Cancer Association of South Africa (CANSA)

Research • Educate • Support

Fact Sheet and Position Statement on Tetrachloroethylene

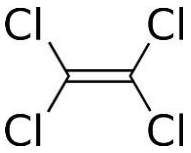
Introduction

[Picture Credit: Dry Cleaning]

Tetrachloroethylene, also known under its systematic name tetrachloroethene and many other names, is a chlorocarbon. It is a colourless liquid widely used for dry cleaning of fabrics and is sometimes called 'dry-cleaning fluid'. It has a sweet odour detectable by most people at a concentration of 1 part per million (1 ppm). It is also used in the cleaning of metal machinery and to manufacture some consumer products and other chemicals. Confirming longstanding scientific understanding and research, the final Environmental Protection Agency (EPA) risk assessment characterises this material as a likely human carcinogen. The assessment provides estimates for both cancer and non-cancer effects associated with exposure to it over a lifetime.

The International Agency for Research on Cancer (IARC) has classified tetrachloroethylene (tetrachloroethene) as a **Group 2A carcinogen**, which means that it is probably carcinogenic to humans.

Its chemical formula is $Cl_2C=CCl_2$.



[Diagram Credit: About.com Chemistry]

Synonyms

Tetrachloroethylene is also known under the following names:

- Ethylene tetrachloride
- PCE

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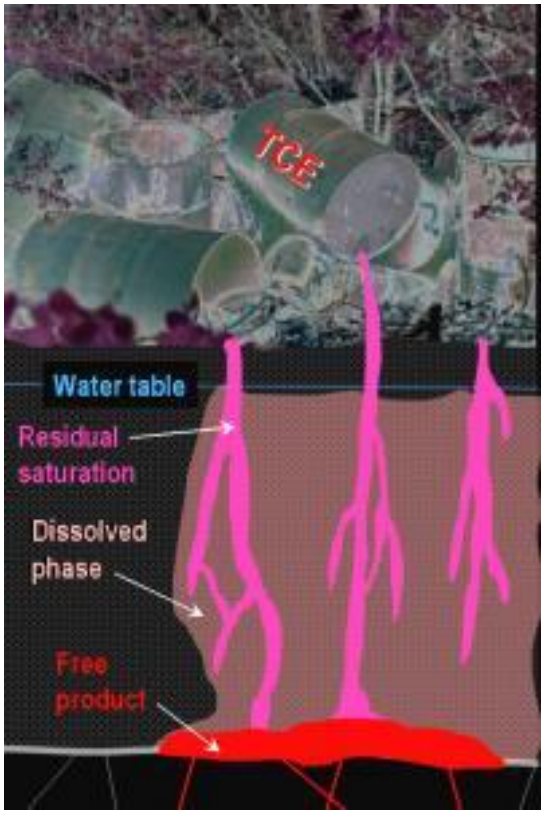
- 'per'
- PER
- PERC
- Perchlorethylene
- Perchloroethene
- Perchloroethylene
- Tetrachlorethylene
- TCE
- 1,1,2,2-Tetrachloroethene
- 1,1,2,2-Tetrachloroethylene

Exposure Routes of Tetrachloroethylene

Exposure to tetrachloroethylene occurs primarily through inhalation and dermal contact where tetrachloroethylene is produced or used. The general population may be exposed via inhalation of ambient air, ingestion of food and drinking water. Contamination of the environment is a major concern.

