waste sites, or near industrial point sources, were not identified. At active and abandoned sites in New Jersey, mean trichloroethylene concentrations ranged from 0.43 to 15.5 μg/m^3 (LaRegina *et al.*, 1986; Harkov *et al.*, 1983), with maximum recorded values of 108 μg/m^3 and 66.5 μg/m^3, respectively.

Concentrations of trichloroethylene in indoor air in approximately 750 homes from across Canada ranged up to 165 μg/m^3, with an overall mean value of 1.4 μg/m^3, based on preliminary results of a pilot study (Otson *et al.*, 1992). Similar levels have been reported in smaller surveys in Toronto (Chan *et al.*, 1990; Bell *et al.*, 1991) and extensive surveys in the U.S. (Wallace *et al.*, 1991; U.S. Environmental Protection Agency, 1987; Pellizari *et al.*, 1989; Shah and Singh, 1988).

Concentrations of trichloroethylene in Canadian surface waters generally do not exceed 1 μg/L, unless the waters receive direct releases. In surface water samples collected from the St. Lawrence River in 1985, Lum and Kaiser (1986) reported levels of trichloroethylene as high as 90.0 μg/L at the mouth of the Yamaska and Saint-François rivers in Lac St. Pierre near Sorel, Quebec. Levels as high as 42 μg/L were measured adjacent to industrial-sewer outfalls in the St. Clair River (COARGLWQ, 1986); however, levels in the St. Lawrence, Niagara, Welland and St. Clair rivers and watersheds were more frequently in the 0.01 to 0.75 μg/L range (Kaiser and Comba, 1983; Strachan and Edwards, 1984; Kaiser and Comba, 1986a; Lum and Kaiser, 1986); Mean concentrations of trichloroethylene in the Great Lakes range from 0.0025 μg/L in Lake Ontario (maximum 0.033 μg/L) [Kaiser *et al.*, 1983] to 0.0094 μg/L in Lake St. Clair (maximum 0.036 μg/L) [Kaiser and Comba, 1986b].

In a pond at an industrial site in Manitoba, levels were 47.7 and 55.4 µg/L (mean 51.6 µg/L) in 1991 (UMA Engineering Ltd., 1992). The source of trichloroethylene in the pond is discharge of overburden groundwater and surface run-off (UMA Engineering Ltd., 1993).

The highest reported concentrations of trichloroethylene in water in Canada occur in groundwater. For example, concentrations ranged from 102 µg/L to 12 950 µg/L in groundwater sampled at or near the Ville Mercier landfill in Quebec (Pakdel *et al.*, 1989; Lesage *et al.*, 1989). Levels ranged from below the detection limit (detection limit = 1 µg/L) to 2 480 µg/L in groundwater collected in May 1988 near a Gloucester, Ontario, municipal landfill following disposal of chlorinated solvents from 1969 to 1980 (Lesage *et al*., 1990). At an industrial site in Vancouver, levels in groundwater ranged from 59.5 to 21 900 µg/L (mean = 770.5 µg/L) [Golder Associates, 1989]. Trichloroethylene has recently been detected in groundwater at and surrounding an industrial site in Manitoba (UMA Engineering Ltd., 1992). The groundwater is part of an aquifer that discharges to a wetland. Concentrations in groundwater below the site were as high as 425 000 µg/L; levels in wells located several kilometres from the site were as high as 490 µg/L. These wells are used for livestock watering and irrigation (UMA Engineering Ltd., 1992). At a chemical transfer and storage facility in Toronto, trichloroethylene formed from the biodegradation of tetrachloroethylene was detected in 2 groundwater samples at concentrations of 1 165 and 1 654 µg/L (Major *et al*., 1991).

With the exception of some groundwater supplies in Prince Edward Island, the majority of drinking water supplies in Canada contain less than 0.2 µg/L trichloroethylene (Environment Canada, 1989a, 1989c; Nova Scotia Ministry of Health, 1991; Quebec Ministry of the Environment, 1990; OME, 1990; Kendall, 1990; Alberta Ministry of the Environment, 1990). Mean concentrations were ® 1.0 µg/L at 30 drinking water treatment facilities across Canada surveyed in 1979 (Otson *et al*., 1982).

Few data are available on levels of trichloroethylene in aquatic sediments and soils in Canada. Following a spill in 1985 in the St. Clair River, levels of trichloroethylene in bottom sediments ranged from below the detection limit (detection limit = 0.01 µg/kg) to 110 000 µg/kg, with a mean concentration of 21 µg/kg (wet or dry weight not specified) [COARGLWQ, 1986]. In soil from a former chemical warehouse and distribution facility in Vancouver, concentrations of trichloroethylene ranged from trace to 4 500 µg/kg (mean = 36 µg/kg) [Golder Associates, 1989]. Concentrations in soil at an industrial site in Manitoba ranged from below the detection limit (detection limit = 0.1 µg/kg) to 1 000 mg/kg (UMA Engineering Ltd., 1992).

Trichloroethylene has been identified (but not quantified) in adult herring gulls from Pigeon Island near Kingston Harbour, Lake Ontario, and from the Kingston garbage dump (Hallett *et al.*, 1982). No other data on levels in tissues in Canadian biota were identified.

The use of trichloroethylene in the preparation of foodstuffs processed in Canada or imported into the country has not been permitted since 1977. In a limited study of 34 food groups in Alberta, 51 and 410 ppb (μg/kg) trichloroethylene was detected (detection limit = 50 ppb or μg/kg) in a cheese/butter composite and fruit pies, respectively (Enviro-Test Laboratories, 1991). Trichloroethylene has been detected in a small percentage of samples of various food items analyzed in total-diet studies and market-basket surveys in the U.S. at concentrations ranging up to 94 μg/kg (with the exception of a single sample of margarine in which 980 μg/kg was detected) [Heikes, 1987; Gartrell, 1986a, 1986b; Daft, 1988, 1989; Entz and Diachenko, 1988].

2.4 Toxicokinetics

Between 25 and 55% of inhaled trichloroethylene is absorbed by humans (Astrand and Ovrum, 1976; Raabe, 1988). Ingested trichloroethylene is rapidly absorbed from the gastrointestinal tract of experimental animals (ATSDR, 1989); the extent to which the compound is absorbed is largely dependent upon the vehicle in which it is administered (i.e., uptake is greater when administered in water than in oil) [Withey *et al.*, 1983]. Once absorbed, trichloroethylene is distributed widely throughout the body via the bloodstream. The primary site of metabolism of trichloroethylene is the liver, although the Clara cells of the lung in experimental animals have also been reported to metabolize the inhaled compound (Bruckner *et al.*, 1989; Dalbey and Bingham, 1978; Odum *et al.*, 1992). Trichloroethylene is metabolized via cytochrome P450 mixed-function oxygenases, generating (possibly) trichloroethylene oxide, chloral hydrate, trichloroacetic acid, trichloroethanol and dichloroacetic acid, along with other minor intermediates, which are subsequently conjugated. This oxidative metabolism of trichloroethylene appears to be qualitatively similar in experimental animals and humans, although there are substantial differences in the quantities of various metabolites formed in various species; e.g., mice appear to metabolize trichloroethylene to a greater extent than rats (see Supporting Documentation for additional details). The formation of a glutathione conjugate in the liver has also been demonstrated in rats; it is converted in the kidney to the cysteine conjugate, which is subsequently cleaved via renal β-lyase to form reactive intermediates (Dekant *et al.*, 1990a, 1990b). This pathway has recently been hypothesized to exist in humans, based on the identification of the cysteine conjugates in the urine of exposed workers (Birner *et al.*, in press). Unmetabolized trichloroethylene is eliminated via exhalation, while its metabolic products are excreted, principally in the urine.

