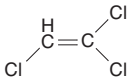
Trichloroethylene

CAS No. 79-01-6

Known to be a human carcinogen

First listed in the *Ninth Report on Carcinogens* (2000)

Also known as 1,1,2-trichloroethene or TCE



Carcinogenicity

Trichloroethylene is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in humans. This conclusion is based on epidemiological studies showing that it causes kidney cancer in humans, together with supporting evidence from toxicological, toxicokinetic, and mechanistic studies demonstrating the biological plausibility of its carcinogenicity in humans. Epidemiological studies also provide limited evidence that trichloroethylene causes non-Hodgkin lymphoma (NHL) in humans. Supporting evidence is provided by studies in experimental animals demonstrating that trichloroethylene causes cancer at several tissue sites, including some of the same sites as seen in humans. The data available from studies in humans are inadequate to evaluate the relationship between trichloroethylene exposure and liver cancer. Trichloroethylene was first listed in the *Ninth Report on Carcinogens* in 2000 as *reasonably anticipated to be a human carcinogen* based on limited evidence of carcinogenicity from studies in humans, sufficient evidence of carcinogenicity from studies in experimental animals, and information from studies on mechanisms of carcinogenesis.

Cancer Studies in Humans

Kidney Cancer

Epidemiological studies have demonstrated that trichloroethylene exposure causes kidney cancer, based on the following evidence: (1) consistent findings of increased risk across studies with different study designs, in different geographical areas, and in different occupational settings, (2) evidence of increasing cancer risk with increasing level or duration of exposure (i.e., an exposure-response relationship), and (3) meta-analyses (combined statistical analyses of the data from several different studies) showing statistically significant increased cancer risk across studies.

Numerous studies, primarily among workers, have evaluated the association between trichloroethylene exposure and kidney cancer, including twelve cohort studies or nested case-control studies (case-control studies conducted within specific cohort studies) and seven case-control studies (NTP 2015). Three of these studies — a cohort study of aerospace workers (Zhao *et al.* 2005), a French case-control study of screw-cutting workers (Charbotel *et al.* 2006, 2009), and a case-control study of occupational exposure to trichloroethylene in central and eastern Europe (Moore *et al.* 2010) — were considered to be the most informative, because they had good exposure assessments, detailed analysis of exposure-response relationships, or presumed high levels of exposure. The most convincing evidence that exposure to trichloroethylene causes kidney cancer comes from these three studies and two additional studies, a Nordic cohort of blue-collar workers in companies using trichloroethylene (Raaschou-Nielsen *et al.* 2003) and a case-control study in an area in Germany where workers in several factories were exposed to high levels of trichloroethylene (Brüning *et al.* 2003). All five studies found that workers with the highest exposure to trichloroethylene had a statistically significant increased risk of kidney cancer, and four of the studies found that the risk of kidney cancer increased with increasing duration, intensity, or cumulative level of exposure.

These findings are supported by weaker associations found in several other cohort studies (Morgan *et al.* 1998, Boice *et al.* 2006, Hansen *et al.* 2013, Bove *et al.* 2014, Silver *et al.* 2014) and case-control studies (Dosemeci *et al.* 1999, Pesch *et al.* 2000). Very high risks of kidney cancer were found among German workers exposed to high levels of trichloroethylene (Henschler *et al.* 1995, Vamvakas *et al.* 1998); however, potential methodological biases in these two studies could have distorted the risk estimate.

Two recent robust meta-analyses found statistically significant increased risks of kidney cancer among workers who had ever been exposed to trichloroethylene (overall relative risks: mRR = 1.27, 95% confidence interval [CI] = 1.13 to 1.43, Scott and Jinot 2011; mRR = 1.32, 95% CI = 1.17 to 1.50, Karami *et al.* 2012). One meta-analysis (Scott and Jinot 2011) found a higher overall relative risk for the highest exposure group across studies (mRR = 1.58, 95% CI = 1.28 to 1.96) than for all subjects ever exposed to trichloroethylene, which provides supporting evidence for an exposure-response relationship between the level of trichloroethylene exposure and risk of kidney cancer.

Several studies, including some large studies (Greenland *et al.* 1994, Radican *et al.* 2008, Lipworth *et al.* 2011, Christensen *et al.* 2013, Vlaanderen *et al.* 2013), found little or no evidence for an association between kidney cancer and trichloroethylene exposure or for an exposure-response relationship. However, these studies were limited by imprecise classification of exposure or low sensitivity to detect an association, either because the exposure levels were low or because few workers had high levels of exposure. In general, these limitations would make it harder to detect a true effect and would not likely result in a false positive association (NTP 2015).