[Picture Credit: TCE]



Inhalation:

The air pathway is a major route of exposure to tetrachloroethylene. Exposure scenarios include inhalation of contaminated air:

- during work with tetrachloroethylene or
- while in the same space as others working with tetrachloroethylene

Tetrachloroethylene may also be inhaled from:

- accidental spills or product use in small, enclosed spaces
- clothing or newly dry-cleaned fabrics in homes
- landfills in which it may have been disposed
- releases to air and water by evaporation or emissions from industrial and dry-cleaning plants
- vapours formed from contaminated water used for bathing and laundering
- vapours rising from contaminated groundwater seeping into a basement or crawl space, and worker's skin

Ingestion:

Ingestion—another major pathway of exposure—may be intentional or accidental. It occurs through swallowing

- food or drinking water contaminated with tetrachloroethylene or breast milk contaminated with tetrachloroethylene

Skin Contact:
Dermal contact also may be a route of tetrachloroethylene exposure in the workplace and among the general public. However, the chemical is less easily absorbed through the skin than through inhalation and the oral exposure route.

Brito-Marcelino, A., Duarte-Tavares, R.J., Marcelino, K.B. & Silva-Neto, J.A. 2020.
Background: Occupational risk factors are associated with many types of neoplasms including cervical cancer.
Objective: To review the specialized literature for evidence on the relationship between cervical cancer and exposure to occupational hazards.
Methods: Literature search in electronic databases using keywords cervical cancer and occupational risk.
Results: Workers occupationally exposed to tobacco, fungi or bacteria, metalworking fluids and tetrachloroethylene used in dry cleaning and for metal degreasing exhibited higher susceptibility to cervical cancer.
Conclusion: Few studies sought to investigate relationships between cervical cancer and occupational hazards, which hinders the attempts at establishing a causal link.

Brito-Marcelino, A., Duarte-Tavares, R.J., Marcelino, K.B. & Silva-Neto, J.A. 2020. Cervical cancer related to occupational risk factors: review. *Rev Bras Med Trab*. 2020 Aug 4;18(1):103-108.
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Physiological Effects of Exposure to Tetracholoroethylene
Exposure to tetrachloroethylene can affect the
- central nervous system (CNS)
- eyes
- kidney
- liver
- lungs
- mucous membranes, and
- skin

Central Nervous System effects have been noted most frequently. Tetrachloroethylene exposure may harm the nervous system, liver, kidneys, and reproductive system, and may be harmful to unborn children. If you are exposed to tetrachloroethylene, you may also be at a higher risk of getting certain types of cancer.

People who are exposed for longer periods of time to lower levels of tetrachloroethylene in air may have changes in mood, memory, attention, reaction time, or vision. Studies in animals exposed to tetrachloroethylene have shown liver and kidney effects, and changes in brain chemistry, but we do not know what these findings mean for humans.

Tetrachloroethylene may have effects on pregnancy and unborn children. Studies in people are not clear on this subject, but studies in animals show problems with pregnancy (such as miscarriage, birth defects, and slowed growth of the baby) after oral and inhalation exposure.

Exposure to tetrachloroethylene for a long time may lead to a higher risk of getting cancer, but the type of cancer that may occur is not well-understood. Studies in humans suggest that exposure to tetrachloroethylene might lead to a higher risk of getting bladder cancer, multiple myeloma, or non-Hodgkin's lymphoma, but the evidence is not very strong. In animals, tetrachloroethylene has been shown to cause cancers of the liver, kidney, and blood system. It is not clear whether these effects might also occur in humans, because humans and animals differ in how their bodies handle tetrachloroethylene.

The EPA considers tetrachloroethylene to be "likely to be carcinogenic to humans by all routes of exposure" based on suggestive evidence in human studies and clear evidence of mononuclear cell leukaemia in rats and liver tumours in mice exposed for 2 years by inhalation or stomach tube.

The International Agency for Research on Cancer considers tetrachloroethylene "probably carcinogenic to humans" based on limited evidence in humans and sufficient evidence in animals. The National Toxicology Program considers tetrachloroethylene to be "reasonably anticipated to be a human carcinogen."

Acute Exposure:
Acute exposure to tetrachloroethylene at air levels of 100 - 200 ppm causes irritation of the skin, eyes and upper respiratory tract. Non-cardiogenic pulmonary oedema, nausea, vomiting, and diarrhoea can occur.