2.5   Effects-related Information

2.5.1   *Experimental Animals and* **In Vitro**

Various effects have been observed in experimental animals following exposure to trichloroethylene. The emphasis in this summary is on those studies in which the lowest effect levels have been reported. The acute toxicity of trichloroethylene is weak in experimental animals following inhalation or ingestion (reported LC_{50}s and LD_{50}s in rodents ranged from approximately 40 000 to 265 000 mg/m^3 and 2 400 to 4 900 mg/kg bw, respectively). Effects on the liver, including increases in liver weight, alterations in enzyme levels and morphological changes, have been reported in mice, rats and gerbils following sub-chronic exposure to trichloroethylene at concentrations as low as 37 ppm (200 mg/m^3) in air (Kjellstrand *et al*., 1983a). Increased kidney weight and altered biochemical parameters have been reported in rats and gerbils at concentrations as low as 75 ppm (405 mg/m$^{3)}$ for 30 days (Kjellstrand *et al*., 1983a). Morphological changes, along with alterations in enzyme activities, have been observed in the Clara cells of the lung in mice exposed to 450 ppm (2 430 mg/m$^{3)}$ trichloroethylene for 2 weeks (Odum *et al*., 1992). Hepatic effects, including alterations in enzyme activities, peroxisome proliferation and histopathological changes, have been reported in mice and rats following sub-chronic ingestion of trichloroethylene, at doses as low as 1 000 mg/L in drinking water (equivalent to 216.7 mg/kg bw/day) for 4 or 6 months (Tucker *et al*., 1982). Increases in relative liver weight have been observed in mice administered doses as low as 100 mg/kg bw/day by gavage for 6 weeks (Buben and O'Flaherty, 1985). Cytomegaly of the renal tubular epithelial cells was reported in rats ingesting doses as low as 1 000 mg/kg bw/day for 13 weeks (National Toxicology Program, 1990), while altered urinary and haematological parameters were noted in mice drinking water containing 2 500 mg/L (equivalent to doses of 393 mg/kg bw/day) for 4 or 6 months (Tucker *et al.*, 1982).

Studies in which experimental animals were chronically exposed to trichloroethylene by inhalation or ingestion are not adequate to derive no-observed-(adverse)-effect-levels (NO(A)ELs) or lowest-observed-(adverse)-effect-levels (LO(A)ELs) for non-neoplastic effects, because, in most cases, such end-points were inadequately assessed (since most of these studies focused principally on investigation of the carcinogenic potential of trichloroethylene) and the exposure levels were relatively high. The incidence of renal tubular cytokaryomegaly was increased in male Sprague-Dawley rats exposed to 300 or 600 ppm (1 620 or 3 240 mg/m^3) for 104 weeks (Maltoni *et al*., 1986, 1988), and in male and female F344, Osborne-Mendel, Marshall, August and ACI rats ingesting 500 or 1 000 mg/kg bw/day for 2 years (National Toxicology Program, 1988, 1990).

Most of the identified carcinogenicity bioassays for trichloroethylene are inadequate, due to limitations of study design or reporting. On the basis of these limited available bioassays, there is consistent convincing evidence that tumours of the liver and lung in mice and testicular tumours in rats are associated with exposure to trichloroethylene.

An exposure-related increase in the incidence of pulmonary adenomas was reported in female B6C3F$_1$ mice exposed to 0, 100, 300 or 600 ppm (0, 540, 1 620 or 3 240 mg/m^3) for 78 weeks and allowed to complete their lifespans (incidence of 2/90, 2/90, 7/90 and 12/90, or, when corrected for the number of animals alive at the time of appearance of the first pulmonary tumour, 16 weeks – 2/90, 2/90, 7/89 and 12/87). The incidence of pulmonary adenomas, adenomas which were suggestive of early adenocarcinomatous transformation and adenocarcinomas (combined), also increased with concentration (2/90, 6/90, 7/90 and 14/90, or, when corrected, 2/90, 6/90, 7/89 and 14/87). No such increase was noted in males (Maltoni *et al*., 1986, 1988). In a similar study in Swiss mice, there was a significant increase in the incidence of adenomatous hyperplasia-early adenomas, adenomas and adenocarcinomas at the highest concentration, although there was no evidence of an exposure-response relationship when only neoplastic lesions were considered. The incidence of "hepatomas" was significantly increased in male Swiss mice at 600 ppm (13/61 versus 4/66 in controls) [Maltoni *et al*., 1986, 1988]. The incidence of pulmonary adenocarcinomas was significantly increased in female ICR mice exposed to 150 or 450 ppm (810 or 2 430 mg/m^3) for 104 weeks, but not at 50 ppm (incidence of 1/49, 3/50, 8/50 and 7/46, with increasing concentration) [Fukuda *et al*., 1983]. An increase in the incidence of malignant lymphoma was noted in female NMRI mice exposed to 100 or 500 ppm (540 or 2 700 mg/m^3) for 18 months, although the authors did not believe that this response was due to any direct carcinogenicity of trichloroethylene (Henschler *et al.*, 1980), and tumours of the haematopoietic system have not been observed in other bioassays.

There was an exposure-related increase in the incidence of tumours of the Leydig cells in the testis (6/135, 16/130, 30/130 and 31/130, or, when corrected for the number of animals alive at the time of appearance of the first Leydig cell tumour, 62 weeks – 6/120, 16/114, 30/114 and 31/120) in male Sprague-Dawley rats exposed to 0, 100, 300 or 600 ppm (0, 540, 1 620 or 3 240 mg/m^3) for 104 weeks (Maltoni *et al*., 1986, 1988). No evidence of carcinogenicity was reported in Sprague-Dawley rats exposed to up to 450 ppm (2 430 mg/m^3) trichloroethylene for 104 weeks (Fukuda *et al*., 1983) or in small groups of Wistar rats exposed to 100 or 500 ppm (540 or 2 700 mg/m^3) for 18 months (Henschler *et al*., 1980).

Ingested trichloroethylene was reported to be hepatocarcinogenic in mice in an earlier bioassay conducted by the National Cancer Institute (1976). This study was repeated by the National Toxicology Program (1990), due to the presence of carcinogenic stabilizers and contaminants in the test compound in the earlier study. A significant

increase in the incidence of hepatocellular carcinomas was again observed in male and female $B6C3F_1$ mice (31/50 versus 8/48 in controls [males] and 13/49 versus 2/48 in controls [females]) administered 1 000 mg/kg bw/day for 103 weeks; as well, the incidence of hepatocellular adenomas was non-significantly increased in males [14/50 versus 7/48] and significantly increased in females (16/49 versus 4/48). Results from other limited bioassays in mice (Van Duuren *et al*., 1979; Herren-Freund *et al*., 1987; Bell *et al*., 1978) are mixed or inconclusive and do not contribute to the weight of evidence for carcinogenicity.

