Trichloroethylene (TCE)

TEACH Chemical Summary

U.S. EPA, Toxicity and Exposure Assessment for Children's Health

This TEACH Chemical Summary is a compilation of information derived primarily from U.S. EPA and ATSDR resources, and the TEACH Database. The TEACH Database contains summaries of research studies pertaining to developmental exposure and/or health effects for each chemical or chemical group. TEACH does not perform any evaluation of the validity or quality of these research studies. Research studies that are specific for adults are not included in the TEACH Database, and typically are not described in the TEACH Chemical Summary.

I. INTRODUCTION

Trichloroethylene (TCE) is a volatile organic chemical (VOC) used primarily as an industrial solvent (1). TCE is a colorless or blue liquid with a sweet, chloroform-like odor. The most common use of TCE is to remove grease from fabricated metal parts and some textiles. It is also an ingredient in adhesives, paint removers, typewriter correction fluids, rug-cleaning fluids, spot removers, and pepper sprays (1-3). The most recent available report of U.S. production stated a production volume of 321 million pounds of TCE in 1991; production capacity in the U.S. was approximately 320 million pounds at that time (1).

TCE has been found in ambient air, surface water, and ground water (1, 4-9). TCE levels above background have been found in industrial settings, in homes undergoing renovation, and in homes using private wells located near TCE disposal or contamination sites (1, 4-6). The most likely TCE exposure route for children is ingestion of contaminated drinking water (1).

Exposure to TCE has been reported to have adverse effects on the central nervous system, immune system, and endocrine (hormonal) system in adults (1). Reported effects often involve the central nervous system, with reported symptoms of fatigue, sleepiness, headache, confusion, and blurred vision (1, 3). Other effects on liver, kidney, gastrointestinal tract, and skin have been reported (1, 3). Available data suggest that exposure to TCE is associated with cancer of the kidney and other organs (1, 10-12). The U.S. EPA IRIS reassessment of TCE is ongoing and includes analysis of noncancer and cancer data (10, 12).

Some studies have reported an association between maternal TCE exposure during pregnancy and increased risk of heart defects (13, 14), other birth defects (15), and very low birth weight (16) in their children. Other studies found no such associations (17, 18). Of three reported studies on childhood TCE exposure and cancer, none of the studies found a significant association (17, 19, 20). Some experimental animal studies suggested *in utero* exposure to TCE may result in an increased incidence of heart abnormalities in the offspring (14-16, 18).

II. EXPOSURE MEDIA AND POTENTIAL FOR CHILDREN'S EXPOSURE[1]

Exposure Media	Relative Potential for Children's Exposure[2,3]	Basis[4]
Drinking Water	Higher	TCE contamination of drinking water can be a concern in areas close to industrial waste sites or industrial facilities. Industrial discharge containing TCE may result in significant contamination of drinking water.
Groundwater	Higher	Groundwater can become contaminated with TCE from discharge from industrial plants and operations.
Indoor Air	Medium	Indoor air contamination occurs as a result of volatilization from contaminated water (e.g., while showering), and also from TCE vapors seeping through basement structures and cracks in foundations from contaminated soils and groundwater. TCE can also contaminate indoor air during home renovation from several sources, including resins, glues, varnish and paint removers, vinyl flooring, and others.
Ambient Air	Medium	Ambient air TCE concentrations are generally expected to be low, although they can be of concern when there is a nearby source of TCE emissions, such as industrial sources.
Soil	Lower	TCE is highly volatile and therefore soil contamination is limited to subsurface soils.
Diet	Lower	Due to its volatility, TCE is not expected to be found in food.
Sediment	Lower	Due to its volatility, TCE is not expected to be found in sediment, although contaminated surface water can contaminate sediments.

[1] For more information about child-specific exposure factors, please refer to the Child-Specific Exposure Factors Handbook (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=55145).

[2] The Relative Potential for Children's Exposure category reflects a judgment by the TEACH Workgroup, U.S. EPA, that incorporates potential exposure pathways, frequency of exposure, level of exposure, and current state of knowledge. Site-specific conditions may vary and influence the relative potential for exposure. For more information on how these determinations were made, go to *http://www.epa.gov/teach/teachprotocols_chemsumm.html*.

