# carbon tetrachloride

| CAS number: | 56-23-5 |
| --- | --- |
| Synonyms: | Tetrachloromethane, carbon tet, methane tetrachloride, perchloromethane, tetrachlorocarbon, freon 10 |
| Chemical formula: | CCl4 |
| Structural formula: | — |

Workplace exposure standard (amended)

| TWA: | **1 ppm (6.3 mg/m3)** |
| --- | --- |
| STEL: | **5 ppm (32 mg/m3)** |
| Peak limitation: | **—** |
| Notations: | **Carc. 2., Sk.** |
| IDLH: | **200 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 1 ppm (6.3 mg/m3) is recommended to protect for hepatotoxicity (liver effects) in exposed workers.

A STEL of 5 ppm (32 mg/m3) is recommended to reduce the acute risk of central nervous system (CNS) depression and observed haematocrit changes.

## Discussion and conclusions

Carbon tetrachloride was traditionally used as a solvent, a dry-cleaning agent and for fluorocarbon manufacture. Historically used as a fumigant, its use is now banned, with all manufacture, import and export controlled in Australia under the *Ozone Protection and Synthetic Greenhouse Gas Management Act 1989*.

A NOAEL of 1 ppm was identified in humans “under industrial exposure conditions” for unaltered serum parameters of hepatotoxicity (SCOEL, 2009). A NOAEL of 5 ppm for liver damage was identified in mice (SCOEL, 2009; USEPA 2010). Rats exposed for one hour per day to 10 ppm (63 mg/m3) showed increased serum enzymes (SCOEL, 2009).

The recommended TWA (1 ppm) is based on the NOAEL of 1 ppm (6.3mg/m3) identified humans and supported by evidence in animals. Acute adverse effects demonstrated in rats (SCOEL, 2009) are within 10 times the TWA concentration requiring a STEL value based on weight of evidence.

## Recommendation for notations

Classified as a category 2 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.

A skin notation is recommended as evidence indicates rapid absorption through the skin and systemic effects in humans.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1995 TWA: 0.1 ppm (0.63 mg/m3) | |
| Acute exposure results in depression of CNS and liver and kidney damage. Chronic exposure may result in optic nerve damage and impaired vision.  TWA based on safety factor of 10 applied to NOAEL in animal studies (1 ppm) and observed adverse effects (LOAEL) in humans at 5 ppm.  Exposure standard considered potentiation of CCl4 toxicity by alcohol and a possibility of simultaneous dermal exposure.  Inadequate evidence for carcinogenicity in humans.  WES documentation and review in 1995 based on *'Review of Toxicity of Carbon Tetrachloride: Recommendation for an Occupational Exposure Standard'* by Karuna Raja, (master’s thesis, University of Sydney). |
| ACGIH 2001 TLV-TWA: 5 ppm (31 mg/m3); TLV-STEL: 10 ppm (63 mg/m3) |
| TLV-TWA and TWA-STEL recommended to minimise potential for hepatotoxicity.  Values may not be sufficiently protective for persons who consume alcohol or have reduced liver function.  Dermal exposure data support skin notation. Suspected human carcinogen notation assigned based on animal studies indicating incidence of liver tumours.  Insufficient data to support a sensitiser notation.  Summary of data:  Human data:   * Dermal absorption observed through detection *via* respiratory exhalation * CNS depression most common symptom of acute exposure * Fatalities from acute liver and kidney necrosis reported to occur following ingestion and inhalation * Wide range of symptoms reported after chronic exposure including nausea, anorexia, altered serum enzyme levels, GIT symptoms, renal failure, blurred vision, coma and death * Exposure at 33–124 ppm led to symptoms of fatigue in workers (<2 h) * No adverse effects on liver function determined with serum iron and transaminase measures reported in 6 male volunteers exposed at 10 ppm for 180 min * Possible liver injury identified in one volunteer 7 d after exposure to 48 ppm for 48 h.   Animal data:   * Not mutagenic to *Salmonella typhimurium* or *Escherichia coli* * Numerous studies indicate broad interspecies variability * Inhalation at 5 ppm for 7 h/d, 5 d/wk over various periods (25–37 wk) reported no observed adverse effects in rats or guinea pigs * LD50: 15,000 mg/kg; (guinea pigs, dermal) * LC50: 7,300 ppm; (rats, 4–6 h) * LC50: 9,526 ppm; (mice, 8 h) * Inhalation studies in squirrel monkeys identified enlarged discoloured livers when exposed continuously for 90 d at 10 ppm: * no observable changes noted when exposed to 1 ppm continuously for the same period * Failed to increase unscheduled DNA synthesis (indicative of damage in hepatocytes) in male or female mice at 20 mg/kg (oral dose) or male rats at 10 mg/kg * Inhalational exposure in pregnant rats (300 or 1000 ppm) for 7 h/d, GD 6­–15 caused significant weight loss and liver damage and reduction in foetal size and weight * Peak carbon tetrachloride blood concentration and peak rate of carbon tetrachloride metabolism were good predictors of carbon tetrachloride-induced liver toxicity * PBPK model predicted that occupational human exposure at 5 ppm results in an internal dose to liver tissue of approximately 0.6 mg/h/kg (i.e. 1/40 of the 10 mg/kg dose in rats with no effect); if 15 min exposures were ≤10 ppm). |
| DFG 2002 MAK: 0.5 mL/m3 |
| MAK recommended to protect for hepatotoxic effects.  Hepatotoxic effects studied with acute toxic effects on the skin, eyes, lungs and nervous system less pronounced.  Exposures of 0.5 mL/m3 (0.5 ppm) for 8 h/d corresponds to daily uptake of 0.5 mg/kg  Dermal absorption demonstrated in both humans and animals.  Sufficient evidence that sensitisation notation is not necessary.  Summary of additional data:  Human data:   * Marginal effects of reduced haematocrit at levels less than 1 mL/m3 observed * Haemoglobin levels, red blood cells and haematocrit significantly changed with exposures greater than 1 mL/m3.   Animal data:   * NOEL: 1 mg/kg (male rats; 12 wk). |
| SCOEL 2009 TWA: 1 ppm (6.4 mg/m3); STEL: 5 ppm (32 mg/m3) |
| TWA and STEL recommended to protect for hepatotoxic effects.  Critical effects observed in the liver through animal studies following repeated exposure. CNS depression leading to death noted at high levels.  Carbon tetrachloride is produced with tetrachloroethylene and as a by-product during the manufacture of chloroform. Traditional use as a solvent is restricted or banned in many countries.  Non-genotoxic carcinogen with a threshold based on mode of action.  Anecdotal sensitisation data in humans, however no indication in animal testing.  No measurement difficulties are foreseen.  Summary of additional data:  Human data:   * Exhaled air concentrations of 3.8 mg/m3 detected following dermal exposures for 30 min decreased to half in 2.5 h * Liver function abnormalities detected at accidental exposure of 300–500 mL/m3 * Airborne level of 1 ppm an established NOAEL “under industrial exposure conditions”; unaltered serum parameters of hepatotoxicity * Indication that it can pass the placental barrier.   Animal data:   * NOAEL: 5 ppm; (mice, 2 yr); liver damage; LOAEL: 25 ppm * Increased serum enzymes in rats treated with 10 ppm (63 mg/m3) carbon tetrachloride for 1 h/d * LC50: 45,000–50,000 mg/m3 (mice). * TWA based on NOAEL of 1 ppm for unaltered serum parameters of hepatotoxicity in humans. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2013 | * Only introduced at small quantities for use by trained personnel for research purposes in laboratories - *Environment tier II assessment* available * The manufacture, import and export is controlled in Australia under the *Ozone Protection and Synthetic Greenhouse Gas Management Act 1989*. |
| US EPA |  | 2010 | * Reference Concentration (RfC) for chronic inhalation exposure: * 0.01 mg/m3 – critical effect noted to be fatty liver changes * Human data: * suggestions of serum enzymes indicating hepatic effects observed at 1–4 ppm * Animal data: * NOAEL: 5 ppm; (mice, 2 yr); LOAEL: 25 ppm. |
| OECD |  | 2011 | * Not considered a mutagen from *in vivo* studies based on weight of evidence. * genotoxic effects observed *in vivo* a response to cell damage and oxidative stress * Un-metabolised CCl4 primarily exhaled in air and excreted in faeces * Animal data: * LD50: >2,130 mg/kg (guinea pigs, unspecified duration) * evidence of weak skin sensitisation in mice. |

