TRICHLOROETHYLENE

CAS number: 79-01-6

Synonyms: 1-Chloro-2, 2-dichloroethylene, ethylene trichloride, TCE, 1,1,2-TCE, tri, acetylene trichloride, trilene

Chemical formula: C_2HCl_3

Workplace exposure standard (retained)

TWA: **10 ppm**

STEL: **40 ppm**

Peak limitation: **—**

Notations: **Carc. 1B**

IDLH: **1,000 ppm**

Sampling and analysis: The recommended value is quantifiable through available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 10 ppm is recommended to protect for effects on the central nervous system (CNS), renal (kidney) toxicity and cancer in exposed workers.

A STEL of 40 ppm is recommended to protect for acute effects on the CNS in exposed workers.

Given the conflicting data about carcinogenicity and the mechanism of action for carcinogenicity available from the primary sources, it is recommended that a review of additional sources be conducted at the next scheduled review.

Discussion and conclusions

Trichloroethylene (TCE) is mainly used for vapour degreasing and cleaning of metal parts, in adhesives, as a solvent and for synthesis in the chemical industry.

The critical effects of exposure are CNS effects, renal toxicity and cancer.

Results of epidemiological studies, including those with occupational studies, are mixed. However, there is a positive association between TCE exposure and cancer of the kidney, non-Hodgkin lymphoma and cancer of the liver in humans. The evidence for cancer of the kidney is stronger than for other cancers (ACGIH, 2018; IARC, 2014; SCOEL, 2009).

Chronic inhalation is reported to cause renal toxicity and tumours in rats and liver and lung tumours in mice. A dose-related increase in the incidence of malignant lymphomas is observed in female mice at 100 ppm for 18 months (ACGIH, 2018). Mechanistic data is inconclusive. TCE and its metabolites are regarded as being weak genotoxic and require high doses to induce a response (ACGIH, 2018). SCOEL (2009) conclude a threshold exists and that preventing renal toxicity is sufficient to prevent renal cancer. Based on this SCOEL (2009) recommend a NOAEC of 10 ppm in humans to derive TWA. Noting there are inconsistent decisions about the carcinogenicity potential and mechanism of

TCE in humans, it is recommended that an investigation of additional data sources is undertaken at the next scheduled review.

Neurotoxic effects including dizziness, headache, sleepiness, nausea, confusion, blurred vision and weakness, are reported to occur in humans at approximately 100 ppm. These acute neurological effects are associated with peak concentrations (ACGIH, 2018).

A TWA of 10 ppm is recommended to be retained. This TWA is consistent across primary sources and is cited to be protective of effects on the CNS, renal toxicity and carcinogenicity. An adverse effect on the CNS is evident at ten times the TWA (100 ppm) in human studies (ACGIH, 2018). Therefore, a STEL of 40 ppm is also recommended to be retained.

Recommendation for notations

Classified as a Category 1B carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Not classified as a skin sensitiser or respiratory sensitiser according to the GHS.

There are insufficient data to recommend a skin notation. However, there is conflicting information between primary sources. A review of additional dermal exposure data is recommended at the next scheduled review.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1995***	***TWA: 10 ppm (54 mg/m^3); STEL: 40 ppm (216 mg/m^3)***
ACGIH	***2007***	***TLV-TWA: 10 ppm (54 mg/m^3); TLV-STEL: 25 ppm (135 mg/m^3)***

TLV-TWA recommended to protect against CNS effects and the potential for other effects including renal toxicity and cancer.

TLV-STEL recommended to minimise CNS effects related to peak exposures.

Summary of data:

- No derivation of TWA or STEL provided
- Primary evidence for recommendation:
  - human exposure produces reversible CNS effects at concentrations >100 ppm
  - cohort studies of exposed workers do not indicate significant increases in cancer incidence
  - case-control studies suggest prolonged exposure to high concentrations (100,000+ ppm) can increase incidence of renal cancer
  - very low acute toxicity by all exposure routes
  - chronic exposure to TCE produces renal toxicity and tumours in rats and liver and lung tumours in mice
  - weakly mutagenic *in vitro* following bioactivation.

