

## Trichloroethylene (TCE)

### 1. Physico-Chemical Properties

Trichloroethylene is a volatile, non-flammable, colourless liquid. Most people can smell it at 100 parts of TCE per million parts of air (ppm), which is equivalent to about 560 mg of TCE per m<sup>3</sup> of air. TCE is somewhat soluble in water and is miscible with most organic solvents. Chemical Abstract Society (CAS) number is 79-01-6. The summary of its relevant physico-chemical properties is presented in table 1 below.

Table 1 Physical and Chemical Properties of Trichloroethylene (Adapted from ATSDR, 1995)

Property	Characteristic
Molecular weight	131.40
Color	Clear, colourless
Physical state	Liquid (at room temperature)
Melting point	-87.1°C
Boiling point	86.7 °C
Density at 20°C	1.465 g/mL
Odour	Ethereal; chloroform- like; sweet
Odour threshold: Air	100 ppm
Solubility: Water at 20°C 25°C Organic solvents	1.070 g/L 1.366 g/L Miscible with many common organic solvents (such as ether, alcohol, and chloroform)
Partition coefficients: Log K <sub>ow</sub> Log K <sub>oc</sub>	2.42 2.03-2.66
Vapour pressure at 25°C	74 mm Hg
Henry's law constants: at 20°C at 25°C	0.020 atm·m <sup>3</sup> /mol 0.011 atm·m <sup>3</sup> /mol
Autoignition temperature	None
Flashpoint	None
Flammability limits at 25°C (explosive limits) volume % in air)	8.0-10.5
Conversion factors Air at 20°C  Water	1 mg/m <sup>3</sup> = 0.18 ppm; 1 ppm = 5.46 mg/m <sup>3</sup> 1 ppm (weight per volume) = 1 mg/L

## **2. Sources and Environmental Fate**

TCE is a synthetic product with no known natural sources. In Canada and the US, most TCE found in the environment is released into the air from degreasing operations (ATSDR, 1995; CEPA, 1993). Other relatively minor releases occur during the manufacture of TCE (according to CEPA, 1993, TCE is currently not produced in Canada) and of other chlorinated hydrocarbons including polyvinyl chloride. Some TCE is released during household and industrial dry-cleaning, from cleaning of electronic components and from adhesives, paints and coatings. Treatment and disposal sites such as water treatment facilities, landfills, municipal and hazardous incinerators may also release TCE. The chemical has been repeatedly detected in the atmosphere and at some distance from any sources even though its predicted half-life is short. This phenomenon has been explained to be resulting from continuous releases of TCE and by the frequent presence of tetrachloroethylene that can break down into TCE.

In the air, about half of TCE is expected to be photochemically transformed primarily into hydroxyl radicals within days in the summer and weeks to months in the winter (CEPA, 1993). However, the half-life for degradation of the remaining TCE may be slower.

Partition of TCE from surface waters to air is rapid with a half-life of several days to several weeks (CEPA, 1993). Evaporation is the primary route of removal of TCE from surface waters whereas photooxidation, hydrolysis and biodegradation play an insignificant role (CEPA, 1993). The situation may be different in the groundwater, where TCE may be biotransformed under suitable anaerobic conditions into dichloroethylene, chloroethane and vinyl chloride with a biodegradation half-life ranging from several months to several years.

Volatilization to the atmosphere is also the primary means of elimination of TCE from the soil. The process is relatively rapid, but more slowly than from surface waters. The half-life ranges from several days to several weeks. Under anaerobic conditions, TCE may be biotransformed into vinyl chloride.

Trichloroethylene is readily mobile in the soil. The mobility is primarily affected by the organic carbon content, which affects sorption to the soil. Experimentally determined  $K_{oc}$  values for the soil ranged from 106 to 460 (Garbarini and Lion, 1986; cited in ATSDR, 1995) for TCE. TCE, which has not volatilized, tends to migrate down towards groundwater. Because its density is higher than water, it tends to settle at or below the lowest groundwater strata. From these pools, TCE may be slowly released over long periods of time.

### **Levels**

In the US, the levels of TCE in the air of industrial cities ranged between 0.24 and 39  $\mu\text{g}/\text{m}^3$  (ATSDR, 1995). In Canada, the levels were generally found to be between 0.1 and 3  $\mu\text{g}/\text{m}^3$ , with some measurements reaching 20  $\mu\text{g}/\text{m}^3$  (CEPA, 1993). The mean value of 1.4  $\mu\text{g}/\text{m}^3$  is typical for Canadian homes, although levels of up to 165  $\mu\text{g}/\text{m}^3$  have been reported (CEPA, 1993).