[3] Childhood represents a lifestage rather than a subpopulation, the distinction being that a subpopulation refers to a portion of the population, whereas a lifestage is inclusive of the entire population.

[4] Information described in this column was derived from several resources (e.g., 1-4) including studies listed in the TEACH Database (*http://www.epa.gov/teach*).

III. TOXICITY SUMMARY[5, 6]

In adults, TCE exposure has been shown to be associated with central nervous system symptoms such as headaches, dizziness, and confusion. Additional effects include liver, kidney, immunological, endocrine, and respiratory problems (1). In adults, TCE exposure was associated with increased risk of liver and biliary tract cancer, and marginally increased risk of non-Hodgkin's lymphoma (1, 11).

Prenatal exposure to TCE via consumption of drinking water may increase the risk of miscarriage, central nervous system defects, neural tube defects, cardiac defects, oral cleft defects (e.g., cleft palate) and low birth weight (13, 21). Other studies found no increased risks of these effects associated with TCE exposure (17, 18, 21, 25). Increased risk of hypertension (high blood pressure) in 9-18 year-old girls was associated with TCE exposure (22). Another study reported increased incidence of autism spectrum disorders in children living in areas with the highest quartile (25%) levels of TCE in air measured in this study (23).

One case of acute exposure of a teenage boy reported symptoms of loss of consciousness, fever, tremors, cardiac sinus tachycardia, and kidney damage (24).

Developmental experimental animal studies have focused on TCE exposure during pregnancy. Observed effects include increased fetal loss (death) (25, 26), altered glucose metabolism in brain (27) or behavior (28) in offspring, delayed organ and bone development (29, 30), and altered cardiac development (31-33). Changes in the immune system have been observed in rat offspring exposed to TCE during pregnancy and lactation; changes included decreased B cell responses, increased delayed-type hypersensitivity responses (involving T lymphocytes), and thymocyte changes in the thymus (34).

Carcinogenicity Weight-of-Evidence Classification[7]: TCE was characterized in the 2001 Draft TCE Health Assessment as "highly likely to produce cancer in humans" based on studies of adults (12); the U.S. EPA is currently reviewing the carcinogenicity assessment (10, 12) (http://cfpub2.epa.gov/ncea/cfm/recordisplay.cfm?deid=23249). Scientific issues related to the assessment of TCE health risks have been reviewed by a National Academy of Sciences panel and the full report is available (35). The World Health Organization International Agency for Research on Cancer (IARC) classifies TCE as a probable (Group 2A) human carcinogen (http://monographs.iarc.fr/ENG/Monographs/vol63/volume63.pdf) (11).

[5] Please refer to research article summaries listed in the TEACH Database for details about study design considerations (e.g., dose, sample size, exposure measurements).

[6] This toxicity summary is likely to include information from workplace or other studies of mature (adult) humans or experimental animals if child-specific information is lacking for the chemical of interest. Summaries of articles focusing solely on adults are not listed in the TEACH Database because the TEACH Database contains summaries of articles pertaining to developing organisms.

[7] For recent information pertaining to carcinogen risk assessment during development, consult "Guidelines for Carcinogen Risk Assessment and Supplemental Guidance on Risks from Early Life Exposure" at *http://www.epa.gov/cancerguidelines*.

IV. EXPOSURE AND TOXICITY STUDIES FROM THE TEACH DATABASE

This section provides a brief description of human and animal studies listed in the TEACH Database. These descriptions generally include the overall conclusion in each study without evaluation or assessment of scientific merit by TEACH. For more details about doses and exposure levels, query the TEACH Database. Any consideration of adverse events should include an understanding of the relative exposure on a body weight basis. In many cases, exposure levels in animal studies are greater than exposure levels normally encountered by humans.