Human data:

- Use as an anaesthetic associated with cardiac arrhythmia in humans exposed at concentrations >15,000 ppm:
  - death occurred at 10,000 ppm and associated with cardiac arrhythmia and massive liver damage
- Neurotoxic effects, including dizziness, headache, sleepiness, nausea, confusion, blurred vision and weakness, occur at ≈100 ppm
- Acute neurological effects in humans and animals associated with peak concentrations rather than 'area-under-the-curve' exposure
- Volunteers exposed at 1,000 ppm for 2 h resulted in adverse effects on visual perception and motor skills:
  - similar exposure at 100 or 300 ppm without any adverse effects
- No adverse effects observed in volunteers exposed at 200 ppm for 7.5 h/d for 5 d
- Investigators report subjective effects such as lassitude and headache at 100 ppm (no exposure frequency or duration provided).

Cancer epidemiology:

- Over 60 cancer epidemiology studies of TCE:
  - a key review of studies was restricted to the key epidemiologic studies and those published in 2000 or later with attention to evidence regarding cancers of the kidney, liver, lung and testes and lymphomas
- No further specific details for the following data are provided

Source	Year set	Standard

- In cancer incidence cohort studies, TCE exposure was associated with an increased risk of kidney cancer, when data on men and women from several studies were combined:
  - RR of 1.7 and 95% confidence interval 1.1-2.7; (N=21)
- In cancer mortality studies, the combined RR was not significantly elevated (1.2; 95% CI, 0.8-1.7; N=37)
- Results from case-control studies were mixed with most designed to identify exposure to dry-cleaning chemicals or solvents, without further specificity
- The largest and most specific case-control study was derived from a proportional mortality ratio study of a large transformer manufacturing plant:
  - classified exposure to TCE as a degreaser
  - results, based on logistic regression analysis, reported as OR for exposure among deaths classified as cancers of the biliary passages and liver (OR, 0.54; 95% CI, 0.30-3.32)
- Results from various case-control studies of kidney cancer and occupational exposure (no further information provided):
  - OR, 10.8; 95% CI, 3.4–34.8
  - OR, 2.16; 95% CI, 1.0–4.6
  - OR, 1.3; 95% CI, 0.9–1.9
  - OR, 1.0; 95% CI, 0.3–3.3
  - OR, 0.8; 95% CI, 0.4–2.0
- No overall significant association with TCE exposure and renal cell cancer in a population-based case-control study with 935 renal cell carcinoma cases and 4,298 controls; questionnaires and two job-exposure matrices to get lifetime agent-specific measures of exposure for each study subject; no dose-response relationship found
- Liver cancer incidence elevated in most of the cancer incidence studies:
  - the overall average SIR of 1.9 (95% CI, 1.0–3.4)
- One liver cancer mortality study; SMR of 1.7; 95% CI, 0.2–16.2
- A combined SMR from 3 studies is reported 1.1 (95% CI, 0–1.7) resulting from analysis of mortality and cancers of the biliary tract and liver
- Combined SIR for studies of NHL of 1.5 (95% CI, 0.9–2.3)
- Combined SMR of 1.2 (95% CI, 0.9–1.7) from NHL cohort mortality studies
- Combined lung cancer SIR of 0.8 (95% CI, 0.6–1.1) for cohort incidence studies
- Combined lung cancer SMR of 1.0 (95% CI, 0.9–1.1) for cohort mortality studies
- Case-control studies of lung cancer and TCE exposure were not found
- Epidemiologic studies of testes cancer and TCE exposure were not found.

Animal data:

- Very low dermal toxicity, LD_{50}: >20 mL/kg (rabbits)
- Very low acute inhalation toxicity with a 4 h LC_{50}: >6,400 ppm and <20,000 ppm in rats
- Slight growth retardation was the only effect observed in rats, guinea pigs, dogs, rabbits and monkeys continuously exposed for 90 d at 35 ppm
- No adverse effects reported in a ‘group of animals’ exposed 8 h/d for 90 d at 700 ppm
- Groups of pigmented rats exposed by inhalation at 2,700, 4,200, 6,000 or 7,200 ppm and effects analysed by recording eye movements upon different stimuli:

