Canadian Environmental Protection Act, 1999

Follow-up Report on a PSL1 Substance for Which Data Were Insufficient to Conclude Whether the Substance Was "Toxic" to Human Health

1,1,2,2-Tetrachloroethane

May 2003

PREFACE

For very few of the PSL 1 substances for which data were considered insufficient to conclude whether they were "toxic" under Section 11 of CEPA 1988, did this conclusion apply both to the environment (under Paragraphs 11(a) and 11(b) of CEPA 1988) and human health (under Paragraph 11(c) of CEPA 1988). 1,1,2,2-Tetrachloroethane is one of these compounds

In the documentation which follows, the impact of critical new data on the initial assessment under CEPA 1988 is considered. These data are presented separately for the environmental and health effects, but cross-referenced, where appropriate. Information relevant to assessment of effects on the environment (i.e., determination of "toxic" under Paragraphs 64(a) and (b) of CEPA '99) is presented initially, followed by human health (determination of "toxic" under Paragraph 64(c)).

TABLE OF CONTENTS

LIST OF TABLES

LIST OF ACRONYMS AND ABBREVIATIONS

CAS	Chemical Abstracts Service
CEPA 1988	*Canadian Environmental Protection Act*
CEPA 1999	*Canadian Environmental Protection Act, 1999*
kg-bw	kilogram body weight
LOAEL	Lowest-Observed-Adverse-Effect Level
NAPS	National Air Pollution Surveillance
NOAEL	No-Observed-Adverse-Effect Level
NTP	National Toxicology Program
PSL1	first Priority Substances List
TD_{05}	dose associated with a 5% increase in tumour incidence
TDL_{05}	95% lower confidence limit of the TD_{05}

SYNOPSIS

1,1,2,2-Tetrachloroethane is not produced in nor imported into Canada, although it is released to the Canadian environment primarily in emissions to ambient air during production of other chemicals and from waste disposal sites; it also enters the Canadian environment as a result of long-range atmospheric transport from other countries. Information concerning the presence of 1,1,2,2-tetrachloroethane in products imported into Canada has not been identified.

1,1,2,2-Tetrachloroethane was included on the first Priority Substances List (PSL1) under the 1988 *Canadian Environmental Protection Act* (CEPA 1988) for assessment of potential risks to the environment and human health. As outlined in the Assessment Report released in 1993, relevant data identified before September 1992 were considered insufficient to conclude whether 1,1,2,2-tetrachloroethane was "toxic" to human health as defined in Paragraph 11(c) under CEPA 1988.

Additional monitoring data were identified during the period following the release of the PSL1 Assessment Report (prior to December 2000), and estimates of exposure were accordingly updated. Additional critical toxicological data in experimental species or humans relevant to assessment of the human health risks for 1,1,2,2-tetrachloroethane have not been identified, although an important 13-week study conducted by the U.S. National Toxicology Program (NTP) is nearing completion. The available data provide some evidence that 1,1,2,2-tetrachloroethane may be carcinogenic in humans, although information is inadequate as a basis for classification in Group II ("probably carcinogenic to humans"). Based on the limited available information, the margin of exposure between concentrations in the principal media of exposure (ambient and indoor air) for the general public and observed effect levels is considered sufficient to protect human health.

Based on available data, it is concluded, therefore, that 1,1,2,2-tetrachloroethane is not entering the environment in a quantity or concentration or under conditions that may constitute a danger to human life or health. Therefore, 1,1,2,2-tetrachloroethane is not considered "toxic" to human health as defined in Paragraph 64(c) of the *Canadian Environmental Protection Act, 1999*.

It is recommended that uses and emissions of this compound continue to be monitored to ensure that exposure does not increase to any significant extent and that the potential impact, if any, on the outcome of this assessment be considered when the final report of the NTP subchronic study is available.

1.0 INTRODUCTION

A common Introduction, which describes the process for the preparation of the updates of the Assessment Reports for the seven substances (including 1,1,2,2-tetrachloroethane) on the first Priority Substances List (PSL1) for which data were considered insufficient to conclude whether the substances were "toxic" to human health under the 1988 *Canadian Environmental Protection Act* (CEPA 1988), is posted on all web sites where the Assessment Reports appear.[1]

The strategy for the literature search to identify critical new data (including commercial activity in Canada, human exposure and effects) on 1,1,2,2-tetrachloroethane is presented in Appendix A of this Assessment Report. Only relevant data acquired prior to December 2000 were considered in the determination of whether 1,1,2,2-tetrachloroethane is "toxic" to human health under Paragraph 64(c) of the *Canadian Environmental Protection Act, 1999* (CEPA 1999).