It is unlikely that the positive findings across studies could be explained by biases or by potential confounding from smoking or co-exposure to other occupational carcinogens (NTP 2015). Most of the case-control studies found positive associations between trichloroethylene exposure and kidney cancer after controlling for smoking. Furthermore, the cohort studies found little evidence for an association between trichloroethylene exposure and lung cancer, which strongly suggests that smoking did not explain the excess kidney cancer risk. Studies of specific industries found positive associations after considering known occupational co-exposures to other carcinogenic substances in their statistical analysis or study design (Zhao *et al.* 2005, Charbotel *et al.* 2006, 2009). Although other cohort and case-control studies did not provide information about occupational co-exposures, those studies included workers in diverse occupations with differing levels and patterns of co-exposures, and the prevalence of any one specific co-exposure across studies was probably low. Furthermore, positive associations between trichloroethylene exposure and kidney cancer were found across studies with different study designs and in different occupational settings and geographical regions.

Non-Hodgkin Lymphoma

Epidemiological studies provide limited evidence that trichloroethylene exposure causes NHL, based on positive associations in several studies and evidence for increased risk of NHL across studies combined in two meta-analyses. The evidence across studies is less consistent than for kidney cancer, and alternative explanations for the associations, such as chance or confounding, cannot reasonably be ruled out (NTP 2015). NHL includes a diverse group of cancers arising in cells of the lymphatic system, most commonly the B lymphocytes, a type of white blood cell involved in the immune response.

Studies evaluating the relationship between exposure to trichloroethylene and NHL (including specific histological subtypes of NHL

and other related B-cell lymphomas) included ten cohort or nested case-control studies (Morgan *et al.* 1998, Raaschou-Nielsen *et al.* 2003, Boice *et al.* 2006, Radican *et al.* 2008, Bahr *et al.* 2011, Lipworth *et al.* 2011, Hansen *et al.* 2013, Vlaanderen *et al.* 2013, Bove *et al.* 2014, Silver *et al.* 2014), four case-control studies (Hardell *et al.* 1994, Persson and Fredrikson 1999, Wang *et al.* 2009, Christensen *et al.* 2013, Deng *et al.* 2013), a pooled analysis of four case-control studies by the International Lymphoma Epidemiology Consortium (InterLymph) (Cocco *et al.* 2013), and two recent meta-analyses. The InterLymph pooled analysis (Cocco *et al.* 2013) was considered to be the most informative study, because of its high-quality exposure assessment, large size, and analyses of exposure levels and durations and NHL subtypes (NTP 2015).

The strongest evidence for an association between trichloroethylene exposure and NHL comes from the InterLymph pooled analysis (P = 0.004 for combined analysis of duration, frequency, and intensity of exposure among individuals with the highest probability of exposure) (Cocco *et al.* 2013) and the two meta-analyses (mRR = 1.23, 95% CI = 1.07 to 1.42, Scott and Jinot 2011; mRR = 1.32, 95% CI = 1.14 to 1.54, Karami *et al.* 2013). The risk of NHL increased with increasing level or duration of exposure in the InterLymph pooled analysis, in one of its component studies (Purdue *et al.* 2011), and in another case-control study (Wang *et al.* 2009).

An association between trichloroethylene exposure and NHL is also supported by increased risks of NHL found in several case-control studies (Hardell *et al.* 1994, Wang *et al.* 2009) and cohort studies (Morgan *et al.* 1998, Raaschou-Nielsen *et al.* 2003, Radican *et al.* 2008, Lipworth *et al.* 2011, Hansen *et al.* 2013). However, the evidence from these studies was not considered to be strong, because most of the studies (except for Wang *et al.* 2009) did not observe exposure-response relationships, and the estimated risks were relatively small or not statistically significant (NTP 2015). Nonetheless, these studies collectively contributed to the statistically significant increased risks found in the meta-analyses.

The remaining studies provided little evidence (Persson and Fredrikson 1999, Christensen *et al.* 2013, Bove *et al.* 2014) or no evidence (Bahr *et al.* 2011, Vlaanderen *et al.* 2013, Silver *et al.* 2014) for an association between trichloroethylene exposure and NHL. These studies were considered inadequate for detecting an association with an uncommon cancer like NHL, either because of inadequate methods for determining whether the subjects were exposed to trichloroethylene, or because of limited exposure information, or because few subjects were exposed (NTP 2015). The study of aerospace workers (Boice *et al.* 2006) was not informative, because it included only one trichloroethylene-exposed worker with NHL.

Few individual subtypes of NHL or related B-cell lymphomas have been studied with respect to trichloroethylene exposure. Among these specific types of lymphoma, the strongest evidence for an association with exposure to trichloroethylene is for chronic lymphocytic leukemia and follicular-cell lymphoma (Purdue *et al.* 2011, Cocco *et al.* 2013).