Environment Canada (CEPA, 1993) reported TCE levels of between over 0.001 µg/L and 100 µg/L in the surface water, with the levels in Ontario waters generally below 1 µg/L. The levels in surface waters generally do not exceed 1 µg/L, unless there are direct releases into the waters. Environment Canada (CEPA, 1993) reported levels ranging from under 1000 µg/L to almost 10<sup>6</sup> µg/L in the groundwater at various contaminated sites. With the exception of some groundwater supplies in Prince Edward Island, the majority of the drinking water supplies in Canada contains less than 0.2 µg/L of TCE.

TCE has been detected in the sediment at 6% of the 388 US observation stations and the median level was 5 µg per kg of dry sediment weight (Staples *et al.* 1985; cited by ATSDR, 1995). The stations consist of a mix of “ambient sites” such as lakes, streams and municipal/industrial effluents. In Canada, high levels (10 to 100 000 µg/L) were reported (CEPA, 1993) following a spill in the contaminated sediment of St. Clair River.

Neither Environment Canada nor Agency for Toxic Substances and Disease Registry (ATSDR) has reported enough data to allow one to form a clear picture of the ranges of levels of TCE in soils in North America or Canada.

### **Situations Likely to Lead to Exposure**

People can be exposed to TCE by inhalation, oral and dermal routes. In most circumstances, the inhalation route and ingestion of drinking water are the primary routes of exposure to TCE. Oral ingestion of soil can be important among children due to their hand to mouth activities. Exposure to TCE from food is generally low. Dermal exposure may be important if there is a direct contact with contaminated soils, such as during gardening or playing on site. Under most circumstances, the primary exposure is from inhalation. Besides occupational inhalation exposures in industries that manufacture or use TCE, the primary concern is exposure indoors, where people spend most of their time. Indoor TCE could originate from indoor sources or outdoor sources. Outdoor sources include the outdoor air and the soil TCE, which volatilizes and enters indoors through building foundations. Other than industrial situations, indoor TCE can be related to new building construction materials, which contain TCE or to home products containing this compound.

## **3. Toxicokinetics**

ATSDR (1995) has reviewed the toxicokinetics of TCE in humans and animals. Based on human data, TCE is rapidly absorbed when inhaled. 37-64% of the inhaled TCE is taken up in the lungs. For the purpose of this study, 50% absorption will be assumed.

There are little data on the oral absorption of TCE in humans. In rodents, oral absorption is rapid (minutes) and almost complete in fasting animals. Absorption is delayed and less complete in animals that have not been fasting or which have received TCE in corn oil. Oils serve as a reservoir for lipophilic material in the gut. For the purpose of this study, oral absorption will be assumed to be complete, although it is recognized that it could be less than complete.

Human data indicate that dermal absorption of TCE can be rapid (minutes). TCE removes the fat from the skin (stratum corneum), thus enhancing its own absorption. Animal data also support the notion of rapid absorption across the skin layer. For the purpose of this study, full absorption is assumed.

Once absorbed, TCE is distributed widely through the bloodstream to most tissues. It is primarily metabolized in the liver, although metabolism in the lungs has also been reported. It is metabolized via cytochrome P-450 oxygenases and the metabolites are conjugated. Unmetabolized TCE is exhaled, while the metabolites are eliminated primarily in the urine.

#### **4. Human Health Effects**

The effects of TCE in humans and experimental animals have been extensively studied and reviewed. The following is only an outline of a few key studies and findings.

At concentrations far exceeding any environmental levels, TCE caused death in humans, presumably due to ventricular fibrillation (a form of heart arrhythmia) or depression of the central nervous system. TCE had been used as an anaesthetic at low doses. More moderate doses may cause headaches, dizziness and damage to the facial nerves. Acute inhalation exposures (1100 mg/m<sup>3</sup> for 5 days, 7 hours/day) caused mild subjective neurological effects, such as fatigue and drowsiness, in the study volunteers (Stewart *et al.* 1970; cited in ATSDR, 1995). Other studies with similar exposure are in general agreement with this study.