An increased incidence of renal tubular adenocarcinomas was reported in male F344/N rats administered 1 000 mg/kg bw/day in corn oil by gavage for 103 weeks (0/33, 0/20 and 3/16 at 0, 500 and 1 000 mg/kg bw/day, respectively), although this study was deemed to be inadequate due to reduced survival in males. No exposure-related increase in tumour incidence was noted in female rats (National Toxicology Program, 1990). In a similar bioassay in Osborne-Mendel, Marshall, August and ACI rats administered 500 or 1 000 mg/kg bw/day trichloroethylene in corn oil by gavage, there was a dose-related increase in the incidence of testicular interstitial cell tumours in Marshall rats (17/46, 21/48 and 32/48 at 0, 500 and 1 000 mg/kg bw/day, respectively). There was also a significant increase in the incidence of renal tubular cell adenomas in Osborne-Mendel rats receiving the lower dose, but not in the high-dose group (0/50, 6/50 and 1/50, with increasing dose); however, this study was judged to be inadequate due to reduced survival, chemical toxicity and deficiencies in the conduct of the study (which did not relate to histopathological diagnoses) [National Toxicology Program, 1988]. No significant increase in the incidence of any specific type of tumour was reported in Sprague-Dawley rats administered up to 250 mg/kg bw/day for 52 weeks (Maltoni *et al*., 1986).

Trichloroethylene appears to be weakly mutagenic, based on the results of several *in vitro* and *in vivo* assays (see Supporting Documentation). A significant increase in micronuclei has recently been reported in the bone marrow of mice exposed to 5 ppm (27 mg/m^3) trichloroethylene for 6 hours (Kligerman *et al*., 1992). As effects have been reported primarily in the presence of metabolic activation, it is likely that the mutagenicity is due to metabolites rather than the parent compound.

Although not unequivocally proven, available data indicate that peroxisome proliferation may play an important role in the hepatocarcinogenesis of trichloroethylene in rodents. There appears to be considerable variability in the proliferative response of peroxisomes to trichloroethylene between mice and rats. Doses of 50 to 2 000 mg/kg bw administered by gavage induced peroxisome proliferation in mice but not in rats (Elcombe *et al*., 1985; Knuckles, 1990). These differences in species susceptibility may be due to variations between mice and rats in the metabolism of trichloroethylene to active metabolites. Available data indicate that the dose at which the metabolism of trichloroethylene to trichloroacetic acid is

saturated is greater in mice than in rats (ATSDR, 1989; California Air Resources Board, 1990). The capacity of cultured hepatocytes from mice to convert trichloroethylene to trichloroacetic was 30-fold greater than in hepatocytes from rats, which in turn was 3-fold greater than in hepatocytes from humans (Elcombe, 1985). Trichloroacetic acid has induced peroxisome proliferation in cultured hepatocytes from mice and rats but not in human hepatocytes from only 2 subjects (Elcombe, 1985).

Both trichloroacetic acid and the minor metabolite dichloroacetic acid induced peroxisome proliferation in mice and rats following *in vivo* exposure (DeAngelo *et al.*, 1989). Oral administration of trichloroacetic acid increased the incidence of hepatocellular tumours in mice (Herren-Freund *et al*., 1987; DeAngelo and Daniel, 1992; Bull *et al*., 1990), but not in rats administered up to 378 mg/kg bw/day in the drinking water for 100 to 104 weeks (DeAngelo and Daniel, 1992). Dichloroacetic acid was also hepatocarcinogenic in mice following chronic oral exposure (DeAngelo *et al.*, 1991) and increased altered foci and hyperplastic nodules in the liver of rats administered concentrations in the drinking water equivalent to doses of 295 mg/kg bw/day (DeAngelo and Daniel, 1992).

Available data also indicate that proliferative responses may play a role in the hepatocarcinogenesis of trichloroethylene in mice. Bull *et al*. (1990) have suggested that the formation of dichloroacetic acid-induced liver tumours may be due to cellular proliferative responses associated with focal necrosis rather than peroxisome proliferation, as the tumours were associated with severe hepatomegaly and cytomegaly in mice exposed to dichloroacetic acid but not trichloroacetic acid; lipofuscin (an indicator of lipid peroxidation) accumulated to a much greater extent in hepatic tissues of mice following administration of trichloroacetic acid than dichloroacetic acid. More recently, Larson and Bull (1992) have demonstrated the ability of both of these metabolites to induce lipid peroxidation in mice and rats, with dichloroacetic acid being the more potent of the two. In addition, it has been proposed that trichloroethylene and/or trichloroacetic acid may interfere with control mechanisms through their ability to inhibit intercellular gap junction communication, which has been demonstrated in hepatocytes from mice but not from rats (Klaunig *et al*., 1989).

It has been proposed that the induction of renal tumours in rats is likely due to the formation of glutathione conjugates, which in turn lead to the formation, via cysteine conjugated intermediates, of reactive metabolites in the kidney, which have been demonstrated to covalently bind to DNA and proteins, to be mutagenic in the Ames test, and to induce unscheduled DNA synthesis in cultured porcine kidney cells at concentrations that did not cause cytotoxicity (Commandeur and Vermeulen, 1990; Commandeur *et al*., 1991; Dekant *et al*., 1990b; Vamvakas *et al.*, 1989). These cysteine conjugates have recently been identified in the urine of workers exposed to trichloroethylene (Birner *et al*., in press). It should be noted, however, that the

marginal increases in renal tumours in male rats occurred at doses that induced damage in the kidney, although nephrosis was also observed in similarly exposed female rats and mice of both sexes, without any increase in the incidence of renal tumours.

It has been suggested that lung tumours in mice associated with exposure to trichloroethylene by inhalation may be due to *in situ* metabolism to reactive metabolites in the Clara cells of the bronchiolar epithelium (Bruckner *et al*., 1989). Trichloroethylene has caused damage to the Clara cells of the lung in CD-1 mice following intraperitoneal administration, including vacuolization and aggregation of the smooth endoplasmic reticulum, necrosis and sloughing, which stimulated a proliferative response resulting in the development of micronodules; it has also been observed to bind to cellular macromolecules in the lung (Forkert *et al*., 1985; Forkert and Troughton, 1987; Forkert and Birch, 1989). More recently, damage to Clara cells in mice, but not in rats, has been reported following inhalation of concentrations of trichloroethylene as low as 20 ppm (108 mg/m^3); this damage was reversible upon continued exposure, but recurred upon renewed administration following a period without exposure (Odum *et al.*, 1992). Odum *et al.* (1992) have demonstrated the accumulation of the genotoxic metabolite, chloral, in the Clara cells of mice exposed to trichloroethylene, likely due to the inability of these cells to form the glucuronide conjugate. Chloral was the agent likely to be responsible for the non-neoplastic changes, as damage similar to that caused by trichloroethylene was induced in mice by exposure to chloral but not the other metabolites, trichloroethanol or trichloroacetic acid. These authors noted that this possible mechanism of action may not be relevant to humans, since, on the basis of limited available data, there are fewer Clara cells in the lungs of humans, and these do not appear to contain smooth endoplasmic reticulum (and therefore possibly do not contain cytochrome p-450 required to catalyse the formation of chloral), although human alveolar type II cells may contain low levels of cytochrome p-450. The relationship between the damage reported in Clara cells and the development of pulmonary tumours has not been established, however. Moreover, there was no indication, upon histopathological examination, of the type of effects described here, which are purported to be associated with a genotoxic metabolite, in the lungs of mice in any of the carcinogenicity bioassays conducted to date.

No information on the mechanism of induction of testicular tumours in rats following exposure to trichloroethylene has been identified, although dichloroacetic acid (a minor metabolite of trichloroethylene) has induced degenerative changes in the testicular epithelium of rats and dogs following oral administration of 500 and 50 mg/kg bw/day and above, respectively, for 3 months (Katz *et al*., 1981). It should be noted, however, that these effects occurred at doses much higher than those likely to be present in the body following metabolism of trichloroethylene.