Central Nervous System effects have also been observed with acute inhalation exposures of 50 - 300 ppm of tetrachloroethylene. At these levels, neuromotor effects may be seen (*e.g.*, the Romberg's test may be positive). Results of certain coordination and behavioural tests may be abnormal. At higher concentrations in air, unconsciousness can occur.

A patient who has a problem with proprioception can still maintain balance by using vestibular function and vision. In the Romberg test, the patient is stood up and asked to close his/her eyes. A loss of balance is interpreted as a positive Romberg's test.

Chronic Exposure:
Chronic exposure to tetrachloroethylene may have adverse effects on the hepatic, renal, and nervous systems, and on the skin. It may increase the risk of adverse effects in foetuses and newborns through maternal exposure.

The U.S. Department of Health and Human Services (HHS) has determined that tetrachloroethylene is 'reasonably anticipated to be a human carcinogen' (National Toxicology Program 2004). The International Agency for Research on Cancer (IARC) classified it as 'probably carcinogenic to humans' (Group 2A).

Carcinogenic Effects of Tetrachloroethylene:
The results of several studies suggest an association between tetrachloroethylene exposure from drinking water and increased incidence of breast cancer, lung cancer, leukaemia, non-Hodgkin's lymphoma and other cancers, although some uncertainties may exist in precision of the associations and exposure classification.

Some epidemiologic studies of dry-cleaning workers have suggested a possible association between chronic tetrachloroethylene exposure and increased cancer risk, including lymphoma and various cancers of the lung, oesophagus, skin, cervix, uterus, liver, kidney, and bladder, however, subjects in many of those studies had been simultaneously exposed to other solvents. Most studies lacked information of exposure dose; and many studies failed to control for smoking, socioeconomic status, and other relevant risk factors.

In studies using mice or rats, high-dose oral administration of tetrachloroethylene was associated with an increased incidence of hepatocellular (liver) carcinoma in mice of both sexes. Inhalation exposure was associated with leukaemia in male and female rats, renal tubular cell adenomas and adenocarcinomas in male rats, and hepatocellular neoplasms in mice of both sexes. However, some studies indicated that tetrachloroethylene metabolism is significantly higher in rats than in humans, thus, using rat tumourigenicity data for human risk assessment of tetrachloroethylene exposure may overestimate human tumour.

Opinions vary on the predictive validity of mouse liver and kidney tumours in assessing carcinogenic (cancer causing) risk in humans. In general, one should be careful in extrapolating evidence of liver and kidney tumours in experimental animals-to-human risk. Significant increases in the understanding of how tetrachloroethylene and its metabolites act in the liver and kidney should help improve the precision of risk assessment.

Tetrachloroethylene has been clearly identified as a carcinogen in experimental animals. The IARC considers it to be 'probably carcinogenic to humans' (Group 2A) and HHS believes it is 'reasonably anticipated to be a human carcinogen'.

Meta-analysis conducted by the researchers demonstrated an increased risk of bladder cancer in dry cleaners, and was reported in both cohort and case-control studies, and some evidence for an exposure-response relationship. Although it was found that dry cleaner workers incurred mixed exposures, tetrachloroethylene could be responsible for the excess risk of bladder cancer because it

is the primary solvent used and it is the only chemical commonly used by dry cleaners that is currently identified as a potential bladder carcinogen (Vlaanderen, *et al*., 2014).

Toxicokinetic modelling aided in characterising the complex metabolism and multiple metabolites that contribute to Perchloroethylene (PCE) toxicity. The exposure assessment approach - a key evaluation factor for epidemiological studies of bladder cancer, non-Hodgkin lymphoma, and multiple myeloma-provided suggestive evidence of carcinogenicity. Bioassay data provided conclusive evidence of carcinogenicity in experimental animals. Neurotoxicity was identified as a sensitive non-cancer health effect, occurring at low exposures: a conclusion supported by multiple studies. Evidence was integrated from human, experimental animal, and mechanistic data sets in assessing adverse health effects of PCE. PCE is likely to be carcinogenic to humans. Neurotoxicity is a sensitive adverse health effect of PCE (Guyton, *et al*., 2014).

