# Methyl Chloride

| CAS number: | 74-87-3 |
| --- | --- |
| Synonyms: | Chloromethane |
| Chemical formula: | CH3Cl |
| Structural formula: |  |

Workplace exposure standard (amended)

| TWA: | **20 ppm (42 mg/m3)** |
| --- | --- |
| STEL: | **80 ppm (167 mg/m3)** |
| Peak limitation: | **—** |
| Notations: | **Carc. 2, Sk., DSEN** |
| IDLH:  Sampling and analysis: | **2,000 ppm** |

## Recommendation and basis for workplace exposure standard

A TWA of 20 ppm (42 mg/m3) is recommended to protect for neurotoxic effects in exposed workers. It is considered to be protective of ocular and central nervous system (CNS) effects and changes to the performance of complex tasks.

A STEL of 80 ppm (167 mg/m3) is recommended to protect for symptoms of moderate exposure, such as diplopia (double vision) and difficulty focusing.

## Discussion and conclusions

Methyl chloride is used as a methylating agent in the production of a range of chemical products including silicones, plastics, pesticides and pharmaceuticals.

Methyl chloride is a gas under standard conditions and its critical effects are on the CNS. Animal studies have shown that methyl chloride is non-genotoxic due to its rapid metabolism. Extreme exposures (greater than those required to elicit neurotoxic effects) in animals lead to the development of renal tumours. However, the experimental conditions of these studies do not allow extrapolation to exposure in humans (SCOEL, 2016).

The TWA is derived from a NOAEL of 150 ppm presented in an animal study (ACGIH, 2001; SCOEL, 2016) with uncertainty factors of 5 and 2.5 to account for human inter-individual differences and interspecies differences, respectively. The recommended STEL is derived from an occupational chronic exposure study in which no symptoms of intoxication were reported at 100 ppm per day (ACGIH, 2001).

## Recommendation for notations

Classified as a category 2 carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Classified as a skin sensitiser and not a respiratory sensitiser according to the GHS.

