# Vinylidene chloride

| CAS number: | 75-35-4 |
| --- | --- |
| Synonyms: | 1,1-Dichloroethene, 1,1-dichloroethylene, VDC, vinylidene dichloride |
| Chemical formula: | C2H2Cl2 |

Workplace exposure standard (retained)

| TWA: | **5 ppm (20 mg/m3)** |
| --- | --- |
| STEL: | **20 ppm (79 mg/m3)** |
| Peak limitation: | **—** |
| Notations: | **Carc. 2** |
| IDLH: | **—** |
| **Sampling and analysis:** The recommended value is quantifiable through available sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A TWA of 5 ppm (20 mg/m3) is recommended to protect for kidney and liver damage in exposed workers.

A STEL of 20 ppm (79 mg/m3) is recommended to protect for local irritation in exposed workers.

## Discussion and conclusions

Vinylidene chloride is used as a monomer in the production of thermoplastics and synthetic textiles.

The critical effects of exposure are kidney and liver damage and mucous membrane irritation.

Occupational exposure at 5 to 50 ppm is not associated with adverse effects in the available epidemiological data (ACGIH, 2018; DFG, 1997; SCOEL, 2008). However, most of these studies are limited by small sample sizes and mixed exposures. Irritation of the eyes and upper respiratory tract is reported above 25 ppm in exposed humans in a poorly documented study without further details (DFG, 1997). In mice, a NOAEC of 10 ppm and LOAEC of 25 ppm for kidney toxicity and kidney cancer are reported in a chronic inhalation study (ACGIH, 2018; DFG, 1997); whereas a LOAEC of 25 ppm for transient liver toxicity is reported in similarly exposed rats without evidence of carcinogenicity. Evidence of carcinogenicity in animals is equivocal and is not expected to act *via* a genotoxic mechanism of action (ACGIH, 2018; DFG, 1997; IARC 2019).

The LOAEC of 25 ppm for transient liver damage in rats is used as a point of departure in the evaluation by ACGIH (2018) and SCOEL (2008). DFG (1997) used the LOAEC of 25 ppm for nephrotoxicity and kidney cancer in mice to derive the MAK. The human relevance of the carcinogenic endpoint observed in mice is uncertain. In view of the available human and animal data, the current TWA of 5 ppm is expected to be protective of potential kidney and liver damage and is recommended to be retained in accordance with the evaluation by ACGIH (2018). The STEL of 20 ppm is also recommended to be retained and is expected to be protective of potential acute local irritation based on poorly documented evidence for mucous membrane irritation above 25 ppm in humans.