A. *HUMAN EXPOSURE AND EFFECTS*

- One study in Minnesota measured TCE in outdoor, indoor, and personal air samples in or near homes with children (36). One significant finding reported in the study was that indoor air samples in the studied urban areas had higher concentrations of TCE than indoor air samples from the studied rural areas (36).
- Increased incidence of miscarriage was associated with occupational exposure of mothers to TCE in one study (21). Another TCE study reported no increase in the incidence of still births for occupationally-exposed women (18).
- Some evidence suggests that maternal exposure to TCE during pregnancy may result in heart malformations in their children. One study reported that the incidence of congenital heart abnormalities in infants was associated with maternal exposure to drinking water contaminated with TCE and dichloroethylene (13). Another study reported increased incidence of congenital heart defects in infants born to mothers who lived within 1.5 miles of a TCE-contaminated site; TCE levels were not directly measured in this study (14).
- Maternal exposure to TCE during pregnancy and risk of abnormalities at birth in their children has been studied. In one study, concentrations of TCE in drinking water for pregnant women were associated with an increased incidence of birth defects in their children, including central nervous system, neural tube, and cleft palate defects (15). Other studies found no such associations (17, 18). A large study in Arizona reported a correlation between very low birth weight and maternal exposure to drinking water contaminated with TCE (16). Changes in the immune system (fewer interferon-gamma-producing T lymphocytes in cord blood) were significantly associated with bedroom TCE air concentrations (5).
- No statistically significant associations between TCE exposure of children and cancer have been reported. Residents of Woburn, Massachusetts were studied for possible links between TCE in drinking water and an increased incidence of childhood leukemias, but the presence of other contaminants in drinking water complicated the analysis (17, 19). A study in California found no association between childhood cancer and exposure to TCE in drinking water (20).
- Neurobehavioral effects in children exposed to TCE in drinking water have been reported in one study. A clinical case series study of individuals of varying ages from three states found significant neurological or cognitive defects (e.g. sensory defects, tremor, and reflex abnormalities) in children and adults exposed to TCE and other organic solvents in drinking water (37).

- Other health effects of TCE exposure have been investigated. One study reported that increased risk of several health effects (e.g., anemia, arthritis, skin rashes) was associated with TCE exposure of children, with the highest elevated risk for hypertension (high blood pressure) in 9-18 year-old girls (22). Another study reported increased incidence of autism spectrum disorders in children living in areas with the highest quartile (25%) levels of TCE in air measured in this study (23).

B. *EXPERIMENTAL ANIMAL EXPOSURE AND EFFECTS*

- A modeling estimate of exposure of pregnant rats to TCE and its metabolite (or breakdown product) trichloroacetic acid has been performed using physiologically-based pharmacokinetic (PBPK) modeling in rats (38).
- Effects of TCE exposure on sperm have been studied in experimental animals. When male rabbits were exposed to TCE during development (during pregnancy and lactation via maternal ingestion), the quality and quantity of sperm was reduced in the offspring during adulthood (39). When male rats were exposed to TCE during adulthood via gavage (tube) feeding, sperm were not significantly affected (40).
- Evidence of reproductive toxicity following maternal TCE exposure during pregnancy remains contradictory. Increased full litter absorption and fetal loss were observed following maternal gavage exposure of rats during pregnancy to TCE in some studies (25, 26); but such increases were not observed following maternal gavage or injection of TCE in mice (41), or maternal inhalation exposure of rabbits and rats (42). In other studies, there was no observed effect on pregnancy success and outcome following prenatal exposure of mice (43), or pre-pregnancy and prenatal exposure of rats (44).
- Effects of maternal TCE exposure during pregnancy (*in utero*) on later neurodevelopment in offspring have been studied in mice and rats. Maternal ingestion exposure to TCE during pregnancy resulted in altered neurochemistry in the brains of exposed offspring (27). Increases in certain behaviors (e.g., exploratory and locomotor wheel-running activities) were noted in one study of adult rats who were exposed to TCE *in utero* and during breastfeeding via maternal ingestion (28). Another study of *in utero* TCE exposure via maternal inhalation reported no significant effects on general activity levels in offspring during adulthood (29).
- Delayed development of tissues and bones was observed in fetal and newborn offspring following maternal inhalation exposure of rats (29), and following maternal injection of TCE in mice (30). Observed effects included delayed lung (29, 30), soft tissue (29), and skeletal (29) development.
- Increased incidence of cardiac defects in offspring was observed following *in utero* exposure of rats to TCE (31, 32) or to the TCE metabolite, tricholoracetic acid (25) via maternal ingestion of drinking water containing TCE. In one study, the incidence of cardiac defects (e.g., atrial, ventricular, and aortic valve defects) in offspring was higher following both prenatal and lactational exposure, as compared to prenatal exposure alone (32). A third study reported no increased incidence of cardiac defects associated with maternal gavage exposure to TCE (45). *In utero* exposure to TCE has also been demonstrated to alter fetal expression of cardiac-specific genes (33).