No effects on reproductive ability were reported in a 2-generation, continuous breeding study in F344 rats (National Toxicology Program, 1986), while reduced sperm motility and increased weights of testis and epididymis were noted in a similar study in CD-1 mice administered diets containing 0.60% trichloroethylene (equivalent to 652.5 to 750.0 mg/kg bw/day) [National Toxicology Program, 1985]. Effects on copulatory behaviour, as determined by the number of mounts and intromissions, and latency of mounts and ejaculation, have been observed in rats administered oral doses of 1 000 mg/kg bw/day (Zenick *et al.*, 1984).

The effects of maternal exposure to airborne trichloroethylene during pregnancy on the development of offspring of mice, rats, rabbits and gerbils have been investigated. Foetotoxic and embryotoxic but no consistent teratogenic effects have been reported at concentrations as low as 100 ppm (540 mg/m^3) [Healy *et al*., 1982], although maternal effects were not assessed in this study. Increased resorptions and malformations of the eye have been observed in the pups of rats ingesting doses of 475 mg/kg bw/day trichloroethylene and above during gestation; maternal toxicity was also evident at all doses (Narotsky *et al.*, 1990). Neurological effects, consisting of physiological and behavioral changes, have been reported in the offspring of rats exposed to trichloro-ethylene in the drinking water at concentrations of 312 mg/L or greater during gestation (Isaacson and Taylor, 1989; Taylor *et al.*, 1985).

Neurophysiological effects, including changes in membrane composition of lipids and proteins and alterations in behaviour, have been reported in rats and gerbils at concentrations of trichloroethylene as low as 270 mg/m^3 for 12 months (Kyrklund *et al.*, 1983) and oral doses as low as 5.5 to 8.5 mg/day administered over a period of 8 weeks (Isaacson *et al.*, 1990). Neuro-opthalmotoxicity has been observed in rabbits following exposure to airborne concentrations of 350 ppm (1 890 mg/m^3) or greater for 12 weeks (Blain *et al.*, 1992). Behavioral changes have been observed in rodents exposed to concentrations of trichloroethylene as low as 150 ppm (810 mg/m^3) for 71 or 106 days (Kjellstrand *et al*., 1981a). Cell-mediated immunity was depressed in mice administered 24 mg/kg bw/day for 14 days and following consumption of drinking water containing 5 000 mg/L for 6 months (Sanders *et al.*, 1982).

2.5.2   *Humans*

A variety of disorders, including hepatic and cardiovascular effects, renal damage, pneumatosis cystoides intestinalis, systemic lupus erythematosus, scleroderma, progressive systemic sclerosis, Stevens-Johnson syndrome and Raynauds phenomena have been associated with exposure to trichloroethylene in case reports and limited investigations in small groups of individuals; however, no consistent pattern of adverse effects has emerged.

Neurotoxic effects have been reported in several clinical studies in volunteers and epidemiological investigations in occupationally-exposed populations. A slight, non-significant increase in mortality due to amyotrophic lateral sclerosis was noted in a historical cohort study of 14 457 workers at an aircraft maintenance facility, although the authors noted that local rates were also elevated compared to national rates (Spirtas *et al.*, 1991). The prevalence of subjective symptoms of neurotoxicity was significantly greater in studies in workers exposed to concentrations of trichloroethylene up to 100 ppm (540 mg/m^3) [Liu *et al.*, 1988]. The prevalence of subjective symptoms was also increased in exposed workers in several other studies, although in most of these studies there was no clinical confirmation of neurological effects, monitoring data were limited and the workers were often exposed to other solvents. A significant difference in the mean conduction latency of blink-reflex functions was observed in a cross-sectional study of a group of 21 people whose drinking water contained 63 to 400 ppb (or µg/L) trichloroethylene, along with other solvents, compared to 27 "unexposed" controls (Feldman *et al*., 1988).

The carcinogenicity of trichloroethylene has been investigated in several epidemiological studies in exposed populations. An association between any specific type of cancer and exposure to trichloroethylene has not been consistently observed in these studies. In the largest study conducted to date, excesses in multiple myeloma, non-Hodgkin's lymphoma and cancers of the biliary passage and liver were noted in 14 457 aircraft maintenance workers; however, there were no significant excesses when only those workers who had been exposed specifically to trichloroethylene were considered (Spirtas *et al*., 1991). Increases in incidence or mortality due to various other types of cancer have occasionally been reported in other studies (e.g., Axelsson *et al.*, 1984; Sharpe *et al*., 1989; Fredriksson *et al.*, 1989), although these investigations were usually limited in terms of the small size of the study group, lack of data on exposure, and exposure to other agents.

There has been no consistent convincing evidence presented in the limited number of studies conducted to date which indicates that exposure to trichloroethylene adversely affects human reproduction or development. The frequency of structural chromosomal aberrations in lymphocytes was significantly increased in a small group of workers exposed to unspecified concentrations of trichloroethylene (Rasmussen *et al*., 1988), although inconclusive results were obtained for other genetic end-points in human lymphocytes and pulmonary cells (Nagaya *et al.*, 1989; Seiji *et al.*, 1990; Perococco and Prodi, 1981; Beliles *et al.*, 1980).

2.5.3   *Ecotoxicology*

In the following section, studies involving species particularly sensitive to trichloroethylene have been emphasized. A summary of the biological effects of trichloroethylene in the Canadian environment is presented in Figures 1 and 2.

Several acute toxicity tests have been performed to determine the effects of trichloroethylene on *Daphnia* species. The 48-hour EC_{50} for immobilization of 4- to 6-day-old *Daphnia magna* was 7.8 mg/L trichloroethylene (Abernethy *et al.*, 1986). The corresponding 48-hour LC_{50} for young *Daphnia magna* (< 24-hour old) was 18.0 mg/L. These studies were conducted under static test conditions, and only nominal concentrations of trichloroethylene were reported.

In a field experiment on a natural pond community in Germany conducted in 1981, Lay *et al.* (1984) observed complete mortality of *Daphnia magna* in two test ponds within 3 days after exposure to an initial concentration of 110 mg/L. Approximately 70% mortality was observed after 3 days at an initial concentration of 25 mg/L (the half-life of trichloroethylene in these experiments was 2.7 days). At the end of the observation period (43 days), the daphnid population had recovered. Species richness and abundance of phytoplankton, however, remained severely depressed at the end of the observation period following exposure to 25 mg/L. The results of subsequent field studies in natural pond communities indicated that similar effects occurred following continuous exposure to lower concentrations of trichloroethylene for longer periods of time (Herrmann, 1985; Lay and Herrmann, 1991). For example, exposure to 1.0 to 1.5 mg/L trichloroethylene for 11 weeks caused fluctuations in the population densities of phytoplankton and zooplankton, reductions of up to 70% in the population of *Daphnia pulex*, a 50% reduction in primary productivity and inhibition of cell multiplication in sensitive cryptomonad species (Herrmann, 1985; Lay and Herrmann, 1991).