Neurological effects were reported also in rodent inhalation studies of intermediate duration (15 days to 364 days). Wistar rats exposed to about 270 mg/m<sup>3</sup> for 6 weeks, 5 days a week, 8 hours a day showed signs of decreased wakefulness, decreased post-exposure heart rate and slow wave sleep (Arito *et al.* 1993; cited in ATSDR, 1995). These findings are supported by reports of organic solvent-induced sleep apnea in humans (see ATSDR, 1995 for references).

Direct exposure of the skin to TCE may cause rashes. Liver and kidney damage has been reported after high level of oral or inhalation exposures in animals. Exposures to TCE have also caused developmental effects in mouse pups and developing mouse fetuses after short term and intermediate duration exposures. Oral exposures of mouse pups or pregnant rats to TCE had led to behavioral (NOAEL = 50mg/kg/day based on the study of Frederickson *et al.* 1993; ATSDR, 1995) or heart abnormalities (No Observable Adverse Effect Level (NOAEL) = 0.18 mg/kg/day, based on the study by Dawson *et al.* 1993; ATSDR, 1995). Both findings are supported by other studies. For references, see ATSDR (1995).

There is some evidence from human epidemiological studies and strong evidence from animal studies that TCE may cause cancer. International Agency for Research on Cancer (IARC, 1995) rates TCE as *probably carcinogenic to humans* (Group 2A) based on *limited evidence* from several human epidemiological studies and on *sufficient evidence* from animal studies. Health Canada (CEPA, 1993) also rates TCE as *probably carcinogenic to humans* (Group II), based on *sufficient weight of evidence* of carcinogenicity in two animal species (rats and mice). USEPA has withdrawn its earlier ranking (Group B2 – *probable human carcinogen*) of this compound from the IRIS database. Its earlier assessment was based on experimental animal data.

## 5. Potency Estimates

The unit risk range of  $3.5 \times 10^{-7}$  to  $1.0 \times 10^{-6}$  ( $\mu\text{g}/\text{m}^3$ )<sup>-1</sup>, derived from Health Canada (CEPA, 1993) TD<sub>0.05</sub> range of  $2.03 \times 10^5$  to  $5.97 \times 10^5$   $\mu\text{g}/\text{kg}$  bw/day (see Table 2) is recommended for assessment of cancer risk. The Health Canada model is recommended because it has applied more stringent criteria to data selection than the California's CARB (1990) study. Health Canada's assessment is similar to the recent assessment by World Health Organization (WHO, 1996) in its data selection, assumptions and outcome (unit risk estimates ranging from  $9.3 \times 10^{-8}$  to  $4.3 \times 10^{-7}$  ( $\mu\text{g}/\text{m}^3$ )<sup>-1</sup>). Health Canada's approach is favored, because it provides a more complete description of the process it has used. A two- to four-fold difference between the two assessments is negligible and the small difference reflects the similarity of the two assessments rather than the low level of uncertainty in these assessments.

### Sources of Uncertainty

The risk assessment of TCE is associated with significant uncertainty, perhaps spanning orders of magnitude. The key issues that need to be considered are listed below.

- TCE present in soil or groundwater can be transformed under anaerobic conditions into vinyl chloride, which is far more toxic than TCE. In situations where vinyl chloride has been identified on the site indicating that this transformation is taking place, risk management actions need to address not only the risk posed by TCE itself but also TCE as a precursor of vinyl chloride.
- The Health Canada (CEPA, 1993) dose response assessment is based on studies where TCE induced tumors in the lungs of mice and in the testes of rats. There is *some doubt regarding the relevance of the pulmonary tumors observed in mice to humans* (CEPA, 1993). If the mechanisms by which these two types of tumors are induced in rodents were found to be not relevant in a human situation, the assessment would have to be revised.
- Although most of the assessments are conducted on the assumption that TCE is a non-threshold carcinogen, this may not be the case as evidence for its ability to act as an initiator is weak. If TCE carcinogenicity has a threshold, the risk from TCE would be substantially lower than the risk estimated by Health Canada (CEPA, 1993) and cancer may not be the most sensitive endpoint. A brief discussion of these issues follows.

### TCE - threshold or non-threshold carcinogen

Most agencies regulate TCE based on its cancer effects assuming a non-threshold mechanism. This approach is conservative because it assumes some (small) risk even at very low concentrations. The assumption of a non-threshold has a good scientific basis when the compounds are strong initiators (such as nitrosamines). Initiators are generally mutagens. Unlike promotion, initiation requires that a mutation take place. The data in support of mutagenicity of TCE are equivocal, however, and ATSDR (1995) considers TCE a weak, indirect mutagen.