Liver Cancer

The data available from studies in humans are inadequate to evaluate the relationship between trichloroethylene exposure and liver cancer (NTP 2015). The available database for liver cancer included twelve cohort or nested case-control studies (Greenland *et al.* 1994, Morgan *et al.* 1998, Ritz 1999, Raaschou-Nielsen *et al.* 2003, Boice *et al.* 2006, Radican *et al.* 2008, Bahr *et al.* 2011, Lipworth *et al.* 2011, Hansen *et al.* 2013, Vlaanderen *et al.* 2013, Bove *et al.* 2014, Silver *et al.* 2014) and two meta-analyses (Alexander *et al.* 2007, Scott and Jinot 2011). The only available case-control study (Christensen *et al.* 2013) was not informative, because it included only one trichloroethylene-exposed worker with liver cancer. The epidemiological data suggest that trichloroethylene may be associated with a modest increase in the risk of liver cancer, based primarily on the two meta-analyses. However, the findings are inconsistent across studies, and there was little evidence for exposure-response relationships in the individual studies or the meta-analyses. In addition, the role of chance or confounding by one or more common occupational co-exposures or lifestyle factors could not be completely ruled out.

Cancer Studies in Experimental Animals

Trichloroethylene caused tumors in mice and rats at several different tissue sites by two different routes of exposure. In rats, exposure to trichloroethylene by inhalation or stomach tube caused kidney cancer (tubular adenocarcinoma) and testicular tumors (interstitial-cell tumors) in males (Maltoni *et al.* 1988, NTP 1988, 1990). In mice, exposure to trichloroethylene by inhalation or stomach tube caused benign and malignant liver tumors (hepatocellular adenoma and carcinoma) in both sexes (NCI 1976, Maltoni *et al.* 1988, NTP 1990, IARC 1995), and inhalation exposure also caused lung tumors in both sexes and lymphoma in females (Henschler *et al.* 1980, IARC 1995).

Studies on Mechanisms of Carcinogenesis

Two distinct metabolic pathways for trichloroethylene have been identified that have been found in all mammalian species studied: oxidation by a cytochrome P450 (CYP) enzyme and binding (conjugation) by the compound glutathione (GSH). These two metabolic pathways usually modify substances that enter the body to make them less toxic and more likely to be eliminated by excretion. However, in some cases (as with trichloroethylene), the chemical modifications can instead make the substance more toxic. Although the GSH-conjugation and CYP-oxidation pathways operate in parallel, the oxidative pathway predominates in all species studied (Lash *et al.* 2014). However, genetic differences among individuals or exposure to substances that induce or inhibit the action of CYP can alter the balance between oxidation and GSH conjugation of trichloroethylene, and their effects may be greater at higher trichloroethylene concentrations. Kidney cancer most likely occurs as a result of GSH conjugation of trichloroethylene (EPA 2011, Rusyn *et al.* 2014), whereas liver cancer most likely occurs as a result of the CYP-oxidation pathway (EPA 2011, Rusyn *et al.* 2014). Trichloroethylene metabolites most likely play a role in the development of non-Hodgkin lymphoma; however, less information is available for this type of cancer.

Kidney Cancer

Toxicokinetic and mechanistic data in both humans and experimental animals provide evidence for a biologically plausible mechanism by which trichloroethylene causes kidney cancer (NTP 2015). The evidence indicates that trichloroethylene causes genotoxicity (such as DNA and chromosomal damage) and cytotoxicity as a result of being metabolized into products that can damage DNA or cells (EPA 2011, Chiu *et al.* 2013, Lash *et al.* 2014). The following key events are likely involved: (1) GSH-conjugated metabolites are either produced in the kidneys or produced elsewhere in the body and transported to the kidneys in the blood, and (2) these metabolites cause mutations, genetic damage, and toxicity in the kidneys (EPA 2011), leading to cancer. Evidence for this proposed mechanism comes from data in both humans and experimental animals. Kidney and liver cells from humans and rodents are able to metabolize trichloroethylene to several GSH-conjugation-derived metabolites, two of which (*N*-acetyl-*S*-dichlorovinyl-L-cysteine and *S*-[2,2-dichlorovinyl]glutathione) have been detected in the urine of humans and experimental animals ex-

posed to trichloroethylene. The importance of the GSH-conjugation pathway in humans is supported by the finding of a significantly increased risk of kidney cancer among trichloroethylene-exposed individuals with a functioning gene that codes for the production of glutathione S-transferase theta 1 (GSTT1) (an enzyme involved in GSH conjugation), but not among individuals who cannot produce GSTT1 (Moore *et al.* 2010).