Erratic movement, altered ventilatory behaviour and increased purge frequency have been observed in bluegill sunfish (*Lepomis macrochirus*) exposed to 0.018 to 0.024 mg/L trichloroethylene for 15 to 30 minutes in a flow-through experiment (Diamond *et al.*, 1990). A return to normal behaviour usually occurred within 2 hours after being placed in clean water. Exposures of longer durations (i.e., up to 24 hours), however, resulted in permanent effects of the same nature (Diamond, 1992). In brook trout (*Salvelinus fontinalis*), there was a significant reduction in swim-up survival, 120-day fry weight, and 120-day growth after exposure to a measured concentration of 0.21 mg/L trichloroethylene in a flow-through test (ATRG, 1988). Loekle (1987) reported that exposure of goldfish (*Carassius auratus*) to 0.1 mg/L trichloroethylene for ≥ 60 days in a static-renewal test resulted in significantly reduced body weight and altered histopathology (primarily, increased fat vacuolation of the liver).

The adverse effects of chloroethylenes (particularly trichloroethylene and tetrachloroethylene) on forests have been studied in Germany and Finland. In these areas, there was an increase in the incidence of chlorosis (bleaching of needles), necrosis (death of needles) and premature needle loss over the last 2 decades in fir (*Abies alba*), Norway spruce (*Picea abies*), beech (*Fagus silvatica*) and other tree

species (Frank and Frank, 1986a, 1986b; Frank, 1989, 1991; Figge, 1990; Frank *et al.* 1992a, 1992b). These effects were attributed to exposure to chloroethylenes (Frank and Frank, 1985, 1986a, 1986b; Frank, 1989, 1991).

In laboratory experiments, Frank and Frank (1986a) observed the effects on Norway spruce needles (*Picea abies*) exposed simultaneously to trichloroethylene and visible/ultraviolet radiation. Concentrations of photosynthetic pigments in the needles that were irradiated and exposed to 10.8 μg/m^3 (2 ppbv) trichloroethylene for 5 hours were significantly depressed. The photosynthetic pigments most severely affected were chlorophyll-a (depressed by 32% relative to controls) and β-carotene (depressed by 41% relative to controls). Exposure without irradiation or irradiation without exposure to trichloroethylene had no effect on the photosynthetic pigments.

Similar effects were observed in a field experiment, in which a 10-year-old Serbian spruce (*Picea omorica*) was continually exposed to trichloroethylene and tetrachloroethylene for 7 months (Frank and Frank, 1985). The effects observed included chlorosis, necrosis and premature loss, particularly on the sun-exposed faces of the needles. Along several of the sun-exposed twigs, a total loss of chlorophyll was observed. The damage intensified after periods of clear, sunny days. The same toxic effects were observed on the sun-exposed leaves of a hornbeam shrub (*Carpinus betulus*) located about 2 metres downwind from the spruce tree. Concentrations of trichloroethylene among the branches of the spruce ranged from 2.7 to 10.8 μg/m^3 (mean = 4.6 μg/m^3) during the study. Concentrations of tetrachloroethylene ranged from 3.4 to 13.7 μg/m^3 (mean = 11.8 μg/m^3). Frank and Frank (1986a) demonstrated that exposure to similar concentrations of trichloroethylene or tetrachloroethylene, in combination with visible/ultraviolet radiation, in the laboratory caused a similar degree of depression in photosynthetic pigments in Norway spruce needles (*Picea abies*).

No information on the toxicity of trichloroethylene to mammalian wildlife or birds was found.

3.0   Assessment of "Toxic" under CEPA

3.1   CEPA 11(*a*): Environment

Trichloroethylene is not produced in Canada but is imported, primarily for use as a cleaning and degreasing solvent in metal-cleaning industries. Due to its volatility and the dispersive nature of this use, trichloroethylene enters the Canadian environment, most often as emissions to air (1.4 kilotonnes/year). Minor releases to the environment include discharging of liquid effluents to surface water, leaching from storage tanks and landfills to soil and groundwater, and emissions to air from dry-cleaning operations and incinerators. Accidental spills of trichloroethylene in the Canadian environment have also occurred. Trichloroethylene has been measured in air across Canada and in surface waters in the Great Lakes and connecting channels. Contamination of groundwater has occurred in several provinces, usually in association with hazardous-waste landfills and industrial sites.

Brook trout (*Salvelinus fontinalis*) and water flea (*Daphnia pulex*) were among the most sensitive aquatic species tested following chronic and acute exposure to trichloroethylene. For brook trout, the 120-day lowest-observed-effects-concentration (LOEC) for reductions in swim-up survival and fry weight is 0.21 mg/L. For *Daphnia pulex*, exposure for several days to 1.0 to 1.5 mg/L trichloroethylene caused reductions of up to 70% in the population present in a natural pond. Dividing the chronic LOEC for brook trout by a factor of 10 to account for differences in species sensitivity and to extrapolate laboratory findings to the field results in an estimated effects threshold for aquatic species of 21 μg/L. Effects on other biota (e.g., fish, aquatic invertebrates, algae and bacteria) have been observed at concentrations within two orders of magnitude of this estimated effects threshold. Although levels at several sites close to industrial sources exceed the estimated effects threshold, concentrations of trichloroethylene in Canadian surface waters are generally less than this threshold, usually by more than an order of magnitude.

Concentrations of trichloroethylene in groundwater in several locations across Canada have been considerably higher than those in surface waters. Since the sources of contamination involve metal-degreasing facilities or landfills, for which similar sites exist across Canada, the extent of groundwater contamination with trichloroethylene is likely widespread. Groundwater is part of an integrated hydrological cycle that enables the recharge of surface waters, serving as sources of water to aquatic ecosystems and wildlife. The concentrations of trichloroethylene detected in a pond at an industrial site (47.7 and 55.4 μg/L, caused by groundwater recharge and surface run-off) exceed the

estimated effects threshold for aquatic species (21 µg/L), suggesting that adverse effects could occur in aquatic biota at this site, or at similar sites that may exist elsewhere in Canada.

An effects threshold for wildlife has been developed on the basis of studies in laboratory rodents (summarized in Section 2.5.1). Effects on the liver have been consistently reported in numerous sub-chronic investigations in rodents. Increases in relative liver weight have been reported in mice administered doses as low as 100 mg/kg bw/day by gavage for 6 weeks (Buben and O'Flaherty, 1985). Although immunological effects have been reported at lower doses (e.g., Sanders *et al.*, 1982), these effects have not been extensively investigated or consistently reported.

Exposure to animals in the wild has been estimated for mink (*Mustela vison*) as the model species. This species is an opportunistic carnivore, with aquatic organisms comprising up to 100% of its diet, depending on the season. Based on the data presented in Table 1, the estimated worst-case exposure to mink is 330 µg/kg bw/day, based on the highest levels recorded in air and water in Canada. This exposure is three orders of magnitude higher than that estimated for a rural environment (maximum concentration in air at Walpole Island, Ontario of 0.46 µg/m^3, and maximum concentration in Lake St. Clair of 0.036 µg/L). Assuming a lowest-observed-effect-level (LOEL) of 100 mg/kg bw/day and dividing by a factor of 10 to extrapolate from the laboratory to the field, the estimated effects threshold is 10 mg/kg bw/day. Exposure estimated on the basis of the worst-case scenario is 30 times less than this effects threshold, while that based on the more realistic rural exposure scenario (0.38 µg/kg bw/day) is 26 000 times less than the effects threshold. Therefore, trichloroethylene is not anticipated to cause effects on mammalian wildlife. No data are available to evaluate effects on birds.