Source	Year set	Standard
		○ decrease in the eye movements ○ prolonged the duration of nystagmus ○ decrease in ability to cancel nystagmus elicited by vestibular stimulation in conflict with a visual input ○ no further information on concentrations and effects • Groups of rats, mice and hamsters exposed 6 h/d, 5 d/w for 18 mo at 100 or 500 ppm: ○ a dose-related increase in the incidence of malignant lymphomas observed in female mice ○ 17/30 at 100 ppm and 18/28 at 500 ppm versus 9/29 in controls ○ observation believed to be a nonspecific activation of a virus infestation ○ no statistically significant increase in tumour formation observed in any of the other groups • Groups of rats and mice exposed 7 h/d, 5 d/wk for 104 wk at 50, 150 or 450 ppm of reagent grade TCE: ○ tumours found mainly in the hematopoietic system, lungs and mammary glands of mice and in pituitary and mammary glands of rats ○ average number of lung tumours/mouse in groups exposed at 150 and 450 ppm more than threefold the control incidence ○ incidences of pulmonary adenocarcinomas in mice exposed at 150 and 450 ppm were 16% and 15%, respectively; significantly higher than the controls (2%) ○ incidences of other types of tumours not significantly different ○ incidence of tumours in rats and mice exposed at 50 ppm not significantly different • Male and female rats and mice exposed at 7 h/d, 5 d/wk for 8 wk at 100 or 600 ppm and for 104 wk (rats) and 78 wk (mice) at 100, 300 and 600 ppm: ○ 8 wk exposure in rats did not result in increased tumour incidences observed at 164 wk ○ slight increases noted in leukaemia and renal adenocarcinomas in male and not female rats exposed at 600 ppm ○ lung tumours and hepatomas increased in male mice exposed at 300 and 600 ppm and for hepatomas at 600 ppm ○ increases seen in female mice with the increase in lung tumours at 600 ppm statistically significant • Groups of 50 male and 50 female rats and mice administered epichlorohydrin-free TCE by gavage, 5/wk for 103 wk; doses 500 or 1,000 mg/kg/d for rats and 1,000 mg/kg/d for mice: ○ incidence of renal tubular adenocarcinomas in male rats increased (low dose: 0/49 and high dose: 3/49 vs controls: 0/48) ○ combination of renal tubular adenomas and adenocarcinomas occurred with a positive trend (2/49 for low dose and 3/49 for high dose vs 0/48 for control) ○ one high-dose female rat had a renal tubular adenocarcinoma ○ combined incidence of renal tubular and renal pelvis tumours in male rats (3/49 for low dose and 4/49 for high dose vs 0/48 for control) occurred with a positive trend ○ in mice, a statistically significant increase in incidence of hepatocellular carcinomas was observed: 8/48 for low dose, 30/50 for high dose in males and 2/48 for low dose and 13/49 for high dose in females ○ incidence of hepatocellular adenomas significantly increased in females (2/48 for low dose and 8/49 for high dose)

Source	Year set	Standard
		○ increased incidence of alveolar/bronchiolar adenomas noted in females (0/48 for low does and 4/48 for high dose). Genotoxicity: • Weakly mutagenic in the presence of a metabolic activation system in the Ames Salmonella assay • The author of a review of data available on the genotoxic effects concluded that with indicator tests *in vitro*, there was no indication of chromosomal damage in yeast, no effect in bacteria and no induction of unscheduled DNA synthesis (UDS) • Concluded TCE and its metabolites are weakly genotoxic and required high doses to induce a response. Insufficient data to warrant a sensitiser notation or STEL. Skin notation not warranted based on low dermal toxicity.
DFG	***2014***	***Not assigned***
		No MAK recommended based on carcinogenic evidence in humans noted below. Summary of additional data: • 2 case–control studies revealed an increased risk of renal cancer after long-term occupational exposure and exposure to high concentrations (cited by ACGIH, 2018) • An increased risk only for exposed females identified in 2 other case-control studies (cited by ACGIH, 2018).
SCOEL	***2009***	***TWA: 10 ppm (54.7 mg/m^3); STEL: 30 ppm (164.1 mg/m^3)***
		TWA recommended to avoid renal toxicity as a threshold to renal carcinogenicity Summary of additional data: • The key target of human TCE toxicity and carcinogenesis is the kidney, notably the proximal tubule • Human renal cell cancer observed in highly and repetitively exposed workers, having used TCE mostly in metal degreasing activities • Observations in experimental systems and in occupationally exposed and diseased persons, lead to the conclusion that human renal cell cancer risk is avoided if exposure to nephrotoxic concentrations of TCE do not occur, including concentrations leading to sub-clinical renal changes • Occupational field study on 70 workers with mean exposure at 32 ppm (range 0.5–252 ppm); minor sub-clinical alterations in renal functional parameters observed • No increase in urinary excretion of NAG marker protein in workers exposed at 6–10 ppm: ○ NOAEC of 10 ppm • Classed as a genotoxic carcinogen, for which a practical threshold is supported by studies on mechanisms and/or toxicokinetics • OEL established based on a NOAEC of 10 ppm in exposed humans relating to the avoidance of renal toxicity • Reports high TCE peak exposures critical in development of human renal cell cancer and taking into account 32 ppm mean exposure concentration in worker study, a STEL of 30 ppm is recommended.