GSH-conjugated metabolites of trichloroethylene have been shown to cause genetic damage to cultured cells from both humans and experimental animals, most notably kidney cells, to transform cultured rat kidney cells into cancer cells, and to damage DNA and cause micronucleus formation in kidney cells from rats exposed to trichloroethylene. Also potentially contributing to trichloroethylene's carcinogenicity are its toxicity to cells and the associated increase in proliferation of cells in response to cell death (EPA 2011). Studies in humans also provide evidence that trichloroethylene causes kidney toxicity (Brüning *et al.* 1999a,b, Brüning and Bolt 2000, Bolt *et al.* 2004, Vermeulen *et al.* 2012), supporting the relevance of this mechanism in humans.

This proposed mechanism is also consistent with the findings of increased risk of kidney cancer mainly among workers with high exposure to trichloroethylene. Some of the mixed results across studies could be partly explained by differences among the study populations in genetic characteristics or co-exposures to substances that could affect trichloroethylene metabolism and the balance between the GSH-conjugation and CYP-oxidation metabolic pathways (NTP 2015).

Non-Hodgkin Lymphoma

The mechanisms by which trichloroethylene could cause lymphoma are largely unknown. Immune disorders, including suppression of immune function and attacks on the body by its own immune system (autoimmunity), are strongly linked to NHL (Hardell *et al.* 1998, Baecklund *et al.* 2014, Ponce *et al.* 2014). In both types of immune disorder, chronic stimulation of the immune system can activate B cells to produce antibodies against host antigens (autoimmunity) or pathogens (immunosuppression) through a mechanism (somatic hypermutation) in which the B cells undergo complex rearrangements of their DNA to code for these antibodies. Because this process is subject to errors, it is proposed that the increased activation of the B cells can lead to a proliferation of mutated cells, possibly resulting in lymphoma (NTP 2015). Although trichloroethylene or its metabolites can cause both immunosuppression and autoimmunity in humans and animals (EPA 2011), the results from studies in humans and animals that measured indicators of immune function (such as B-cell activation) were not entirely consistent with this hypothesis (Peden-Adams *et al.* 2006, 2008, Keil *et al.* 2009, Lan *et al.* 2010, Hosgood *et al.* 2012, Bassig *et al.* 2013). However, neither the proposed model nor the potential association between lymphoma and trichloroethylene-induced immune effects has been directly tested in either humans or animals.

Liver Cancer

The mechanism by which trichloroethylene causes liver cancer in mice is unknown, but likely is complex, involving key events in several molecular pathways (EPA 2011). Studies in experimental animals provide evidence for several potential modes of action, including genetic damage, oxidative stress, peroxisome proliferation, epigenetic events, and autoimmune hepatitis (EPA 2011, Wang *et al.* 2013). Oxidative metabolites are considered to be more important than GSH-conjugated metabolites in liver carcinogenicity, because trichloroethylene and its oxidative metabolites trichloroacetic acid, dichloroacetic acid, and chloral hydrate have similar toxic effects on the liver. These oxidative metabolites are formed in humans and have been reported to cause genetic damage in several *in vitro* and *in vivo* test systems. Although species differences in sensitivity to the proposed modes of action are likely, no data suggest that trichloroethylene causes liver tumors in mice by mechanisms that are not relevant to humans (NTP 2015).

Properties

Trichloroethylene is a halogenated alkene that exists at room temperature as a clear, colorless, or blue freely flowing liquid with an ethereal odor. It is slightly soluble in water, soluble in ethanol, acetone, diethyl ether, and chloroform, and miscible in oil. It is relatively stable, but oxidizes slowly when exposed to sunlight in air (HSDB 2014). Upon combustion, trichloroethylene produces irritants and toxic gases, which may include hydrogen chloride. In the presence of moisture and light, it breaks down into hydrochloric acid. Physical and chemical properties of trichloroethylene are listed in the following table.

Property	Information
Molecular weight	131.4
Specific gravity	1.4642 at 20°C/4°C
Melting point	–84.7°C
Boiling point	87.2°C
Log K_{ow}	2.61
Water solubility	1.28 g/L at 25°C
Vapor pressure	69 mm Hg at 25°C
Vapor density relative to air	4.53

Source: HSDB 2014.

Stabilizers, in the form of antioxidants or acid receptors (such as phenolic, olefinic, pyrrolic, or oxiranic derivatives and aliphatic amines), are usually added to commercial trichloroethylene in concentrations that normally range from 20 to 600 mg/kg but may be as high as 5,000 mg/kg. The specific stabilizers used depends on patent ownership and technical specifications (IPCS 1985).