A draft follow-up report was made available for a 60-day public comment period (between September 28, 2002 and November 27, 2002). No comments were received.

2.0 SUMMARY OF THE HUMAN HEALTH RISK ASSESSMENT FOR 1,1,2,2-TETRACHLOROETHANE CONDUCTED UNDER CEPA 1988 (BASED ON INFORMATION IDENTIFIED UP TO SEPTEMBER 1992) (GOVERNMENT OF CANADA, 1993)[2]

1,1,2,2-Tetrachloroethane (Chemical Abstracts Service [CAS] registry number 79-34-5; $Cl_2CHCHCl_2$; acetylene tetrachloride) is a highly volatile synthetic chemical that is used principally as an intermediate in the synthesis of other chlorinated hydrocarbons. At the time of completion of the PSL1 Assessment Report, 1,1,2,2-tetrachloroethane was not produced in nor imported into Canada, although it was released in emissions to air (during production of vinyl chloride and ethylene dichloride and from waste disposal sites); it also enters the Canadian environment as a result of long-range atmospheric transport from other countries.

Data available at the time of release of the PSL1 assessment were sufficient to serve as the basis of exposure estimates for five age groups of the general population of Canada. These estimates were based on mean concentrations in indoor air and ambient air in national surveys and the range of detection limits in drinking water (since 1,1,2,2-tetrachloroethane had only rarely been detected). Intake in food was not included in these estimates, based on the lack of detection of 1,1,2,2-tetrachloroethane in two surveys of foodstuffs in Canada (34 food groups) and the United States (231 food items) and expectation that food would be an insignificant source of exposure due to the high volatility and low potential for bioaccumulation of this substance.

---

[1] See "Introduction to Assessment Reports for Reconsideration of PSL1 Substances for Which Data Were Insufficient to Conclude Whether the Substances Were 'Toxic' to Human Health (Paragraph 11(c), CEPA 1988; Paragraph 64(c), CEPA 1999)" at the following web site: http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

[2] The PSL1 Assessment Report for 1,1,2,2-tetrachloroethane is available on the Health Canada web site: http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

Due to their limitations, the available epidemiological data were considered inadequate to assess the carcinogenicity of 1,1,2,2-tetrachloroethane in humans. In chronic studies identified at the time of release of the PSL1 assessment, there was a highly statistically significant dose-related positive trend ($p < 0.001$) in the incidence of hepatocellular carcinomas in male and female $B6C3F_1$ mice exposed by gavage (in corn oil) to time-weighted-average daily doses of 142 or 284 mg technical-grade 1,1,2,2-tetrachloroethane/kg-bw per day, 5 days per week, for up to 78 weeks (1/18, 13/50 and 44/49 in males and 0/20, 30/48 and 43/47 in females in the vehicle controls, low-dose group and high-dose group, respectively (NCI, 1978). The incidence was statistically significant in all exposed groups, with tumours being observed earlier in mice administered the higher dose. There was no statistically significant increase in the incidence of any type of neoplastic or non-neoplastic lesion in male or female Osborne-Mendel rats similarly administered 1,1,2,2-tetrachloroethane (at time-weighted-average daily doses of 43–108 mg/kg-bw per day) for 78 weeks, although there were two males with hepatocellular carcinomas and one with a hepatic neoplastic nodule in the highest dose group (NCI, 1978), which is noteworthy in view of the relative resistance of this strain to chemical induction of liver tumours.

Based on the weight of evidence in *in vitro* and *in vivo* studies, 1,1,2,2-tetrachloroethane was considered, at most, weakly genotoxic. However, little additional relevant information was identified concerning the mechanism(s) of tumour induction in mice.

Available data were also considered inadequate to develop a Tolerable Daily Intake for 1,1,2,2-tetrachloroethane, as none of the identified studies was of sufficient quality to determine a No-Observed-(Adverse-)Effect Level (NO(A)EL) or Lowest-Observed-(Adverse-)Effect Level (LO(A)EL) for non-neoplastic endpoints, due to either a lack of information presented in the published accounts or limitations in study design (e.g., small numbers of animals per experimental group, lack of histopathological examination). Results of principally limited short-term and subchronic studies conducted by the oral and inhalation routes were sufficient as a basis to conclude that the liver is likely the most sensitive target organ for non-neoplastic effects.