- The incidence of microthalmia (small eyes) was increased following prenatal exposure to TCE via maternal gavage in rats (26, 46). Another study of maternal gavage of rats reported no measurable effects on fetal eye development (47).
- Immune system effects of developmental TCE exposure have been reported. One study reported decreased B cell responses, increased delayed-type hypersensitivity responses (a type of T lymphocyte response), and increased numbers of T cells in the thymus of rat offspring following maternal exposure to TCE during pregnancy and lactation (34).

V. CONSIDERATIONS FOR DECISION-MAKERS

This section contains information that may be useful to risk assessors, parents, caregivers, physicians, and other decision-makers who are interested in reducing the exposure and adverse health effects in children for this particular chemical. Information in this section focuses on ways to reduce exposure, assess possible exposure, and, for some chemicals, administer treatment.

- Detailed compilations and analyses of information pertaining to exposure and health effects of TCE are available from the U.S. Centers for Disease Control Agency for Toxic Substances and Disease Registry in the Toxicological Profile for TCE (1). The U.S. EPA provides a fact sheet summarizing information about TCE in drinking water (2). A Hazard Summary for TCE is available from the U.S. EPA Technology Transfer Air Toxics Web site (3), which summarizes key exposure and toxicity information for TCE in air, compiled from several sources.
- Vapor intrusion to indoor air pathway may occur from TCE vapors from contaminated soils and groundwater that migrate through the subsurface into air spaces of overlying buildings. An additional source of indoor air exposure is volatilization from contaminated water during showering, bathing, and other household uses of water (e.g., dishwashing, cooking, etc.) (1, 4, 48).
- In view of the U.S. EPA Maximum Contaminant Level Goal (MCLG) of 0 mg/L for TCE in drinking water (see Toxicity Reference Values), caregivers may consider alternative water supplies, e.g. bottled water, where TCE-contaminated groundwater may be impacting drinking water.
- Draft RfD and RfC toxicity values developed as part of the 2001 TCE draft health risk assessment are currently under revision (12, 49). Current review status information for TCE is available (50). This document also includes a range of cancer slope factors based on cancers in an occupational cohort, a community drinking water study, and adult rodents. A critical analysis of this draft health risk assessment by a U.S. EPA Scientific Advisory Board is also available (10). Scientific issues related to the assessment of TCE health risks have been reviewed by a National Academy of Sciences panel and the full report is available (35).
- TCE exposure has been assessed in several regions of the U.S. as part of the U.S. EPA National Human Exposure Assessment Survey (NHEXAS), which evaluated human exposure to several chemicals on a regional scale in 1998 (51, 52). One study reported TCE blood levels in individuals in Region 5 (Midwest region) to be below detection (53).
- The U.S. EPA used 1999 emissions data for TCE for all 50 states to report county-level emissions, modeled ambient air concentration estimates, modeled human inhalation exposure, and estimated risk in the National-Scale Air Toxics Assessment (7).

- Detailed discussions and review articles about TCE exposures and effects are available in one supplemental issue of the journal Environmental Health Perspectives (54), though nearly all of the information focused on adults. One review article included a discussion about children's possible unique sensitivities to TCE (55).
- Consult the "Child-Specific Exposure Factors Handbook," EPA-600-P-00-002B, for factors to calculate children's drinking water consumption and inhalation rates (56). An updated External Draft of the 2006 version of this handbook is available (57).

VI. TOXICITY REFERENCE VALUES

A. Oral/Ingestion

U.S. EPA Maximum Contaminant Level (MCL) for Drinking Water: 0.005 mg/L, based on liver problems and increased risk of cancer in adults (http://www.epa.gov/safewater/contaminants/index.html) (58); last revised 6/03.

U.S. EPA Maximum Contaminant Level Goal (MCLG): 0 mg/L (http://www.epa.gov/safewater/contaminants/index.html) (58); last revised 6/03.