Use

Trichloroethylene is used as an intermediate in production of hydrofluorocarbon refrigerant (83.6%) and as a degreaser for metal parts (14.7%) (EPA 2014a). The remaining 1.7% is attributed to "other uses," which include use as a spot-removal solvent in the drycleaning industry, as a modifier in polyvinyl chloride polymerization, and in several consumer household aerosol products. Starting in the early 1900s, trichloroethylene was primarily used as a degreaser, to remove grease, wax, or dirt from metal parts before painting, plating, or other processes; however, that use in the United States declined beginning in the 1970s (Bakke *et al.* 2007). Although trichloroethylene was used extensively as a degreaser in the aircraft industry beginning in the 1950s, this use ended in the 1980s. Industries that may currently use trichloroethylene in vapor or cold degreasing operations include fabricated metal products, electrical and electronic equipment, transportation equipment, and miscellaneous manufacturing. Trichloroethylene has also been used as an industrial solvent in the rubber industry; in paints, lacquers, varnishes, adhesives, and paint strippers; and in the production of agricultural chemicals such as fungicides and insecticides (IARC 1995, Bakke *et al.* 2007).

Trichloroethylene has been listed as a major ingredient in several consumer products, such as degreasers intended for use in automotive products, home maintenance, or commercial or institutional use and household aerosol products for arts and crafts uses (HPD 2014, EPA 2014b). However, the only U.S. manufacturer of trichloroethylene-containing spray fixatives used in arts and crafts has vol-

untarily reformulated the products to replace trichloroethylene with an alternative chemical (EPA 2016b). Other consumer products identified as containing trichloroethylene include typewriter correction fluids, paint removers and strippers, adhesives, spot removers, and rug-cleaning fluids (Gist and Burg 1995).

In the past, trichloroethylene was used as a drycleaning agent in a batch process for cleaning large quantities of textiles; as an extraction solvent to remove natural fats and oils from plant materials, to manufacture flavoring extracts from spices and hops, and to remove caffeine from coffee; as an anesthetic and analgesic in obstetrics and for minor surgical procedures; and in cosmetics and drug products. However, its use essentially ended by the 1950s for batch drycleaning (although uses for spot cleaning have continued) and by the 1970s for the other food, drug, cosmetic, and surgical uses (IARC 1995, Bakke *et al.* 2007).

Production

Trichloroethylene is a high-production-volume chemical, with combined U.S. production and imports exceeding 100 million pounds in 2015 (as shown in the table below). U.S. imports of trichloroethylene peaked at 60 million pounds in 2007 (USITC 2014). Between 1989 and 2017, annual U.S. exports of trichloroethylene were as high as 107 million pounds, but export volume showed no consistent trends over that period. In 2014, trichloroethylene was available from 101 suppliers worldwide, including 37 U.S. suppliers (ChemSources 2014).

Category	Year	Quantity (million lb)
Production + imports[a]	2015	100 to 250
U.S. imports[b]	2017	3.4
U.S. exports[b]	2017	29.2

Sources: [a]EPA 2016a. [b]USITC 2018.

Trichloroethylene is reported to occur naturally in some algae in temperate to tropical climates and in one red macroalga (IARC 1995).

Exposure

A significant number of people living in the United States are or have been exposed to trichloroethylene because of its widespread presence from past and current uses. In addition to occupational exposure of workers in industries using trichloroethylene, the general population can be exposed to trichloroethylene in ambient air, drinking-water supplies, certain consumer products, and contaminated foods (ATSDR 1997, 2013). Exposure has been documented by measurement of trichloroethylene blood levels in the general population and by direct measurement of trichloroethylene in groundwater, drinking water, and ambient air in workplace and non-workplace environments. However, recent measurements of trichloroethylene blood levels in the general population suggest an overall decrease in exposure. Several additional lines of evidence support this trend, including changes in major uses of trichloroethylene that suggest decreases in both the numbers of exposed workers and occupational exposure levels, particularly the decreased use of trichloroethylene for solvent degreasing in large commercial and industrial settings; recent decreases in total imports of trichloroethylene; and declining environmental releases of trichloroethylene. Nevertheless, exposure to workers and also to the general population from current use, past use, or disposal of trichloroethylene continues, as evidenced by measurements in the environment.

Occupational Exposure

Workers are exposed to trichloroethylene primarily by breathing vapors and through skin contact with vapors or liquid. According to the U.S. Environmental Protection Agency's (EPA's) Office of Chemical Safety and Pollution Prevention (EPA 2014b), an estimated 300,000 workers are exposed in drycleaning facilities that use trichloroethylene to remove spots from garments before or after cleaning them in drycleaning machines. An estimated 30,000 additional workers are potentially exposed to trichloroethylene at small commercial degreasing operations. EPA considered production of hydrofluorocarbon refrigerant and solvent degreasing in large commercial and industrial settings to have low potential for human exposure to trichloroethylene because of the use of closed-loop process systems and regulatory monitoring and controls (EPA 2014b).