In view of the absence of adequate data for characterization of dose–response for non-neoplastic endpoints and the limited available data on carcinogenicity, **data were considered insufficient to conclude whether 1,1,2,2-tetrachloroethane was "toxic" to human health as defined in Paragraph 11(c) of CEPA 1988.**

3.0 POST-PSL1 ANALYSIS (BASED ON INFORMATION IDENTIFIED BETWEEN SEPTEMBER 1992 AND DECEMBER 2000)

3.1 Production, importation, use and release [3]

Identified information on the commercial activity for 1,1,2,2-tetrachloroethane in Canada confirms that this substance continues not to be produced in nor imported into Canada (CIS, 2001), although very small amounts (e.g., 0.47 tonnes in 1999) may be emitted into the environment as fugitive releases from chemical manufacturing plants (Environment Canada, 2000a). Information on the presence of this substance in consumer products imported into Canada (or elsewhere) has not been identified.

3.2 Population exposure [3]

In a more recently identified relevant study, Fellin *et al*. (1992) reported the outcome of analysis of additional data on concentrations in indoor air (12-month versus 10-month sampling) in the national pilot survey for which preliminary results were reported previously in Otson *et al.* (1992). Reported mean and maximum concentrations of 1,1,2,2-tetrachloroethane in residential indoor air of approximately 750 homes in 10 Canadian provinces were <0.1 $\mu g/m^3$ and 5.2 $\mu g/m^3$, respectively; the highest levels of 1,1,2,2-tetrachloroethane were detected in "single family dwellings" (Fellin *et al*., 1992). Based on recent monitoring studies conducted as part of the National Air Pollution Surveillance (NAPS) Program, mean concentrations of 1,1,2,2-tetrachloroethane in samples (n = 3062) of ambient air collected from sampling locations in seven Canadian provinces (during 1998 and 1999) ranged from 0.02 to 0.05 $\mu g/m^3$, with individual values ranging from non-detectable (estimated detection limit 0.04 $\mu g/m^3$) to 1.7 $\mu g/m^3$ (in Sarnia, Ontario) (Environment Canada, 2001).

In addition, methodology for exposure assessment has evolved since completion of PSL1. Deterministic estimates of the total daily intake of 1,1,2,2-tetrachloroethane for six age groups (versus five groups, previously) of the population of Canada have been revised, therefore, to incorporate developments (EHD, 1998) and the monitoring data from the small number of relevant identified studies (Fellin *et al.*, 1992; Environment Canada, 2001). These revised estimates of total daily intake of 1,1,2,2-tetrachloroethane for the general population and worst-case estimates for high-exposure subgroups are presented in Tables 1 and 2, respectively. The assumptions on which these estimates are based are delineated in footnotes to the tables.

Estimated total daily intakes of 1,1,2,2-tetrachloroethane for six distinct age groups of the general population range from <0.02 to <0.06 µg/kg-bw per day, while worst-case estimates for highly exposed populations range from 0.94 to 2.87 µg/kg-bw per day; the highest estimate of exposure was for children aged 7 months to 4 years. Based on the available data, the principal medium of exposure to 1,1,2,2-tetrachloroethane for the population of Canada is indoor air,

[3] (see also Environment Canada Follow-up Report on 1,1,2,2-Tetrachloroethane)

although it should be noted that these estimates are based on the limit of detection for this medium (since 1,1,2,2-tetrachloroethane was generally not detected in indoor air).

3.3 Hazard characterization and dose–response analyses

Recent identified toxicological data are limited to genotoxicity studies in which negative results have been observed for mitotic recombination in *Drosophila* (Vogel and Nivard, 1993), transformation in BALB cells (Colacci *et al*., 1996) and DNA damage in rodents exposed *in vivo* (Kitchin and Brown, 1994; Sasaki *et al*., 2000), as well as limited short-term studies in which neurotoxicity (Frantik *et al*., 1994; Kanada *et al*., 1994; Anon, 1996) and renal toxicity (NTP, 1996) were examined in rodents exposed orally or via inhalation. The preliminary results of subchronic studies conducted by the National Toxicology Program (NTP, 1994) have also been identified. In these bioassays, groups (n = 10 per sex) of F344 rats and $B6C3F_1$ mice were administered microencapsulated 1,1,2,2-tetrachloroethane in feed at doses equivalent to 18–300 mg/kg-bw per day and 88–1400 mg/kg-bw per day, respectively, for 13 weeks. The results of this unpublished study are currently under review by the NTP Pathology Working Group and thus are not available for hazard characterization or dose–response analysis for 1,1,2,2-tetrachloroethane at this time.