### 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 2 |
| NICNAS | NA |
| EU Annex | Carcinogenicity – category 2 |
| ECHA | NA |
| ACGIH | Carcinogenicity – A2, Skin |
| DFG | Carcinogenicity – 4, H (skin) |
| SCOEL | Carcinogenicity – D, Skin |
| HCOTN | NA |
| IARC | Carcinogenicity – Group 2B |
| 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 |
| --- |
| |  |  |  |  | | --- | --- | --- | --- | | Adverse effects in human case study: | yes | 4.00 |  | | Dermal LD50 ≤1000 mg/kg: | no |  |  | | Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  | | Dermal LD50/Inhalation LD50 <10: |  |  |  | | *In vivo* dermal absorption rate >10%: |  |  |  | | Estimated dermal exposure at WES >10%: |  |  |  | |  |  |  | **a skin notation is warranted** | |

### IDLH

| Is there a suitable IDLH value available? | Yes |
| --- | --- |

## Additional information

| Molecular weight: | 153.8 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = Number mg/m3; 1 mg/m3 = Number 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

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7th Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the [*TLVs® and BEIs® Guidelines section*](http://www.acgih.org/tlv-bei-guidelines/policies-procedures-presentations) on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (2012) Carbon tetrachloride – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2009) Recommendation from the Scientific Committee on Occupational Exposure Limits for carbon tetrachloride. SCOEL/SUM/31.

International Agency for Research on Cancer (IARC) (2001) Volume 79 some thyrotropic agents. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2013): Methane, tetrachloro-: Human health tier I assessment – IMAP report.

Organisation for Economic Cooperation and Development (OECD) (2011) SIDS initial assessment profile – Tetrachloromethane (carbon tetrachloride).

Tenth Adaptation to Technical Progress Commission Regulation (EU) No 2017/776 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the CLP Regulation).

US Environmental Protection Authority (US EPA) (2010) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Carbon tetrachloride.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – Carbon tetrachloride.