U.S. ATSDR Minimal Risk Level (MRL): 0.2 mg/kg-day (acute oral), based on developmental effects (http://www.atsdr.cdc.gov/mrls/index.html) (59); last revised 9/97.

B. Inhalation

U.S. ATSDR Minimal Risk Level (MRL): 2 ppm (acute inhalation), based on neurological effects; 0.1 ppm (intermediate inhalation), based on neurological effects (http://www.atsdr.cdc.gov/mrls/index.html) (59); last revised 9/97.

VII. U.S. FEDERAL REGULATORY INFORMATION

- Currently the U.S. EPA has set a Maximum Contaminant Level (MCL) for drinking water of 0.005 mg/L, and the U.S. ATSDR has set Minimal Risk Levels (MRL) for inhalation and oral routes (see Toxicity Reference Values above). The U.S. EPA regulates drinking water for public water systems and drinking water wells that serve at least 25 people (60); information is available for owners of private wells (61).
- TCE is one of 188 hazardous air pollutants (HAPs) listed under section 112(b) of the 1990 Clean Air Act Amendments and is regulated for more than 170 industrial source categories (4, 62).
- TCE is ranked as number 16 out of 275 substances on the 2005 Priority List of Hazardous Substances for the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) section 104 (i), as amended by the Superfund Amendments and Reauthorization Act (SARA). This is a ranking in the order of priority of concern of substances most commonly found at sites listed on the National Priorities list (NPL) (63).
- The U.S. EPA requires reporting of quantities of certain chemicals that exceed a defined reportable quantity, and that quantity varies from chemical to chemical. Under the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313 "Toxic Chemicals," quantities of TCE greater than 25,000 pounds manufactured or processed, or greater than 10,000 pounds otherwise used, must be reported; under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), reporting releases of TCE of any quantity exceeding 100 pounds is required (63).

VIII. BACKGROUND ON CHEMICAL

A. CAS Number: 79-01-6

B. Physicochemical Properties: TCE is a colorless or blue liquid with a sweet odor, and is highly volatile (evaporates quickly from liquid form). For more information, go to the National Library of Medicine ChemID Web site (*http://chem.sis.nlm.nih.gov/chemidplus*) and search for TCE.

C. Production: TCE does not occur naturally in the environment, and its presence in groundwater sources and surface waters is the result of the manufacture, use, and disposal of the chemical (64). Estimates of annual production of TCE in the U.S. have increased from over 260 million pounds in 1979 (65), to 320 million pounds in 1991 (1).

D. Uses: TCE is used primarily as a solvent to remove grease from metal parts. This use is closely associated with the metal and automotive industries. It is also an ingredient in adhesives, paint and varnish removers, typewriter correction fluids, rug-cleaning fluids, spot removers, sheet vinyl flooring, and pepper sprays (2). Total TRI reported disposals and releases in 2005 were over 5.6 million pounds, with releases occurring primarily from steel pipe and tube manufacturing industries (66).

E. Environmental Fate: TCE is highly soluble and can persist in groundwater (1). At high concentrations in confined groundwater aquifers, TCE may form a DNAPL (dense non-aqueous phase liquid) (1). In settings where groundwater charges surface water, contaminated groundwater can lead to contaminated surface water and sediment. When released into the air, this material may be moderately degraded through reaction with photochemically-produced hydroxyl radicals to then form phosgene, dichloroacetyl chloride, and formyl chloride (1). The half-life of TCE in air is approximately 7 days (1). TCE does not easily evaporate from subsurface soils and can leach to groundwater.

F. Synonyms and Trade Names: Ethylene trichloride, TCE, Trichloroethene, Trilene 1,1,2-Trichloroethylene, Acetylene trichloroethylene, Algylen, Anameth, Benzinol, Chlorilen, CirCosolv, Germalgene, Lethurin, Perm-a-chlor, Petzinol, Philex, TRI-Plus M, Vitran (2).

Additional information on TCE is available in the TEACH Database for TCE, and at the following Web sites:

www.epa.gov/ttn/atw/nata/
www.epa.gov/sab/pdf/ehc03002.pdf
www.epa.gov/safewater/dwh/c-voc/trichlor.html

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