Limitations of currently available data preclude confident characterization of dose–response for non-neoplastic effects and, hence, development of a tolerable intake or tolerable concentration for 1,1,2,2-tetrachloroethane. Based on the limited data available, effects in rodents at lowest concentrations (i.e., 13 mg/m^3) following repeated inhalation of 1,1,2,2-tetrachloroethane have been observed only at levels more than 130 000 times greater than mean concentrations in ambient (i.e., 0.02–0.05 $\mu g/m^3$) and indoor air (<0.1 $\mu g/m^3$), the principal media of exposure.

The toxicological endpoint for which dose–response is best characterized is the statistically significant increase in hepatocellular carcinomas in mice exposed to 1,1,2,2-tetrachloroethane, reported in the long-term bioassay conducted by the National Cancer Institute (NCI, 1978). Measures of tumorigenic potency have been developed, therefore, principally to additionally inform in relation to dose-response though the weight of evidence of carcinogenicity is inadequate as a basis for classification of the compound in Group II ("probably carcinogenic to humans") (Health Canada, 1994). Tumorigenic potency was estimated based on multistage modelling of the incidence of these tumours using GLOBAL82 (Howe and Crump, 1982). The incidences of tumours on which the estimates of potency are based, degrees of freedom, parameter estimates and nature of any adjustments for mortality or period of exposure are presented in Table 3.

Tumorigenic $Dose_{05}$s (TD_{05}, the dose associated with a 5% increase in tumour incidence) range from 5.8 to 28 mg/kg-bw per day,[4] while TDL_{05}s (95% lower confidence limits of the TD_{05}s) range from 3.2 to 18 mg/kg-bw per day (Table 3). While these measures of dose–

[4] These TD_{05}s correspond to airborne concentrations of 5.3–90.6 $\mu g/m^3$ based on inhalation volumes and body weights for six age groups (EHD, 1998).

response are presented to provide at least a crude benchmark with which estimates of exposure can be compared, it should be noted that the weight of evidence for the carcinogenicity of 1,1,2,2-tetrachloroethane is limited. A statistically significant increase in tumour incidence has been observed in only one species in a single study, and 1,1,2,2-tetrachloroethane is, at most, only weakly genotoxic.

3.4 Human health risk characterization

Based on a statistically significant increase in hepatocellular carcinomas in mice, a non-statistically significant increase in hepatocellular tumours in rats and the genotoxic potential demonstrated in some *in vitro* studies, there is some evidence of carcinogenicity of 1,1,2,2-tetrachloroethane, though it is considered inadequate as a basis for classification as "probably carcinogenic to humans". Based on comparison of estimated exposure with carcinogenic potency (for which data on dose-response are most robust), it is concluded that non-neoplastic effects will be protective for tumours (i.e., Margins between estimates of exposure based on limits of detection in the principal media of exposure and the TD_{05} range from 100,000 to 1,4000,000).

Based on the limited data available, effects in rodents at lowest concentrations (i.e., 13 mg/m^3) following repeated inhalation of 1,1,2,2-tetrachloroethane have been observed only at levels more than 130 000 times greater than mean concentrations in ambient (i.e., 0.02 –0.05$\mu g/m^3$) and indoor air (<0.1 $\mu g/m^3$), the principal media of exposure.

On this basis, 1,1,2,2-tetrachlorethane is not considered "toxic" as defined in Paragraph 64(c) of the *Canadian Environmental Protection Act, 1999*.

3.5 Uncertainties and degree of confidence in human health risk characterization

There is a moderate degree of confidence in the data that form the basis for the estimates of intake derived for the population of Canada. These estimates are based on relatively recent monitoring studies in which a large number of samples was collected from various locations across Canada. However, the analytical methodology in most of these investigations was not sufficiently sensitive to quantify levels of 1,1,2,2-tetrachloroethane in various media (i.e., this substance was generally not detected in food, drinking water or indoor air). As a result, potential exposure has likely been overestimated, though the magnitude of this uncertainty cannot be quantified.