Table 1
Estimated Total Daily Exposure to Trichloroethylene for Mink near the St. Lawrence River in Southern Quebec

Exposure Route	Environmental Levels[a]	Daily Rate of Consumption (per kg bw)[b]	Daily Intake (µg/kg bw/d)
Air	19.98 µg/m3	0.55 m^3/d	11
Surface Water	90.0 µg/L	0.1 L/d	9
Biota	2.0 µg/g	155.0 g/d	310
Total	–	–	330

a. The level in air is the maximum level measured in Montréal, Quebec in 1990; the level in surface water is the maximum level measured in the St. Lawrence River in 1985; the level in fish is predicted based on the K_{ow}, using the equation of Veith *et al.* (1979) and the above concentration in water.

b. Inhalation rate from Stahl (1967); drinking rate from Calder and Braun (1983); ingestion rate from Nagy (1987), assuming a diet of 75% fish.

In Germany and Finland, phytotoxic effects of chloroethylenes, including trichloroethylene, in forests have been reported at elevations where exposure to ultraviolet radiation from natural sunlight is high (i.e., mountains). Effects observed include chlorosis, necrosis and premature needle loss. These effects occurred at environmental concentrations of 0.2 to 1.1 $\mu g/m^3$ trichloroethylene in Germany, which are comparable to concentrations measured in air in Canada. In the laboratory, spruce (*Picea abies*) was identified to be sensitive to exposure to trichloroethylene, with significant reductions in the photosynthetic pigments, chlorophyll-a and β-carotene being observed following exposure to concentrations of trichloroethylene as low as 10.8 $\mu g/m^3$ for 5 hours with simultaneous irradiation. In the field, reductions in photosynthetic pigments would likely be associated with reduced photosynthetic capacity and, eventually, reduced growth of the tree (Frank and Frank, 1986a). Dividing the laboratory effect level of 10.8 $\mu g/m^3$ by a factor of 10 to account for interspecies variation in sensitivity and to extrapolate the results of a laboratory study to the field results in an estimated effects threshold of 1.08 $\mu g/m^3$. This threshold is similar to concentrations of trichloroethylene in air at a rural location, is approximately equal to concentrations in 24-hour composite air samples collected in several cities in Canada and averaged over periods varying from 1 month to 1 year, and is approximately 2 to 20 times less than the maximum concentrations of trichloroethylene in Montreal, Toronto, Winnipeg, Calgary and Vancouver. Furthermore, a field study was conducted in which simultaneous exposure of a Serbian spruce (*Picea omorica*) to trichloroethylene (4.6 $\mu g/m^3$) and tetrachloroethylene (11.8 $\mu g/m^3$) led to chlorosis, necrosis and premature loss of the sun-exposed needles. Toxic effects in a nearby hornbeam shrub (*Carpinus betulus*) downwind of the spruce were similar. At similar concentrations, trichloroethylene and tetrachloroethylene elicited responses at a comparable magnitude in a laboratory study. Therefore, demonstrated field effects can be attributed proportionally to trichloroethylene and tetrachloroethylene.

Therefore, on the basis of available information, trichloroethylene 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, contamination of groundwater-recharged surface water in Canada could be significant, particularly in areas where there is inappropriate disposal of trichloroethylene. There is limited data suggesting that atmospheric concentrations of trichloroethylene may be sufficient to cause adverse effects to terrestrial plants, notably trees, in Canada, particularly in urban areas. It is concluded that trichloroethylene 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 trichloroethylene in Canada is less than 6 months, and its halogenated degradation products are short-lived (Colborn, 1990; Bunce, 1992). These degradation products are also water soluble and will, therefore, be removed quickly by precipitation. The migration time of trichloroethylene is estimated to be over 5 years (Rowland, 1990), and, consequently, only minute amounts of trichloroethylene may reach the stratosphere. It is considered unlikely, therefore, that trichloroethylene is involved in the destruction of stratospheric ozone (WHO, 1985; Bunce, 1992). Trichloroethylene absorbs radiation in the infrared region, and therefore has the potential to be a "radiatively active gas"; however, it is generally present at low concentrations in the atmosphere, and has a relatively short half-life. It is considered likely, therefore, that trichloroethylene makes only a minor contribution to global climate change. Trichloroethylene is also considered to be a minor precursor in the production of ground-level ozone (Singh, 1976; Singh *et al*., 1977; Tuazon *et al*., 1988).

Therefore, on the basis of available data, trichloroethylene is not thought to contribute to the depletion of stratospheric ozone, or to the formation of ground-level ozone or global climate change. It is concluded, therefore, that trichloroethylene 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 Exposures

Estimated daily intake (on a body-weight basis) of trichloroethylene for various age groups of the general population in Canada, and the assumptions upon which these estimates are based, are presented in Table 2. Total daily intake of trichloroethylene from ambient and indoor air, drinking water and food is estimated to range from 0.37 to 0.60 µg/kg bw/day for various age groups of the general population in Canada. Based on the estimates presented in Table 2, indoor air is clearly the major source of exposure to trichloroethylene in the general population, while ambient air, drinking water and food make only minor contributions. It should be noted, however, that a national survey of foodstuffs in Canada of adequate sensitivity has not been identified.

Table 2
Estimated Average Daily Intake of Trichloroethylene by the
General Population in Canada

Medium	Estimated Intake (µg/kg bw/day)				
	0 - 0.5 yr[1]	0.5 - 4 yr[2]	5 - 11 yr[3]	12 - 19 yr[4]	20 - 70 yr[5]
Ambient air[6]	0.003 – 0.02	0.004 – 0.03	0.005 – 0.03	0.004 – 0.03	0.004 – 0.02
Indoor air[7]	0.33	0.45	0.52	0.43	0.38
Drinking Water[8]	0.02	0.01	0.007	0.005	0.004
Food[9]	0.02	0.02 – 0.04	0.01 – 0.04	0.006 – 0.02	0.004 – 0.01
Total Intake	0.37 – 0.39	0.48 – 0.53	0.54 – 0.60	0.45 – 0.49	0.39 – 0.41

1. Assumed to weigh 7 kg, breathe 2 m^3 per day and drink 0.75 L of water per day (Environmental Health Directorate, 1992).
2. Assumed to weigh 13 kg, breathe 5 m^3 of air per day and drink 0.8 L of water per day (Environmental Health Directorate, 1992).
3. Assumed to weigh 27 kg, breathe 12 m^3 of air per day and drink 0.9 L of water per day (Environmental Health Directorate, 1992).
4. Assumed to weigh 57 kg, breathe 21 m^3 of air per day and drink 1.3 L of water per day (Environmental Health Directorate, 1992).
5. Assumed to weigh 70 kg, breathe 23 m^3 of air per day and drink 1.5 L of water per day (Environmental Health Directorate, 1992).
6. Based on the range of mean concentrations of trichloroethylene in 12 sites across Canada of 0.07 to 0.45 µg/m^3 (Dann, 1992) and an estimated 4 hours/day spent outdoors (Environmental Health Directorate, 1992).
7. Based on the mean concentration of trichloroethylene in indoor air reported in preliminary results of a survey of approximately 750 homes from 10 provinces across Canada of 1.4 µg/m^3 (Otson *et al*., 1992); (similar mean levels of trichloroethylene have been measured in 2 smaller surveys in Toronto (0.5 to 15.7 µg/m^3) [Chan *et al*., 1990; Bell *et al.,* 1991] and larger surveys in the United States (0.22 to 7.48 µg/m^3) [Wallace *et al*., 1991; U.S. Environmental Protection Agency, 1987; Pellizzari *et al*., 1989; Shah and Singh, 1988]) and an estimated 20 hours/day spent indoors (Environmental Health Directorate, 1992).
8. Based on a concentration of trichloroethylene of 0.2 µg/L, which is not exceeded in most Canadian supplies (Environment Canada, 1989a, 1989b, 1989c; Nova Scotia Ministry of Health, 1991; Quebec Ministry of the Environment, 1990; OME, 1990; Kendall, 1990; Alberta Ministry of Environment, 1990).
9. Based on concentrations of trichloroethylene reported for various foodstuffs in the United States (Heikes, 1987; Daft, 1989; Heikes and Hopper, 1986; Entz and Hollifield, 1982; Entz and Diachenko, 1988; Ferrario *et al*., 1985, Gossett *et al.*, 1983) and average daily food consumption patterns per age group (Environmental Health Directorate, 1992). No quantitative data were identified on levels of trichloroethylene in breast milk in Canada or elsewhere; therefore, it was assumed that infants consumed prepared foodstuffs.