Reproductive/Developmental Effects of Tetrachloroethylene:

Some adverse reproductive effects, such as menstrual disorders, altered sperm structure, and reduced fertility, have been reported in studies of workers occupationally exposed to tetrachloroethylene. However, the evidence is inconclusive.

Some studies of residents exposed to drinking water contaminated with tetrachloroethylene and other solvents during pregnancy suggest an association of tetrachloroethylene exposure with birth defects, however firm conclusions cannot be drawn due to several limitations of these studies.

Increased foetal resorptions and effects to the foetus have been reported in animals exposed to high levels of tetrachloroethylene by inhalation.

Aschengrau, A., Winter, M.R., Gallagher, L.G., Vieira, V.M., Butler, L.J., Fabian, M.P., Carwile, J.L., Wesselink, A.K., Mahalingaiah, S., Janulewicz, P.A., Weinberg, J.M., Webster, T.F. & Ozonoff, D.M. 2020.

"Tetrachloroethylene (PCE) is a common contaminant in both occupational and community settings. High exposure levels in the workplace have been shown to have adverse impacts on reproduction and development but few epidemiological studies have examined these effects at the lower levels commonly seen in community settings. We were presented with a unique opportunity to examine the reproductive and developmental effects of prenatal exposure to PCE-contaminated drinking water resulting from the installation of vinyl-lined water pipes in Massachusetts and Rhode Island from the late 1960s through 1980. This review describes the methods and findings of two community-based epidemiological studies, places their results in the context of the existing literature, and describes the strengths and challenges of conducting epidemiological research on a historical pollution episode. Our studies found that prenatal exposure to PCE-contaminated drinking water is associated with delayed time-to-pregnancy, and increased risks of placental abruption, stillbirths stemming from placental dysfunction, and certain birth defects. No associations were observed with pregnancy loss, birth weight, and gestational duration. Important strengths of this research included the availability of historical data on the affected water systems, a relatively high exposure prevalence and wide range of exposure levels, and little opportunity for recall bias and confounding. Challenges arose mainly from the retrospective nature of the exposure assessments. This research highlights the importance of considering pregnant women and their developing fetuses when monitoring, regulating, and remediating drinking water contaminants."

Habib, S., Ahmed, H.O., Al-Muhairi, N. & Ziad, R. 2018.
BACKGROUND: Perchloroethylene (PERC) is a widely spread cleaning solvent, used in nearly all dry-cleaning facilities. It has been declared as "probable human carcinogen" by the International Agency for Research on Cancer (IARC) due to its hazardous and toxic effects on human health. The study aimed at assessing the exposure of PERC among dry-cleaning workers at four different dry-cleaning facilities in the UAE.
METHODS: The four dry-cleaning facilities, using PERC in one of the cities of the UAE, were selected. Draeger perchloroethylene 10/b detector tubes along with a Draeger accuro pump were used to estimate the levels of PERC exposure in three main selected positions in each of the facilities.
RESULTS: The results showed that the second selected position had the highest amounts of PERC exposure above the international and local standards in 3 out of 4 selected facilities. The workers at position 2, who were not using any of the provided personal protective equipment, were at the highest risk of developing PERC-related health problems.
CONCLUSION: It is important to install local exhaust ventilation systems and monitoring devices of PERC concentrations in these facilities, along with raising the awareness of workers about the health effects of PERC and the importance of using personal protective equipment (PPE) while performing their job.