A skin notation is recommended, supported by evidence from human observations.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 2011 TWA: 50 ppm (103 mg/m3); STEL: 100 ppm (207 mg/m3) | |
|  |
| ACGIH 2001 TLV-TWA: 50 ppm (103 mg/m3); TLV-STEL: 100 ppm (207 mg/m3) |
| TLV-TWA recommended to minimise the potential for subtle changes in performance of complex tasks. The TLV-TWA should also protect for other CNS effects such as drowsiness, headache, dizziness, blurred vision, speech difficulties, mental confusion and staggering gait. Principal route of absorption is inhalation; however, dermal absorption is possible.  Summary of data:  Human data:   * Moderate exposure characterised by ocular symptoms that include mistiness, diplopia and difficulty focusing. Symptoms may persist for several weeks * Moderate to high exposure associated with kidney and liver damage, CNS depression, respiratory failure, coma and death * Severe acute exposure may lead to nausea, vomiting, abdominal pain, and diarrhoea * Chronic and subacute exposure in humans can result in ataxia, staggering gait, tremors, vertigo, slurred speech, and blurred vision * Report of moderate to severe exposure (>500 ppm) in rubber manufacturing found workers were disabled for ≤30 d prior to recovery * Available data does not suggest irreversible adverse effects to body organs after repeated exposures at 100–200 ppm/d * Safety margin in TLV-TWA incorporated to protect against impairment in completing complex tasks * Skin notation recommended due to systemic intoxication through skin absorption * Insufficient data available to recommend a sensitiser notation.   Animal data:   * LC50: 2,760 ppm (undisclosed species, 4 h) * Renal tumours observed in male mice chronically exposed to 1,000 ppm/d * Male and female mice experienced limb muscle impairment and degeneration of the cerebellum * Highest NOAEL: 150 ppm (fertility, male F344 rats). |
| DFG 1984 MAK: 50 ppm (100 mg/m3) |
| MAK established provisionally on the basis of one workplace study and animal studies. Skin notation revised in 1998.  Summary of additional data:  Human data:   * Odour threshold 10 ppm * Liquid contact with skin can cause blisters due to chilling * Human population may be divided into two groups based on their capacity to metabolise methyl chloride (one considerably faster than the other).   Animal data:   * Toxicity varies greatly among different animal species * Fertility NOAEL: 150 ppm (male F344 rats) used to support MAK * Teratogenic NOAEL: 250 ppm (mice) * Direct mutagen in bacterial study, but insufficient evidence in animals to be classified as genotoxic. Infertility of severely exposed rats due to inflammatory action rather than a mutagenic pathway. |
| SCOEL 2016 8-hour TWA: 20 ppm (42 mg/m3) |
| TWA based on NOAEL of 150 ppm in F344 susceptible rats. Uncertainty factor of 5 applied for inter-individual variations combined with an uncertainty factor of 2.5 for differences in interspecies susceptibility (overall uncertainty factor of 7.5).  Summary of additional data:   * Most workplace exposures are acute; very few reported chronic cases * Metabolism in humans depends on GSTT1-1 (glutathione S-transferase (GST) theta), which is deficient in 20% of the European population. This sub-population may be more resistant to intoxication and is reflected in the application of uncertainty factors to derive the recommended TWA * Prolonged skin contact with liquid methyl chloride is unlikely as the substance is a gas under standard conditions. Exposure through skin absorption is considered to be very low * Carcinogenicity group and skin notation not assigned * Animal study indicated LOAEL of 400 ppm (cerebellar degeneration, C57BL/6 mice) * Insufficient data are available to derive a STEL. |
| OARS/AIHA NA NA |
| No report |
| HCOTN 2004 NA |
| Summary of additional data:   * No human fertility, developmental or lactation studies found regarding effects of exposure. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2014 | * Harmful systemic effects following acute and repeated inhalation exposure * NOAEC of 100–200 mg/m3 (50–100 ppm) for neurotoxicity indicated from human case studies. |
| IARC |  | 1999 | * Inadequate evidence of carcinogenicity in animals. |
| OECD |  | 2002 | * Human data consistently indicate a NOEL of 100–200 mg/m3/d (50–100 ppm/d) for all neurotoxic effects (inhalation) * ≤200 mg/m3/d (100 ppm/d) produces no adverse effect in repeated, prolonged daily occupational exposure. However, CNS effects occurred at long-term average exposure of 400 mg/m3/d (200 ppm/d). |

### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | Yes |
| --- | --- |
| Is the chemical carcinogenic with a mutagenic mechanism of action? | No |
| **The chemical is not a non-threshold based genotoxic carcinogen.** |  |

## Notations

| Source | Notations |
| --- | --- |
| SWA | Carc. 2, Skin |
| HCIS | Carcinogenicity – category 2 |
| NICNAS | Carc. Cat. 3 |
| EU Annex | NA |
| ECHA | Carcinogenicity – category 2 |
| ACGIH | Carcinogenicity – A4, Skin |
| DFG | Carcinogenicity – 3B, H (skin) |
| SCOEL | — |
| HCOTN | — |
| IARC | Carcinogenicity – Group 3 |
| US NIOSH | — |

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: | N/A |  |  | | 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: | 50.49 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 2.09 mg/m3; 1 mg/m3 = 0.477 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) (1984, 2001) Methyl Chloride (1984, 2001) – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2016) – SCOEL/REC/191 Chloromethane – recommendation report.

Health Council of the Netherlands (HCOTN) (2004) Methylchloride. Health-based recommended occupational cancer risk values. The Hague: Health Council of the Netherlands; publication no. 2012/32.

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

Organisation for Economic Cooperation and Development (OECD) (2002), Chloromethane – SIDS initial assessment report.

US National institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life and health concentrations – Methyl chloride.