# Chloroform

| CAS number: | 67-66-3 |
| --- | --- |
| Synonyms: | Formyl trichloride, methane trichloride,  methenyl trichloride, trichloroform, trichloromethane |
| Chemical formula: | CHCl3 |
| Structural formula: | — |

Workplace exposure standard (amended)

| TWA: | **0.5 ppm (2.5 mg/m3)** |
| --- | --- |
| STEL: | — |
| Peak limitation: | — |
| Notations: | Carc. 2, Sk. |
| IDLH: | 500 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 0.5 ppm (2.5 mg/m3) is recommended to protect for liver and kidney effects in exposed workers.

## Discussion and conclusions

Chloroform is used as a raw material in the chemical industry in the manufacture of fluorocarbons and as an extractant and industrial solvent.

A quarter of workers (total 68) had enlarged livers following exposures of 10 to 200 ppm with employment periods between one to four years (ACGIH, 2018). A NOAEC of 5 ppm for kidney and liver effects is reported in mice and rats. A 104-week inhalation study also reported a NOAEC of 5 ppm in mice and 10 ppm in rats for kidney tumours (DFG, 2012; NICNAS, 2014). A LOAEL for liver and kidney effects is reported at 25 ppm in rats, rabbits and guinea pigs (SCOEL, 1995). Adverse effects on the foetus are reported at 30 ppm in rats (ACGIH, 2001), with no reported embryotoxicity at 10 ppm (DFG, 2012). Evidence in animals suggests dermal uptake results in effects in the kidneys and significantly contributes to total body burden of chloroform.

A TWA of 0.5 ppm is derived using the NOAEC of 5 ppm in animal studies and applying an uncertainty factor of 10 to account for interspecies variability. This TWA is considered to protect for liver and kidney effects including kidney tumours in exposed workers.

## 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.

While the data available are limited, a skin notation is recommended based on evidence of dermal absorption in animals and potential contribution to systemic effects.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 2001 TWA: 2 ppm (10 mg/m3) | |
|  |
| ACGIH 2001 TLV-TWA: 10 ppm (49 mg/m3) |
| TLV-TWA recommended to minimise the potential for liver toxicity and embryotoxicity.  Summary of data:  Human data:   * Workers exposed at 80–240 ppm reported severe fatigue, digestive disturbance and mental dullness * less severe symptoms reported at 20–70 ppm (no further information) * A study of 68 workers exposed at 10–200 ppm reported 25% with enlarged livers; employed durations of between 1 and 4 yr.   Animal data:   * Mice exposed at 100 ppm for 4 h produced fatty infiltration in the liver with liver necrosis at higher concentrations (no further information) * No organ injury reported in rats exposed at 25–30 ppm 7 h/d, 5 d/wk for 6 mo * liver and kidney injury reported at ≥50 ppm same frequency and duration * severity is concentration dependant * Rats more sensitive species * Significant increases in epithelial tumours of the kidney in rats and hepatocellular carcinomas in mice fed with 90–180 mg/kg bw chloroform in corn oil for 111 days * Considered embryotoxic; in rats exposed for 7 h/d on GD 6–15 at 30, 100 or 300 ppm: * decreased conception rate and high incidence of foetal resorption at 300 ppm * retarded foetal development at 30, 100 and 300 ppm * decreased foetal body measurements at 30 and 300 ppm.   Insufficient evidence to recommend skin notation, sensitiser notations or a STEL. |
| DFG 2010 MAK: 0.5 ppm (2.5 mg/m3) |
| MAK established provisionally in 1999 to protect for liver and kidney effects reported in animal studies.  Summary of additional data:   * NOEL 5 ppm (rats and mice, 13 wk) for increased cell proliferation in liver and kidney: * no increase in tumour incidence * cytotoxic effects seen from 10 ppm * More recent study reports no embryotoxic effects in rats at 10 ppm * MAK based on NOAEL of 5 ppm; assumed factor of 10 applied (no further information); supported by PBPK modelling * Skin notation: * evidence in dermal exposure studies in rats, concluded that dermal uptake could be much higher than uptake by inhalation at the recommended MAK * dose-dependent degenerative changes in kidneys of rabbits after single application to skin * Increased incidence of kidney tumours in male mice following inhalation; mechanisms of tumour development are non-genotoxic based on negative results *in vitro,* also tumour development only when there are also cytotoxic effects. |
| SCOEL 1995 TWA: 2 ppm (10 mg/m3) |
| TWA recommended to protect for liver and kidney damage.  Summary of additional data:   * LOAEL for kidney and liver damage: 25 ppm (124 mg/m3) (rats, rabbits and guinea pigs, 6 mo) * TWA derived from LOAEL of 25 ppm with factor of 10 applied to account for no NOAEL and rounded down. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN 2000 Not assigned |
| Summary of additional data:  A lack of appropriate data precludes the assessment of chloroform for effects on fertility. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2014 | * NOAEC: 25 mg/m3 (5.15 ppm) renal effects and atypical tubule hyperplasia; (mice, 104 wk) * NOAEC: 5 ppm kidney tumours; (mice) 10 ppm (rats); 104 wk * NOAEC: 10 ppm developmental toxicity (rats, gestation days 7 to 16) * Not likely to be a skin sensitiser * No direct mutagenic or genotoxic potential. |

### 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 | Carc. Cat. 3 |
| EU Annex | Carcinogenicity – category 2 |
| ECHA | — |
| ACGIH | Carcinogenicity – A3 |
| DFG | Carcinogenicity – 1, H (skin) |
| SCOEL | 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: |  |  |  |  |  | | Dermal LD50 ≤1000 mg/kg: |  |  |  |  |  | | Dermal repeat-dose NOAEL ≤200 mg/kg: |  |  |  |  |  | | Dermal LD50/Inhalation LD50 <10: |  |  |  |  |  | | *In vivo* dermal absorption rate >10%: |  |  |  |  |  | | Estimated dermal exposure at WES >10%: | yes | 2.00 |  |  |  | |  |  | 2 | **insufficient data to assign a skin notation** | | | |

### IDLH

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

## Additional information

| Molecular weight: | 119.38 |
| --- | --- |
| 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) Chloroform – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (1995) Recommendation from the Scientific Committee on Occupational Exposure Limits for chloroform. SEG/SUM/30.

Health Council of the Netherlands (HCOTN) (2000) Chloroform. Evaluation of the effects on reproduction, recommendation for classification. The Hague: Health Council of the Netherlands; publication no. 2000/07OSH.

International Agency for Research on Cancer (IARC) (1999) Volume 73 some chemicals that cause tumours of the kidney or urinary bladder in rodents and some other substances. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2014) Methane, trichloro: Human health tier II assessment – IMAP report.

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