N.B. Insufficient data were available to estimate intake from soil.

Effects

Although some excesses in mortality due to different types of cancer have been observed in some epidemiological studies of populations occupationally exposed to trichloroethylene, there has been no consistent convincing pattern.

The carcinogenic potential of trichloroethylene administered by inhalation or orally has been examined in several studies in experimental animals. In some of the earlier studies, the test compound to which the animals were exposed contained impurities or stabilizers, such as epichlorohydrin, which has induced tumours predominantly at the site of contact; thus, the results of these studies are of limited value in assessment of the weight of evidence of carcinogenicity of trichloroethylene. In more recent studies, in which epoxide-free compound has been administered, there is consistent convincing evidence that tumours of the liver and lung in mice and testicular tumours in rats are associated with exposure to trichloroethylene. In addition, small increases in the incidence of relatively rare renal tumours in male rats have been reported at doses toxic to the kidney in several studies, although an exposure-response relationship has not been observed consistently. Although increases in the incidence of tumours of other organs have occasionally been reported in experimental animals exposed to trichloroethylene, they have not been observed consistently, and/or may be attributable to the presence of contaminants or stabilizers. Negative results in several small bioassays are most likely due to the limited sensitivity of these studies; however, there are limitations in all of the bioassays conducted to date, which complicate the assessment of the weight of evidence for carcinogenicity of trichloroethylene.

A significant increase in the incidence of hepatocellular tumours in male and female B6C3F$_1$ mice following chronic exposure to trichloroethylene via ingestion has been reported by the National Toxicology Program (1990) and the National Cancer Institute (1976), although the carcinogenicity of trichloroethylene could not be firmly established in the latter study due to the presence of epichlorohydrin. The incidence of "hepatomas" was increased in male Swiss mice exposed to trichloroethylene by inhalation (Maltoni *et al*., 1986, 1988), although no significant increase was noted in this strain following ingestion of trichloroethylene (Henschler *et al*., 1984).

If the hepatocarcinogenesis of trichloroethylene in mice is attributable to increased peroxisome proliferation stimulated by the metabolite trichloroacetic acid (which occurs to a greater extent in mice than rats) [Section 2.5.1], and trichloroacetic acid does not induce such proliferation in human hepatocytes (based on an *in vitro* study in a small number of individuals), then the induction of hepatic tumours in mice but not rats following exposure to trichloroethylene is likely to be a species-specific response for which humans are much less sensitive. Similarly, if it is related to other epigenetic mechanisms, such as proliferative responses induced only by high concentrations (Section 2.5.1), humans may be less sensitive.

An increased incidence of renal tubular adenocarcinomas was reported in male F344/N and Osborne-Mendel rats following administration of trichloroethylene by gavage (National Toxicology Program, 1988, 1990) and in Sprague-Dawley rats following exposure via inhalation (Maltoni *et al.*, 1986, 1988); however, the studies conducted by the National Toxicology Program were considered to be inadequate to evaluate the carcinogenic potential of trichloroethylene in rats due to reduced survival, chemically induced nephrotoxicity or deficiencies in the conduct of the study (not related to histopathological diagnoses of lesions) [National Toxicology Program, 1988, 1990], while the statistical significance of the increase in the incidence of renal tumours was not reported in the studies by Maltoni *et al.* (1986, 1988). In addition, an exposure-response relationship was observed in the study in F344/N rats, in which the number of animals surviving until the end of the study was small (National Toxicology Program, 1990), but not in the bioassay in Osborne-Mendel rats, in which survival was greater (National Toxicology Program, 1988). It should be noted that these small increases in tumour incidence in male rats were observed only at doses sufficient to cause toxic nephropathy (cytomegaly in renal tubular cells), although nephropathy, but not renal tumours, was also observed in female rats and male and female mice.

An increased incidence of lung tumours has been reported in 3 strains of mice (B6C3F$_1$, Swiss and ICR) following exposure to trichloroethylene by inhalation and in one study following ingestion. Maltoni *et al*. (1986, 1988) observed an exposure-response relationship between airborne concentration of trichloroethylene and pulmonary adenomas and adenomas and adenocarcinomas (combined) in female B6C3F$_1$ mice, but not in males. Similarly, Fukuda *et al*. (1983) reported a significant increase in the incidence of pulmonary adenocarcinomas in female ICR mice exposed to trichloroethylene by inhalation; however, the trichloroethylene to which the mice were exposed in this study contained epichlorohydrin, benzene, carbon tetrachloride and 1,1,2-trichloroethane, although the authors believed that the concentrations of these impurities were too low to have caused the increase in tumour incidence. This observation appears to be at least partially justified, on the basis of the estimated unit risk for epichlorohydrin.[1] In addition, in an earlier study conducted by the National Cancer Institute (1976), the incidence of combined lung adenomas and adenocarcinomas was increased in mice administered trichloroethylene by gavage; however, this study was deemed to be inadequate, due to the presence of epichlorohydrin in the test compound, although lung tumours have not been observed following oral administration of epichlorohydrin, a compound for which tumour induction has been restricted to the site of contact. Although the potential mechanism

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1. Based on the estimated unit excess cancer risk for inhaled epichlorohydrin of 1.2×10^{-3} $(mg/m^3)^{-1}$ (as developed by the U.S. Environmental Protection Agency [IRIS, 1992]), the risk at the highest concentration in this study is 5.5×10^{-4} or 0.055%, or very low compared to the observed incidence (24%).

of induction of lung tumours in mice exposed to trichloroethylene (i.e., by reactive metabolites in the Clara cells, which are less likely to be formed in humans) warrants further investigation, available data are not sufficient to rule out the possibility that these tumours are relevant to humans.

The incidence of Leydig-cell tumours of the testes increased in an exposure-related manner in Sprague-Dawley rats exposed to trichloroethylene by inhalation (Maltoni *et al.*, 1986, 1988). Similarly, an increased incidence of interstitial-cell tumours of the testes was reported in Marshall rats administered trichloroethylene by gavage in the 2-year bioassay conducted by the National Toxicology Program (1988). Although this study was judged to be inadequate to determine the carcinogenic potential of trichloroethylene due to reduced survival, chemically-induced toxicity and deficiencies in the conduct of the study, these inadequacies did not affect the histopathological diagnoses of the lesions. No information has been identified on the mechanism of induction of testicular tumours in rats following exposure to trichloroethylene.