Exposure in occupational settings such as solvent degreasing in large commercial or industrial facilities has decreased over time as a result of regulatory monitoring and controls, but high levels of trichloroethylene in workplace air have still been reported in recent years, particularly in the metals and rubber industries. Based on 1,229 trichloroethylene measurements across industries from the 1930s to 1990s, an average exposure concentration of 38.2 ppm was calculated, and the highest levels were reported for vapor degreasing (44.6 ppm) (Bakke *et al.* 2007). In statistical modeling of trichloroethylene exposures over time, the highest values were found in the 1950s to 1970s (Hein *et al.* 2010). The Occupational Safety and Health Administration (OSHA) Chemical Exposure Health Database (which includes results for 3,600 air samples from 1984 to 2011) reported that from 2000 to 2010, 92 samples exceeded the OSHA permissible exposure limit of 100 ppm, and two exceeded the National Institute for Occupational Safety and Health "immediately dangerous to life or health" level of 1,000 ppm (OSHA 2013).

Exposure of the General Population

The general population is exposed to trichloroethylene primarily by consuming contaminated drinking water and inhaling contaminated indoor air. Water and air become contaminated by releases of trichloroethylene from active industries or from hazardous waste sites. Exposure from consumer products and food also is possible. Results from the third National Health and Nutrition Examination Survey (NHANES), conducted from 1988 to 1994 (in which 677 whole-blood samples were tested for trichloroethylene), suggested that approximately 10% of the U.S. population had detectable levels of trichloroethylene in their blood (limit of detection = 0.01 ng/mL) (Wu and Schaum 2000). However, the NHANES survey data for 2001 to 2002 (922 samples), 2003 to 2004 (1,228 samples), 2005 to 2006 (3,178 samples), and 2007 to 2008 (2,952 samples) detected trichloroethylene in the blood of less than 5% of people in all age groups, genders, and races or ethnicities studied in the surveys (CDC 2009a,b, 2011, 2016).

Environmental Releases

According to EPA's Toxics Release Inventory (TRI) database, environmental releases of trichloroethylene from 211 U.S. facilities in 2011 totaled 2.3 million pounds (TRI 2014). Based on historical TRI data, environmental releases of trichloroethylene have declined by more than 95% since 1988, when over 57 million pounds were released. Trichloroethylene is a common groundwater and drinking-water contaminant (Gist and Burg 1995, IARC 1995, ATSDR 1997, 2013, Heneghan 2000, Wu and Schaum 2000). Trichloroethylene tends to be persistent in groundwater, because its rate of biodegradation is relatively slow, with a half-life of months to years (Howard *et al.* 1991). Industrial wastewater is a source of trichloroethylene released into surface-water systems. Trichloroethylene background levels in 1995 were 0.001 ppb (µg/L) in the Gulf of Mexico, 0.007 ppb in the northeastern Atlantic Ocean, and 0.0008 to 0.039 ppb in rainwater and snow (Gist and Burg 1995). In EPA's Contract Laboratory Program

Statistical Database, trichloroethylene was reported in about 3% of surface-water samples and 19% of groundwater samples (IARC 1995). Based on its past widespread use for industrial and maintenance processes (e.g., as a metal degreasing agent) at U.S. military installations, trichloroethylene is also a common groundwater contaminant at military sites (NRC 2006, 2009). For example, the U.S. Marine Corps discovered in 1982 that the water supply from a water-treatment plant at Camp Lejeune, North Carolina, contained trichloroethylene, as a result of contamination of supply wells from leaking underground storage tanks, industrial area spills, and waste-disposal sites (ATSDR 2016). Exposure to contaminated groundwater can also potentially occur near National Priorities List (Superfund) sites, and trichloroethylene has been found in at least 1,045 of the 1,699 sites identified by EPA (ATSDR 2015).

Trichloroethylene in Tap Water

Based on a trichloroethylene concentration of 3.0 μg/L in drinking water (the median concentration in a large California water survey) and daily water consumption of 2 L, average daily trichloroethylene exposure through drinking water was estimated as 6 μg (Wu and Schaum 2000), which is consistent with the Agency for Toxic Substances and Disease Registry's estimate of 2 to 20 μg for daily exposure of the general population (ATSDR 1997). EPA has set a maximum contaminant level for trichloroethylene of 0.005 mg/L (5 μg/L) for drinking water (see Regulations).