The database on toxicity is limited primarily by the absence of data relevant to assessment of the mode of liver tumour induction by 1,1,2,2-tetrachloroethane in mice; therefore, these data, in addition to *in vivo* genotoxicity studies, are desirable to interpret the relevance of these tumours to humans. For a complete investigation of the potential effects of exposure to 1,1,2,2-tetrachloroethane on human health, adequate subchronic and carcinogenicity studies conducted by the inhalation route (the most relevant route of exposure for humans) would be useful. Once the final results of the subchronic oral NTP study (NTP, 1994) are available, these data may be useful in the assessment of human health risk of this substance. Data concerning the

developmental toxicity, reproductive toxicity and immunotoxicity of 1,1,2,2-tetrachloroethane are also not available.

3.6 Considerations for follow-up

Based upon current use patterns, investigation of options to reduce exposure is not considered to be a priority at this time. Uses and emissions of this compound should continue to be monitored to ensure that exposure does not increase to any significant extent. The potential impact, if any, on the outcome of this assessment should also be considered when the final report of the NTP study is available.

4.0 REFERENCES

Anon. 1996. TSCA test rule submissions include nervous system effects for 1,1,2,2-tetrachloroethane. Pestic. Toxic Chem. News 24: 4.

ATSDR (Agency for Toxic Substances and Disease Registry). 1994. Toxicological profile for 1,1,2,2-tetrachloroethane (Draft). U.S. Department of Health and Human Services, Atlanta, Georgia.

ATSDR (Agency for Toxic Substances and Disease Registry). 1996. Toxicological profile for 1,1,2,2-tetrachloroethane (Update). U.S. Department of Health and Human Services, Atlanta, Georgia.

CIS (Camford Information Services). 2001. 1,1,2,2-Tetrachloroethane. Chemical Process Industries (CPI) Product Profiles. Scarborough, Ontario.

Colacci, A., M. Vaccari, P. Perocco, C. Da Via, P. Silingardi, E. Manzini, W. Horn and S. Grilli. 1996. Enhancement of BALB/c 3T3 cells transformation by 1,2-dibromoethane promoting effect. Carcinogenesis 17: 225–231.

Ecobichon, D.J. and M.C. Allen. 1990. New Brunswick public water supplies data summary report 1990. New Brunswick Water Quality Surveillance Program, Department of Health and Community Services.

EHD (Environmental Health Directorate). 1998. Exposure factors for assessing total daily intake of Priority Substances by the general population of Canada. December 1998. Priority Substances Section, Environmental Health Directorate, Health Canada, Ottawa, Ontario (unpublished).

Environment Canada. 1992. Unpublished data from T. Dann, Pollution Measurement Division, River Road Environmental Technology Centre, Ottawa, Ontario.

Environment Canada. 2000a. Search (conducted December 2000) of the National Pollutant Release Inventory, 1994–2000 (http://www.ec.gc.ca/pdb/npri/).

Environment Canada. 2000b. Personal communication (August 2000) with Y. Bovet and E. Dowdall, Use Patterns and Controls Implementation Section, Commercial Chemicals Evaluation Branch, Hull, Quebec.

Environment Canada. 2001. 1,1,2,2-Tetrachloroethane air data. Personal communication (February 14, 2001) with D. Dubé, Commercial Chemicals Evaluation Branch, Hull, Quebec.

Fellin, P., S.E. Barnett and Q.A. Tran. 1992. Results of a national pilot survey of airborne volatile organic compounds in Canadian residences. Prepared by Concord Environmental Corporation for Health and Welfare Canada, Ottawa, Ontario.

Frantik, E., M. Hornychova and M. Horvath. 1994. Relative acute neurotoxicity of solvents: isoeffective air concentrations of 48 compounds evaluated in rats and mice. Environ. Res. 66: 173–185.

Government of Canada. 1993. *Canadian Environmental Protection Act*. Priority Substances List Assessment Report. 1,1,2,2-Tetrachloroethane. Ministry of Supply and Services, Ottawa, Ontario. 27 pp. (ISBN 0-662-20852-8).

Health Canada. 1994. *Canadian Environmental Protection Act* — Human health risk assessment for Priority Substances. Minister of Supply and Services, Ottawa, Ontario. 36 pp. (Catalogue No. En40-215/41E).

Health Canada. 2000. Personal communication (August 2000) with G. Moore, Submission Management and Information Division, Pest Management Regulatory Agency, Ottawa, Ontario.