Callahan, C.L., Stewart, P.A., Blair, A. & Purdue, M.P. 2019.
BACKGROUND: Dry cleaning workers are commonly exposed to tetrachloroethylene, a suspected bladder carcinogen, and other organic solvents. The health risks associated with solvent exposures in this industry are unclear.
METHODS: We extended mortality follow-up of 5,369 dry cleaning union members in St. Louis to further investigate solvent-related risks. We added 22 years of follow-up, from 1993 through 2014, via linkage to the National Death Index. Using Cox proportional hazards modeling, we computed hazard ratios (HRs) and 95% confidence intervals (CIs) relating cause-specific mortality with levels of a solvent exposure index previously developed by an industrial hygienist based on workers' job titles from union records. The models were fit adjusting for age, sex, and decade of union enrollment, and assuming different exposure lags.
RESULTS: In internal analyses of estimated solvent exposure with a 20-year lag, we observed exposure-response relationships for bladder cancer (HR medium exposure = 4.2; 95% CI = 0.7, 24.5 and HR high exposure = 9.2; 95% CI = 1.1, 76.7 vs. no exposure; Ptrend = 0.08) and kidney cancer (HR = 4.1; 95% CI = 0.7, 22.5 and 24.4; 2.9, 201.6; Ptrend = 0.004). High exposure was also associated with heart disease (HR = 1.6; 95% CI = 1.1, 2.2) and lymphatic/hematopoietic malignancies (HR = 4.3; 95% CI = 1.4, 13.6).
CONCLUSIONS: These findings are, to the best of our knowledge, the first cohort evidence relating solvent exposure levels among dry cleaners to elevated risks of selected cancers and heart disease. Additional studies employing solvent-specific exposure assessment are needed to clarify cancer risks associated with tetrachloroethylene.

Aschengrau, A., Gallagher, L.G., Winter, M., Butler, L. Patricia, F.M. & Vieira, V.M. 2018.
BACKGROUND: Residents of Massachusetts and Rhode Island were exposed to tetrachloroethylene-contaminated drinking water from 1968 through the early 1990s when it leached from the vinyl lining of asbestos cement water distribution pipes. While occupational exposure to solvents during pregnancy has consistently been linked to an increased risk of certain birth defects, mixed results have been observed for environmental sources of exposure, including contaminated drinking water. The present case-control study was undertaken to examine further the association between prenatal

exposure to tetrachloroethylene-contaminated drinking water and the risk of central nervous system defects, oral clefts and hypospadias.
METHODS: Cases were comprised of live- and stillborn infants delivered between 1968 and 1995 to mothers who resided in 28 Massachusetts and Rhode Island cities and towns with some PCE-contaminated water supplies. Infants with central nervous system defects (N = 268), oral clefts (N = 112) and hypospadias (N = 94) were included. Controls were randomly selected live-born, non-malformed infants who were delivered during the same period and geographic area as cases (N = 771). Vital records and self-administered questionnaires were used to gather identifying information, birth defect diagnoses, and other relevant data. PCE exposure during the first trimester was estimated using water distribution system modeling software that incorporated a leaching and transport model. Prenatal PCE exposure was dichotomized as "high" or "low" exposure at the level corresponding to an estimated average concentration of 40 µg/L, the criterion for remediation when PCE contamination was discovered in 1980.
RESULTS: Mothers with "high" levels of exposure to PCE-contaminated drinking water during the first trimester (> 40 µg/L) had increased odds of having a child with spina bifida (OR: 2.0, 95% CI: 0.8-5.4), cleft lip with or without cleft palate (OR: 3.8, 95% CI: 1.2-12.3) and hypospadias (OR: 2.1, 95% CI:0.5-8.3). No increases in the odds of other defects were observed in relation to "high" exposure levels.
CONCLUSIONS: The results of the present study suggest that mothers with "high" PCE exposure levels during the first trimester have increased odds of having a child with spina bifida, cleft lip with or without cleft palate, and hypospadias. These findings support several prior studies that observed an increased risk of selected birth defects following prenatal exposure to solvents in occupational and environmental settings. Even though PCE contamination from vinyl lined pipes was remediated many years ago, it remains a widespread contaminant across the U.S and so environmental regulations must be guided by a precautionary perspective that safeguards pregnant women and their offspring.