Trichloroethylene volatilizes readily from contaminated tap water, and inhalation exposure to volatilized trichloroethylene may equal or exceed the exposure from ingestion of contaminated drinking water. One study estimated that inhalation exposure from a 10-minute shower in trichloroethylene-contaminated water would equal the exposure expected from drinking the contaminated water (McKone and Knezovich 1991), and another study (Weisel and Jo 1996) determined that approximately equal amounts of trichloroethylene entered the body via inhalation, absorption through the skin, and ingestion during typical daily activities where contaminated tap water was used for drinking and bathing (including showering). However, a modeling study of trichloroethylene exposure of workers showering with trichloroethylene-contaminated water at a metal degreasing facility (Franco *et al.* 2007) estimated that dermal exposure contributed more than inhalation exposure to carcinogenic risk.

Trichloroethylene in Indoor and Outdoor Air

In studies of the concentration of trichloroethylene in air conducted since the 1980s, trichloroethylene levels are generally lower in recent samples, consistent with the overall decrease in releases to the air and in blood levels in the general population. According to monitoring data from EPA's Air Quality System, trichloroethylene levels in ambient air remained fairly constant from 1999 to 2006, with a mean level of approximately 0.3 μg/m^3 (0.000056 ppm); however, the data were not from a statistically based survey and may not be nationally representative (EPA 2011). As part of the Minnesota Children's Pesticide Exposure Study, personal, indoor-air, and outdoor-air trichloroethylene concentrations were measured from May to September 1997 in 284 households with children. The median values for indoor, outdoor, and personal sampling were all between 0.5 and 1 μg/m^3 (0.00009 and 0.0002 ppm) (Adgate *et al.* 2004). Trichloroethylene concentrations in ambient air were also measured during EPA's large-scale Total Exposure Assessment Methodology studies conducted in Maryland, New Jersey, and California from 1981 through 1987 (Wallace *et al.* 1996). Median personal trichloroethylene exposure concentrations measured with personal air monitors carried by 750 individuals for 24 hours ranged from 0.3 to 3.0 μg/m^3 (0.00006 to 0.0006 ppm).

Migration of volatile chemicals from the subsurface into overlying buildings (vapor intrusion) likely makes an important contribution to indoor air levels of trichloroethylene in offices or residences located near soil or groundwater with high contamination levels (EPA 2011). Contamination of residential indoor air could also result from release of trichloroethylene directly from consumer products into the indoor environment (McHugh *et al.* 2011); however, some previously marketed consumer products have been reformulated to replace trichloroethylene (as discussed under Use, above). Environmental occurrences of trichloroethylene have been reported in locations near sites of past use or disposal (e.g., Superfund sites). Elevated levels of trichloroethylene in indoor air at Superfund sites were reported for office buildings in Mountain View, California (Rust and Drange 2013), and homes in Asheville, North Carolina (Morrison 2014). Trichloroethylene concentrations were as high as 110 μg/m^3 in office buildings at the Mountain View site when the heating, ventilation, and air conditioning system was not operating (Welt and Bice 2013) and 14 μg/m^3 in the basement of a house at the Asheville site.

Trichloroethylene in Consumer Products or Food

Trichloroethylene has been a major ingredient in several consumer products. For example, it constituted 80% to 100% of three aerosol spray fixative products for arts and crafts uses and other products intended for use as cleaners or degreasers in automobile or home maintenance (EPA 2014b, HPD 2014). However, an EPA risk assessment (EPA 2014b) was not able to estimate the numbers of consumers or bystanders exposed to trichloroethylene from arts and crafts spray products or degreasers.

The U.S. Food and Drug Administration (FDA) Total Diet Study identified 72 food items containing trichloroethylene, including fruits, beverages, and many foods prepared with oils and fats. The highest mean concentration (0.012 ppm) was found in samples of raw avocado (FDA 2006). Other studies also have found trichloroethylene in a variety of foods, with the highest levels in meats and margarine. Although trichloroethylene has not been used as a solvent for extraction of natural fats and oils, spices, hops, or caffeine (from coffee) since the FDA imposed limitations on these uses in 1977, foods can still be contaminated with trichloroethylene through the use of contaminated water in food processing or the use of food-processing equipment cleaned with trichloroethylene (ATSDR 1997).

Regulations

Coast Guard (Dept. of Homeland Security)

Minimum requirements have been established for safe transport of trichloroethylene on ships and barges.

Department of Transportation (DOT)

Trichloroethylene is considered a hazardous material, and special requirements have been set for marking, labeling, and transporting this material, including transporting it in tank cars.

Environmental Protection Agency (EPA)

Clean Air Act

National Ambient Air Quality Standards: Controlled as a volatile organic compound under state regulations implementing the standards for ozone.

National Emission Standards for Hazardous Air Pollutants: Listed as a hazardous air pollutant.