Howe, R.B. and K.S. Crump. 1982. GLOBAL82: A comprehensive program to extrapolate quantal animal toxicity data to low doses. Science Research Systems, Ruston, Louisiana.

IPCS (International Programme on Chemical Safety). 1998. 1,1,2,2-Tetrachloroethane. Concise International Chemical Assessment Document (CICAD) No. 3. World Health Organization, Geneva.

Kanada, M., M. Miyagawa, M. Sato, H. Hasegawa and T. Honma. 1994. Neurochemical profile of effects of 28 neurotoxic chemicals on the central nervous system in rats. (1) Effects of oral administration on brain contents of biogenic amines and metabolites. Ind. Health 32: 145–164.

Kitchin, K.T. and J.T. Brown. 1994. Dose–response relationship for rat liver DNA damage caused by 49 rodent carcinogens. Toxicology 88: 31–49.

Lachmaniuk, P. 1991. Personal communication (letter and telephone conversation). Drinking Water Assessment Specialist, Water Resources Branch, Ontario Ministry of the Environment.

NCI (National Cancer Institute). 1978. Bioassay of 1,1,2,2-tetrachloroethane for possible carcinogenicity. National Cancer Institute, National Institutes of Health, Public Health Service, U.S. Department of Health, Education and Welfare, Bethesda, Maryland (NTIS PB277 4537GA; DHEW/PUB/NIH-78-827).

NTP (National Toxicology Program). 1994. 13-week subchronic microencapsulated dosed feed toxicity study of 1,1,2,2-tetrachloroethane in F344 rats and B6C3F$_1$ mice. April 1, 1994. Final report prepared by Microbiological Associates, Inc. for the National Toxicology Program, National Institutes of Health, National Institute of Environmental Sciences, Research Triangle Park, North Carolina.

NTP (National Toxicology Program). 1996. Technical report on renal toxicity studies of selected halogenated ethanes administered by gavage to F344/N rats. National Institutes of Health, Research Triangle Park, North Carolina (NTP Toxicity Report Series No. 45).

Otson, R., D.T. Williams and P.D. Bothwell. 1982. Industrial chemicals — 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 VOC's in residences — design and progress. Presented at the 1992 Environmental Protection Agency/Air and Waste Management Association Symposium on Measurement of Toxic and Related Air Pollutants, May 4–8, 1992, Durham, North Carolina (unpublished).

Sasaki, Y.F., K. Sekihashi, F. Izumiyama, E. Nishidate, A. Saga, K. Ishida and S. Tsuda. 2000. The Comet assay with multiple mouse organs: comparison of Comet assay results and carcinogenicity with 208 chemicals selected from the IARC Monographs and the U.S. NTP Carcinogenicity Database. CRC Crit. Rev. Toxicol. 30: 629–799.

U.S. EPA (United States Environmental Protection Agency). 2000. Toxic Release Inventory database (http://www.epa.gov/enviro/html/tris/tris_info.htm). On-line search conducted December 2000.

Vogel, E.W. and M.J.M. Nivard. 1993. Performance of 181 chemicals in a *Drosophila* assay predominantly monitoring interchromosomal mitotic recombination. Mutagenesis 8: 57–81.

Table 1: Estimated average total daily intake of 1,1,2,2-tetrachloroethane for various age groups of the general population in Canada

Medium	Estimated intake (µg/kg-bw per day)					
	0–6 months[1]	**7 months–4 years[2]**	**5–11 years[3]**	**12–19 years[4]**	**20–59 years[5]**	**60+ years[6]**
Ambient air[7]	7×10^{-4} – 1.8×10^{-3}	1.5×10^{-3} – 3.8×10^{-3}	1.2×10^{-3} – 2.9×10^{-3}	7.0×10^{-4} – 1.7×10^{-3}	6.0×10^{-4} – 1.4×10^{-3}	5.0×10^{-4} – 1.2×10^{-3}
Indoor air[8]	<0.02	<0.05	<0.04	<0.02	<0.02	<0.02
Drinking water[9]	<0.001–<0.03	$<6.45 \times 10^{-4}$ – <0.01	$<6.45 \times 10^{-4}$ – <0.01	$<3.37 \times 10^{-4}$ – <0.007	$<2.82 \times 10^{-4}$ – <0.006	$<2.77 \times 10^{-4}$ – <0.006
Total intake	**<0.02–<0.05**	**<0.05–<0.06**	**<0.04–<0.05**	**<0.02–<0.03**	**<0.02–<0.03**	**<0.02–<0.03**