Safe Handling of Products that Contain Tetrachloroethylene
Safe handling of products that contain tetrachloroethylene requires the following:

- minimal contact with the skin
- avoidance of undue inhalation of fumes
- avoiding ingestion of anything that has come into contact with the product

To further protect oneself against tetrachloroethylene:

- do not eat or drink while working with any product that contains tetrachloroethylene
- do not smoke while working with any product that contains tetrachloroethylene
- wash hands thoroughly with soap and water after working with any product that contains tetrachloroethylene
- apply tetrachloroethylene-containing fluids in well ventilated spaces, preferably outdoors if possible
- If work needs to be done indoors, apply product in short episodes to facilitate maximum dilution with air and thereby minimising inhalation of fumes
- keep products containing tetrachloroethylene out of reach of children, pets and animals
- allow clothes from a dry cleaner to hang in a well ventilated room (at least overnight) before using
- Be knowledgeable of the First Aid measures of products which contain tetrachloroethylene

Position of the Cancer Association of South Africa (CANSA)
CANSA supports the eradication of all carcinogens from the environment.

In this instance attention is specifically focused on IARC Group 2A carcinogens. Products listed as Group 2A by IARC have been shown to cause cancers in laboratory animals and are probably carcinogenic (cancer causing) to humans. This means that there is not sufficient evidence to be quite certain that Group 2A products will definitely cause cancer in humans although the total information is strongly suggestive thereof.

Occupational exposure (out of, and in the course of employment) to carcinogens is a major concern to CANSA. In the case of tetrachloroethylene, IARC has labelled this as a Group 2A carcinogen with special reference to the dry cleaning industry where high concentrations of tetrachloroethylene fumes form in the air that could be responsible for causing various cancers in humans.

CANSA noted according to ChemicalWatch that tetrachloroethylene has been identified for total banning in France in 2012. Tetrachloroethylene has also been banned for use in the dry-cleaning industry in the State of California in 2007 (Natural Resources Defense Council). CANSA is busy investigating whether similar legislation would be appropriate in South Africa.

Tetrachloroethylene has also been banned under the Montreal Protocol (substances used in production). The **Montreal Protocol on Substances that Deplete the Ozone Layer** (a protocol to the Vienna Convention for the Protection of the Ozone Layer) is an international treaty designed to protect the ozone layer by phasing out the production of numerous substances that are responsible for ozone depletion. It was agreed on September 16, 1987, and entered into force on January 1, 1989 (The Ericsson Lists of Banned and Restricted Substances; Wikipedia).

A search of the scientific literature on tetrachloroethylene did not reveal any cancer threat with the incidental use of tetrachloroethylene in multi-purpose lubricants which is mainly used in workshops and in the home. Notwithstanding this, CANSA wishes to inform casual users of products containing tetrachloroethylene to make sure that:

- there is no contact with the skin – in the event of accidental skin contact, appropriate personal hygiene should be practised
- the product is not ingested
- fumes from the product is not inhaled
- the product is kept away from children and animals, especially pet animals

Care should also be exercised that working with such products does not happen over extended periods of time which may cause the air space to become contaminated with tetrachloroethylene fumes that may result in the inhalation of tetrachloroethylene fumes.

Tetrachloroethylene-containing products should be kept safely out of the reach of children and pets.

Medical Disclaimer

This Fact Sheet and Position Statement is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet and Position Statement. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet and Position Statement.

Whilst the Cancer Association of South Africa (CANSA) has taken every precaution in compiling this Fact Sheet and Position Statement, neither it, nor any contributor(s) to this Fact Sheet and Position Statement can be held responsible for any action (or the lack thereof) taken by any person or organisation wherever they shall be based, as a result, direct or otherwise, of information contained in, or accessed through, this Fact Sheet and Position Statement.

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