National Volatile Organic Compound Emission Standards for Aerosol Coatings: Trichloroethylene is included in product-weighted reactivity (PWR) calculations of aerosol coating products (trichloroethylene reactivity factor = 0.60 g O_3/g VOC).

New Source Performance Standards: Manufacture of trichloroethylene is subject to certain provisions for the control of volatile organic compound emissions.

Urban Air Toxics Strategy: Identified as one of 33 hazardous air pollutants that present the greatest threat to public health in urban areas.

Clean Water Act

Designated a hazardous substance.

Effluent Guidelines: Listed as a toxic pollutant.
Water Quality Criteria: Based on fish or shellfish and water consumption = 2.5 µg/L; based on fish or shellfish consumption only = 30 µg/L.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 100 lb.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Listed substance subject to reporting requirements.

Resource Conservation and Recovery Act

Characteristic Hazardous Waste: Toxicity characteristic leaching procedure (TCLP) threshold = 0.5 mg/L.
Listed Hazardous Waste: Waste codes for which the listing is based wholly or partly on the presence of trichloroethylene = U228, F001, F002, F024, F025, K018, K019, K020.
Listed as a hazardous constituent of waste.

Safe Drinking Water Act

Maximum contaminant level (MCL) = 0.005 mg/L.

Toxic Substances Control Act

Manufacturers (including importers) or processors of trichloroethylene for use in a consumer product except for use in cleaners and solvent degreasers, film cleaners, hoof polishes, lubricants, mirror edge sealants, and pepper spray are required to notify EPA at least 90 days before commencing, to allow EPA to evaluate the intended use and to regulate prospective manufacturers or processors of trichloroethylene before the use occurs, provided that regulation is warranted under Toxic Substance Control Act section 5(e), 5(f), 6, or 7.

Food and Drug Administration (FDA, an HHS agency)

Maximum permissible level in bottled water = 0.005 mg/L.
Trichloroethylene may be used as a solvent in the manufacture of modified hop extract provided the residue does not exceed 150 ppm.
Trichloroethylene may be used as a solvent in the manufacture of specified foods, with maximum residue levels ranging from 10 to 30 ppm.

Occupational Safety and Health Administration (OSHA, Dept. of Labor)

This legally enforceable PEL was adopted from the United States of America Standards Institute (USAI) (later the American National Standards Institute, ANSI) shortly after OSHA was established. The PEL may not reflect the most recent scientific evidence and may not adequately protect worker health.
Permissible exposure limit (PEL) = 100 ppm (8-h TWA).
Acceptable ceiling concentration = 200 ppm.
Acceptable maximum peak above the acceptable ceiling concentration = 300 ppm (5 min in any 2 h).

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted average (TLV-TWA) = 10 ppm.
Threshold limit value – short-term exposure limit (TLV-STEL) = 25 ppm.
Biological exposure indices: Trichloroacetic acid in urine (end of shift at end of workweek) = 15 mg/L; trichloroethanol in blood (without hydrolysis; *n*-hexane, methyl *n*-butyl ketone, and trichloroethylene, end of shift at end of workweek) = 0.5 mg/L.

Environmental Protection Agency (EPA)

Integrated Risk Information System (IRIS) oral reference dose (RfD) = 0.0005 mg/kg b.w. per day.
Interim Acute Exposure Guideline Levels (AEGLs): AEGL-1 (non-disabling) = 77 ppm; AEGL-2 (disabling) = 240 ppm; AEGL-3 (lethal) = 970 ppm (8-h TWAs). These AEGLs are available for use as deemed appropriate on an interim basis by federal and state regulatory agencies and the private sector.
IRIS inhalation reference concentration (RfC) = 0.0004 ppm [0.4 ppb, or 2 µg/m^3].
IRIS oral cancer slope factor = 5×10^{-2} per mg/kg b.w. per day.
IRIS inhalation unit risk = 2×10^{-2} per ppm [4×10^{-6} per µg/m^3].
Regional Screening Levels (formerly Preliminary Remediation Goals): residential soil = 0.44 mg/kg; industrial soil = 2.0 mg/kg; residential air = 0.21 µg/m^3; industrial air = 0.88 µg/m^3; tap water = 0.26 µg/L; maximum contaminant level (MCL) = 5.0 µg/L.

National Institute for Occupational Safety and Health (NIOSH, CDC, HHS)

Recommended exposure limit (REL) = 25 ppm (10-h TWA).
Ceiling recommended exposure limit = 2 ppm (60-min ceiling) during use as an anesthetic agent.
Immediately dangerous to life and health (IDLH) limit = 1,000 ppm.
Listed as a potential occupational carcinogen.

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