1 Assumed to weigh 7.5 kg, breathe 2.1 m^3 of air per day and drink 0.2 L of water per day (EHD, 1998).

2 Assumed to weigh 15.5 kg, breathe 9.3 m^3 of air per day and drink 0.2 L of water per day (EHD, 1998).

3 Assumed to weigh 31.0 kg, breathe 14.5 m^3 of air per day and drink 0.4 L of water per day (EHD, 1998).

4 Assumed to weigh 59.4 kg, breathe 15.8 m^3 of air per day and drink 0.4 L of water per day (EHD, 1998).

5 Assumed to weigh 70.9 kg, breathe 16.2 m^3 of air per day and drink 0.4 L of water per day (EHD, 1998).

6 Assumed to weigh 72.0 kg, breathe 14.3 m^3 of air per day and drink 0.4 L of water per day (EHD, 1998).

7 Based on the range of mean concentrations of 1,1,2,2-tetrachloroethane in samples (n = 3062) of ambient air collected from 41 NAPS sampling locations in seven Canadian provinces (during 1998–1999) of 0.02–0.05 µg/m^3 (Environment Canada, 2001) and an average of 3 hours per day spent outdoors (EHD, 1998).

8 Based on a mean concentration of <0.1 µg 1,1,2,2-tetrachloroethane/m^3 in indoor air from approximately 750 homes in 10 Canadian provinces (Fellin *et al*., 1992) and an average of 21 hours spent indoors (EHD, 1998).

9 Based on the range of detection limits in a survey (during 1979) of 30 water treatment facilities across Canada (Otson *et al*., 1982) and monitoring programs in Ontario (Lachmaniuk, 1991) and New Brunswick (Ecobichon and Allen, 1990) of <0.05–<1.0 µg/L (conducted between 1988 and 1991), in which 1,1,2,2-tetrachloroethane was generally not detected. Since 1,1,2,2-tetrachloroethane has only rarely been detected in treated drinking water in Canada, these estimates likely overestimate exposure in this medium.

Table 2: Worst-case estimates of daily intake of 1,1,2,2-tetrachloroethane for various age groups of the population in Canada

Medium	Estimated intake (µg/kg-bw per day)					
	0–6 months[1]	**7 months–4 years**[2]	**5–11 years**[3]	**12–19 years**[4]	**20–59 years**[5]	**60+ years**[6]
Ambient air[7]	0.06	0.13	0.09	0.06	0.05	0.04
Indoor air[8]	1.27	2.73	2.13	1.21	1.04	0.90
Drinking water[9]	1.3×10^{-3} – 0.03	6.45×10^{-4} – 0.013	6.45×10^{-4} – 0.013	3.37×10^{-4} – 0.007	2.82×10^{-4} – 0.006	2.77×10^{-4} – 0.006
Total intake	**1.33–1.36**	**2.86–2.87**	**2.22–2.23**	**1.27–1.28**	**1.09–1.10**	**0.94–0.95**

[1] Assumed to weigh 7.5 kg, breathe 2.1 m^3 of air per day and drink 0.2 L of water per day (EHD, 1998).

[2] Assumed to weigh 15.5 kg, breathe 9.3 m^3 of air per day and drink 0.2 L of water per day (EHD, 1998).

[3] Assumed to weigh 31.0 kg, breathe 14.5 m^3 of air per day and drink 0.4 L of water per day (EHD, 1998).

[4] Assumed to weigh 59.4 kg, breathe 15.8 m^3 of air per day and drink 0.4 L of water per day (EHD, 1998).

[5] Assumed to weigh 70.9 kg, breathe 16.2 m^3 of air per day and drink 0.4 L of water per day (EHD, 1998).

[6] Assumed to weigh 72.0 kg, breathe 14.3 m^3 of air per day and drink 0.4 L of water per day (EHD, 1998).

[7] Based on the maximum concentration of 1,1,2,2-tetrachloroethane (i.e., 1.7 µg/m^3) detected in samples (n = 3062) of ambient air collected from up to 41 locations in seven Canadian provinces during 1998–1999 (Environment Canada, 2001) and an average of 3 hours per day spent outdoors (EHD, 1998).

[8] Based on a maximum concentration of 1,1,2,2-tetrachloroethane (i.e., 5.2 µg/m^3) detected in indoor air from approximately 750 homes in 10 Canadian provinces (Fellin *et al*., 1992) and an average of 20 hours spent indoors (EHD, 1998).