For typical non-threshold carcinogens such as polycyclic aromatic hydrocarbons (PAH), tumors are usually observed at concentrations or doses lower than those inducing non-cancer effects. TCE does not seem to behave in the same way. A very comprehensive ATSDR assessment indicates that cancer effects have been observed at exposure levels that are higher than those needed to induce other toxic effects. It is possible that cancer may be induced at lower exposure levels and remains undetected in the experimental studies. It is also possible that the observed cancer effects are secondary to tissue damage and possible cell proliferation in the target organs. Such cytotoxic and proliferative events are thought to have a threshold. If there is a threshold to the cancer effects of TCE, then other toxic endpoints that are considered to have a threshold may be more sensitive than the cancer endpoint.

ATSDR has developed *Minimum Risk Levels* (MRLs) for non-cancer endpoints (see table 3). Although the MRLs are intended to provide a ranking of individual chemical toxicity, it is useful to compare these values with the levels associated with a  $10^{-6}$  cancer risk level. It is apparent that although the exposure levels at which cancer effects were detected are higher than the exposure levels required to induce non-cancer effects, the risk management level is much more stringent for the cancer endpoint due to the non-threshold assumption for TCE carcinogenicity.

Table 2 Unit risks in  $(\mu\text{g}/\text{m}^3)^{-1}$  and slope factors in  $(\mu\text{g}/\text{kg bw}/\text{day})^{-1}$

Agency	Unit risk	Slope factor	Basis	Reference
USEPA	withdrawn	withdrawn	NA	IRIS, 1994
WHO	$9.3 \times 10^{-8}$ to $4.3 \times 10^{-7}$	NA	**	WHO, 1996
CEPA*	$3.5 \times 10^{-7}$ to $1.0 \times 10^{-6}$	$8.4 \times 10^{-8}$ to $2.5 \times 10^{-7}$	***	CEPA, 1993
CARB	$2 \times 10^{-6}$ to $3 \times 10^{-6}$	NA	****	CARB, 1990

\*converted from  $\text{TD}_{0.05}$  range of  $2.03 \times 10^5$  to  $5.97 \times 10^5 \mu\text{g}/\text{kg-bw}/\text{day}$ . This value is equivalent to a slope factor range of  $8.37 \times 10^{-8}$  to  $2.46 \times 10^{-7} (\mu\text{g}/\text{kg-bw}/\text{day})^{-1}$ , which can be translated into unit risk ranges of  $3.5 \times 10^{-7}$  to  $1.0 \times 10^{-6} (\mu\text{g}/\text{m}^3)^{-1}$ , assuming a 70 kg person and an inhalation rate of  $17\text{m}^3/\text{day}$ . There is good evidence indicating that both oral and inhalation routes of exposure have similar effects on the same target tissues and that TCE distributes rapidly throughout the body.

\*\* pulmonary adenomas/carcinomas in B6C3F<sub>1</sub> mice, pulmonary adenomas in Swiss mice and testicular tumors in rats (references not provided)

\*\*\* pulmonary adenomas/carcinomas in B6C3F<sub>1</sub> mice (Maltoni *et al.* 1986, 1988), pulmonary adenomas in ICR mice (Fukuda *et al.* 1983) and testicular tumors in rats (National Toxicology Program, 1988; Maltoni *et al.* 1986, 1988)

\*\*\*\* Included 13 data sets including lymphomas, lung and liver tumors in mice and rats.

Table 3 MRLs for TCE (ATSDR, 1995) – comparison with doses corresponding to a  $10^{-6}$  cancer risk level calculated using CEPA unit risk and slope factor ranges.

Route	Exp. Duration	Effect Observed at	MRL/Risk @ $10^{-6}$	Management Level
inhalation	Acute	109 mg/m <sup>3</sup>	MRL	1.1 mg/m <sup>3</sup> (neurol.)
	Intermediate	27.3 mg/m <sup>3</sup>	MRL	0.546 mg/m <sup>3</sup> (neurol.)
	Chronic	54.6 – 327 mg/m <sup>3</sup>	Risk	0.001 to 0.0029 mg/m <sup>3</sup> (cancer)
Oral	Acute	50 mg/kg/day	MRL	0.2 mg/kg/day (develop.)
	Chronic	1000 mg/kg/day	Risk	0.004 to 0.012 mg/kg/day (cancer)

## 6. References

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