Since the increased incidence of hepatic tumours in mice appears to be induced by one or more mechanisms to which humans are likely to be less sensitive, and the relevance of the small increase in renal tumours in male rats (at doses that induced renal damage) to humans exposed to this substance is unclear at the present time, results considered most pertinent in assessing the weight of evidence of carcinogenicity of trichloroethylene in humans are principally the significant increases in pulmonary tumours in mice reported by Maltoni *et al*. (1986, 1988) and Fukuda *et al*. (1983), and the increases in testicular tumours in rats reported by Maltoni *et al*. (1986, 1988) and the National Toxicology Program (1988). Although there is some doubt regarding the relevance of the pulmonary tumours observed in mice to humans, based on information on the possible mechanism of induction of these tumours in this species it is not currently possible to conclude that the tumours are induced by a mechanism that is not relevant to humans exposed to trichloroethylene. In addition, trichloroethylene appears to be weakly genotoxic in *in vitro* and *in vivo* assays.[2] Thus, in view of the sufficient weight of evidence of carcinogenicity in 2 species of experimental animals, trichloroethylene is categorized in Group II (probably carcinogenic to humans)[3] of the classification scheme developed for the determination of "toxic" under paragraph 11(*c*) of CEPA (Environmental Health Directorate, 1992).

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2. In one study, somatic mutations have been observed in rats exposed by inhalation to relatively low concentrations (5 ppm or 27 mg/m^3) for 6 hours (Kligerman *et al*., 1992).

3. If additional data are generated on mechanisms of induction of the pulmonary tumours in mice or testicular tumours in rats associated with exposure to trichloroethylene, which indicate that these tumours may not be relevant to evaluation of risks for humans, it is recommended that the classification of this substance as "probably carcinogenic to humans" be re-evaluated.

For such substances, where data permit, estimated total daily intake by the general population in Canada is compared to quantitative estimates of carcinogenic potency to characterize risk and to provide guidance for further action under the Act. The carcinogenic potency ($TD_{0.05}$) of trichloroethylene was derived based on the increased incidence of pulmonary adenomas and adenocarcinomas in $B6C3F_1$ mice (with and without correction for the number of animals alive at the time of appearance of the first pulmonary tumour) [Maltoni *et al*., 1986, 1988], pulmonary adenomas in ICR mice (Fukuda *et al*., 1983), and testicular tumours in Marshall rats (National Toxicology Program, 1988) and Sprague-Dawley rats (with and without correction for the number of animals alive at the time of appearance of the first Leydig cell tumour) [Maltoni *et al*., 1986, 1988]. The increases in renal tubular cell tumours observed in rats (National Toxicology Program, 1988, 1990; Maltoni *et al*., 1986, 1988) were not incorporated in the derivation of carcinogenic potency estimates, due to limitations of the studies (i.e., renal toxicity and reduced survival), the lack of observation of a dose-response relationship in the investigation in which a significant increase in the incidence of this tumour was reported, and observation of small increases only at doses that induced renal damage (National Toxicology Program, 1988).

Based on multistage modelling of these data amortized for continuous exposure, estimates of carcinogenic potency ($TD_{0.05}$s) range from 203×10^3 to 597×10^3 µg/kg bw/day. Calculated exposure/potency indices for the range of estimated total daily intakes of trichloroethylene by the general population of 0.37 to 0.60 µg/kg bw/day are 0.62×10^{-6} to 3.0×10^{-6}. The priority for further action (i.e., analysis of options to reduce exposure), based solely on consideration of potential health effects, is, therefore, considered to be low to moderate.

Although physiologically-based pharmacokinetic models, which take into consideration the proportion of trichloroethylene that has been metabolized, have been developed (e.g., U.S. Environmental Protection Agency, 1988; California Air Resources Board, 1990), pharmacokinetic data have not been incorporated in the estimation of carcinogenic potency, since the putative carcinogenic metabolite(s) has (have) not been identified. Moreover, as the $TD_{0.05}$ is in the experimentally observable range, incorporation of information on metabolized dose is not expected to appreciably alter the estimates of carcinogenic potency reported here. Incorporation of a correction factor for the differences in body-surface area between rodents and humans was not considered appropriate, as it is likely that the carcinogenicity of trichloroethylene is due to a metabolite, rather than to the parent compound.

There are several limitations that must be considered in interpreting the estimates of cancer potency. In particular, it should be noted that the animals in the studies conducted by Maltoni *et al*. (1986, 1988) were exposed to trichloroethylene for a fixed period (78 and 104 weeks for mice and rats, respectively), and then observed until spontaneous death. This study design is in contrast to that of studies normally used in

the quantitative estimation of cancer potency, and the values calculated for potency here are not directly comparable to those determined for some of the other substances assessed under CEPA. In addition, the test compound to which mice were exposed in the study conducted by Fukuda *et al.* (1983) contained low concentrations of contaminants. In the bioassay conducted by the National Toxicology Program (1988), there was chemically-induced toxicity, reduced survival and deficiencies in the conduct of the study (which did not relate to the histopathological diagnoses of lesions).

Since trichloroethylene has been classified as being "probably carcinogenic to humans", it has been concluded that this substance may enter the environment in quantities or under conditions that may constitute a danger in Canada to human life or health.

This approach is consistent with the objective that exposure to non-threshold toxicants should be reduced wherever possible, and obviates the need to establish an arbitrary *de minimis* level of risk for the determination of "toxic" under CEPA.

3.4   Conclusions

Based on the available data, it has been concluded that trichloroethylene occurs at concentrations that may be harmful to the environment, and that may constitute a danger in Canada to human life or health. It has been concluded that trichloroethylene occurs at concentrations that do not constitue a danger to the environment on which human life depends.

4.0 Recommendations

Acquisition of additional data in the following areas would enable a more complete evaluation of the potential effects to the health of the general population in Canada. Also, in assessing the entry, exposure, and effects of trichloroethylene on the environment, several data gaps have been identified. It is thus recommended that additional data be obtained in the following environmental areas:

(i)   research on the mechanisms of induction of tumours of the lungs in mice and testicular tumours in rats associated with exposure to trichloroethylene, in order to more confidently determine the relevance of the results obtained in carcinogenicity bioassays in experimental animals to humans;

(ii)   additional studies in which experimental animals are chronically exposed to trichloroethylene, preferably by inhalation, and in which an adequate range of non-neoplastic effects is investigated, in order to establish an "effect level" for non-neoplastic end-points following long-term exposure to trichloroethylene;

(iii) additional data on the immunotoxicity of trichloroethylene and the neurotoxic effects observed in the offspring of rats exposed to relatively low concentrations of trichloroethylene during pregnancy;

(iv)   additional data on the effects of atmospheric trichloroethylene on terrestrial plants (especially trees and Canadian commercial crops) and of dissolved trichloroethylene on aquatic plants (particularly under conditions of light irradiation as are typical for Canadian conditions);

(v)   additional data on concentrations in ambient air (especially in rural areas and in the vicinity of hazardous-waste depots and landfill sites), surface water (especially in "pristine" waters, and after spills), and biota (especially fish and plants);

(vi)   data on the short- and long-term fate and persistence of trichloroethylene released into Canadian surface waters after spills, with more detailed consideration of potential levels of exposure for aquatic organisms (especially due to the puddling of trichloroethylene), coupled with on-site impact assessments of aquatic biota;

(vii) additional data on acute and chronic effects of low levels of trichloroethylene and its biotic and abiotic transformation products on Canadian aquatic invertebrate, amphibian, avian, and mammalian wildlife;

(viii) information on the effects of sediment- and soil-bound trichloroethylene on benthic and soil-dwelling organisms; and

(ix)   additional data on the fate and persistence of trichloroethylene released into Canadian groundwater, sediments and subsurface soils.

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