[9] Based on a range of detection limits in a survey (conducted in 1979) of 30 water treatment facilities across Canada (Otson *et al*., 1982) and monitoring programs in Ontario (Lachmaniuk, 1991) and New Brunswick (Ecobichon and Allen, 1990) of 0.05–1.0 µg/L; since 1,1,2,2-tetrachloroethane has only rarely been detected in treated drinking water in Canada, these estimates likely overestimate exposure in this medium.

Table 3: Tumorigenic doses for hepatocellular carcinomas in $B6C3F_1$ mice exposed by gavage to 1,1,2,2-tetrachloroethane (NCI, 1978)[1]

Liver histopathology	TD_{05} (mg/kg-bw per day)	TDL_{05} (mg/kg-bw per day)	p-value	Chi-square	Degrees of freedom
Incidence of hepatocellular carcinomas in males: 3/36, 13/50, 44/49	27.5	17.9	NA[2]	5.5	0
Incidence of hepatocellular carcinomas in females: 1/40, 30/48, 43/47	5.8	3.2	NA	0	0

[1] Male and female $B6C3F_1$ mice were exposed to 1,1,2,2-tetrachloroethane by gavage (in corn oil) at time-weighted-average daily doses of 0, 142 or 284 mg/kg-bw per day for 5 days per week for up to 78 weeks. A "pooled" vehicle control group was used in the dose–response analysis, which included controls from both the 1,1,2,2-tetrachloroethane study and a separate chloropicrin study, since it included more animals than in the single "matched" vehicle control group.

[2] NA = not applicable.

APPENDIX A: SEARCH STRATEGY — NEW INFORMATION FOR THE ASSESSMENT OF "TOXIC" TO HUMAN HEALTH UNDER PARAGRAPH 64(C) OF CEPA 1999

In the period since the PSL1 Assessment Report was released, more recent information on exposure and effects of 1,1,2,2-tetrachloroethane (up to August 1995) was reviewed by Health Canada for the preparation of a Concise International Chemical Assessment Document (IPCS, 1998), based principally on the Assessment Report for 1,1,2,2-tetrachloroethane (Government of Canada, 1993) and a review prepared by the Agency for Toxic Substances and Disease Registry (ATSDR, 1994).

To identify additional relevant information on production, importation, use and environmental release, searches (conducted up to December 2000) of the National Pollutant Release Inventory (Environment Canada, 2000a), the Toxic Release Inventory (U.S. EPA, 2000), the Pesticide Management Regulatory Agency of Health Canada (Health Canada, 2000) and the Use Patterns and Controls Implementation Section of Environment Canada (Environment Canada, 2000b) were conducted. A product information profile for 1,1,2,2-tetrachloroethane was provided by Camford Information Services (CIS, 2001).

A literature search was conducted (up to March 2000) for monitoring data in Canada (or elsewhere) and toxicological studies in animals and humans, using the strategy of searching by name or CAS registry number in the following databases: Canadian Research Index, CCRIS (Chemical Carcinogenesis Research Information System, U.S. National Cancer Institute), EMIC (Environmental Mutagen Information Center database, Oak Ridge National Laboratory), GENE-TOX (Genetic Toxicology, Office of Toxic Substances, U.S. Environmental Protection Agency), HSDB (Hazardous Substances Data Bank, U.S. National Library of Medicine), IRIS (Integrated Risk Information System, U.S. Environmental Protection Agency) and RTECS (Registry of Toxic Effects of Chemical Substances, U.S. National Institute for Occupational Safety and Health). Name and registry number were searched in the Toxline (U.S. National Library of Medicine; 1994–1999) and Medline (U.S. National Library of Medicine; 1991–2000) databases. A search of the following web sites was also conducted (up to December 2000): Agency for Toxic Substances and Disease Registry, International Agency for Research on Cancer, International Programme on Chemical Safety, National Toxicology Program, Organisation for Economic Co-operation and Development, , TOMES Plus System (composed of CHRIS, ERG2000, HAZARDTEXT, HSDB, INFOTEXT, IRIS, MEDITEXT, New Jersey Fact Sheets, NIOSH Pocket Guide, OHM/TADS and RTECS) and U.S. Environmental Protection Agency. An updated review by the Agency for Toxic Substances and Disease Registry (ATSDR, 1996) was also consulted.