Source	Year set	Standard
OARS/AIHA	***NA***	***NA***
No report		
HCOTN	***2003***	***Not assigned***
• Evaluation of the effects on reproduction and recommendation for classification (not an OEL document) • The human studies on the potential effects of occupational exposure on fertility did not show significant effects.		

Secondary source reports relied upon

Source		Year	Additional information
NICNAS	✓	2000	• No additional data.
IARC	✓	2014	• Recognised positive associations between TCE and cancer of the kidney, NHL and cancer of the liver; concluded that evidence for cancer of the kidney was stronger for non-Hodgkin lymphoma or cancer of the liver • Controlled studies evaluating TCE alone found it to be incapable of inducing gene mutations in most standard assays for bacterial mutagenesis • Has shown potential to affect DNA and chromosomal structure • Unlikely TCE is a direct-acting mutagen • Overall, strong evidence to conclude, after metabolism, TCE can be genotoxic, particularly in the kidney where metabolism *in situ* occurs.
US EPA	✓	2011	• Following 2005 US EPA Guidelines for Carcinogen Risk Assessment, TCE is characterised as "*carcinogenic to humans*" by all routes of exposure • Based on convincing evidence of a causal association between exposure in humans and kidney cancer • Kidney cancer association cannot be reasonably attributed to chance, bias or confounding • Human evidence of carcinogenicity from epidemiologic studies of exposure is strong for NHL: ○ less convincing for kidney cancer and more limited for liver and biliary tract cancer • Clear evidence for carcinogenicity in rats and mice, with multiple studies showing multiple kinds of cancers • Concludes that a mutagenic mode of action is operative in TCE-induced kidney tumours • Cytotoxicity and compensatory cell proliferation suggested to play a role in the mode of action for renal carcinogenesis, as

Source	Year	Additional information
		high incidences of nephrotoxicity have been observed in animals at doses that induce kidney tumours: ○ nephrotoxicity has not been shown to be necessary for kidney tumour induction by TCE in rodents.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? No

The chemical is not a non-threshold based genotoxic carcinogen.

Notations

Source	Notations
SWA	NA
HCIS	Carcinogenicity – category 1B
NICNAS	NA
EU Annex	Carcinogenicity – category 1B
ECHA	Carcinogenicity – category 1B
ACGIH	Carcinogenicity – A2
DFG	Carcinogenicity – 1, H (skin)
SCOEL	Skin
HCOTN	NA
IARC	Carcinogenicity – Group 1
US NIOSH	NA

NA = not applicable (a recommendation has not been made by this Agency); — = the Agency has assessed available data for this chemical but has not recommended any notations

Skin notation assessment

Calculation
Insufficient data to assign a skin notation.

IDLH

Is there a suitable IDLH value available? Yes

Additional information

Molecular weight:	131.39
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 5.45 mg/m^3; 1 mg/m^3 = 0.183 ppm
This chemical is used as a pesticide:	☐
This chemical is a biological product:	☐
This chemical is a by-product of a process:	☐
A biological exposure index has been recommended by these agencies:	✓ ACGIH ✓ DFG ✓ SCOEL

Workplace exposure standard history

Year	Standard
Click here to enter year	

References

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