## 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 not recommended based on the available evidence.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 5 ppm (20 mg/m3); STEL: 20 ppm (79 mg/m3) | |
|  |
| ACGIH 2001 TLV-TWA: 5 ppm (20 mg/m3) |
| TLV-TWA intended to protect for liver necrosis and kidney toxicity as observed in animals and CNS depression at high acute exposures as observed in humans. Not classifiable as a human carcinogen based on equivocal results for limited carcinogenicity in animal bioassays. TLV-STEL of 20 ppm withdrawn in 1998.  Summary of information:  Available carcinogenicity evaluations are conflicting; EPA category II classification is based on chemical similarity to vinyl chloride, positive mutagenicity *in vitro* and positive carcinogenicity in mice in 1 bioassay. Agency notes carcinogenicity in mice only presented once in an unpublished report and contradicted by results of several other animal bioassays. Carcinogenic mechanism of action associated with liver glutathione depletion with subsequent tissue injury and regenerative hyperplasia. Prevention of this liver toxicity would protect for potential carcinogenicity.  Therefore, TLV-TWA based on transient liver cell fatty infiltration observed at 25–75 ppm in rats and supported by industrial experience that suggests average exposure at 5 ppm is not associated with adverse effects.  Human data:   * CNS depression leading to unconsciousness at ≈4,000 ppm (no further details provided) * Pharmacokinetic modelling based on animal data suggest metabolic saturation at 200 ppm * No adverse effects reported in limited cohort study of workers exposed on average at   5–70 ppm with peak of 1,900 ppm (n=138, 21 yr exposure, no further details provided)   * Skin permeability coefficient: 0.016 cm/h.   Animal data:   * Hepatic haemangiosarcomas (mice only) and kidney damage (not specified) at 55 ppm in chronic inhalation study (mice, rats, 6 h/d, 5 d/wk, 7–12 mo):   + tumour incidence in mice:1/35 (female) and 2/35 (male)   + not reproducible at 55 ppm for 1, 3, 6 and 10 mo in follow-up study * Results of several chronic inhalation studies with exposures between 10–150 ppm showed equivocal evidence for tumorigenicity in mice in 1 study, but not other species (mice, rats, hamsters, 4 h/d, 5 d/wk, 1–2 yr):   + increased incidence of kidney adenocarcinomas at 25 ppm (mice) in 1 study   + no increased tumorigenicity in separate study with 3 different strains of mice   + no increase in overall tumours compared to controls, but increase in mammary tumours at 10 ppm (female rats); biological relevance of result uncertain   + no increased tumour incidence at 25 and 75 ppm (rats, 6 h/d, 5 d/wk, 1.5 yr); transient hepatocellular fatty infiltration observed, basis of TLV-TWA * Results of mechanistic study indicate increased tumorigenicity observed in mice was likely due to cytotoxicity rather than genotoxicity; high doses produced cytotoxic metabolites * Mutagenic *in vitro* in bacteria and mammalian cells in the presence of metabolic activation, non-mutagenic *in vivo* at 55 ppm (rats) and 10–50 ppm (mice) in dominant lethal mutation assay (mice, rats, 6 h/d, 5 d/wk, 1–11 wk) * Metabolites bind to liver and kidney biomolecules dose-dependently between 5–200 ppm (mice, rats, 6 h); metabolic saturation reached at 200–300 ppm, 98% of inhaled dose of 10 ppm metabolised in 6 h (rats).   Insufficient data to recommend a TLV-STEL or notations for skin absorption or sensitisation. |
| DFG 1985 MAK: 2 ppm (8 mg/m3) |
| Summary of additional information:  No evidence of adverse effects or carcinogenicity from occupational exposure in available epidemiological data. Limited evidence for carcinogenicity in animals. Previous MAK of 10 ppm based on NOAEC of 30 ppm for reversible liver changes in rats and LOAEC of 25 ppm for chronic liver and kidney damage and carcinogenicity in mice. MAK lowered to 2 ppm in 1985 to account for steep dose-response relationship observed in chronically exposed mice.  Insufficient data to classify as human carcinogen based on equivocal carcinogenicity in animals (Category 3B).  Human data:   * Odour threshold: 50 ppm; irritating to eyes and URT at 25 ppm (no further details provided) * No evidence for liver toxicity reported in 2 workplace studies with average exposure at 5 ppm, co-exposure to vinyl chloride at 300 ppm reported in 1 of these studies (n=49 and 298) * No excess mortality associated with occupational exposure at 50 ppm (10 yr), 10 ppm (10 yr) and <5 ppm (<2 yr) in cohort study of production workers.   Animal data:   * LDLO: 3,700 mg/kg (rabbits) * Non-mutagenic *in vivo* at 10 and 50 ppm (mice, rats, 6 h); dose-dependent kidney necrosis, increased DNA repair in kidneys at 50 ppm; agency concludes kidney tumours observed in chronically exposed mice likely due to non-genotoxic mechanism * Agency concludes carcinogenic potential in animals is weak:   + 18 separate chronic exposure studies with mice, rats and hamsters (including those presented in ACGIH, 2018) reviewed; 1 chronic inhalation study showed evidence for increased tumorigenicity at 25 ppm (mice, 4 h/d, 4 d/wk, 2 yr)   + no signs of toxicity at 10 ppm, increased tumorigenicity and nephrotoxic lesions at 25 ppm, increased mortality at 50 ppm observed in this mouse study; dose-response relationship used as basis for lowering MAK   + no evidence for significant increase in carcinogenicity in remaining chronic exposure studies.   Insufficient data to recommend notations for skin absorption or sensitisation. |
| SCOEL 2008 TWA: 2 ppm (8 mg/m3); STEL: 5 ppm (20 mg/m3) |
| Summary of additional information:  Chronic LOAEC of 25 ppm for transient and reversible fatty infiltration of liver cells in rats used as POD for TWA derivation. This is supported by sub-chronic NOAEC of 25 ppm with corresponding LOAEC of 47.3 ppm for liver and kidney toxicity in several other species. Overall UF of 12.5 applied to account for wide variability in expression of relevant detoxification enzyme in humans to produce TWA of 2 ppm. Excursion factor of 2.5 used to recommend 15-min STEL of 5 ppm, which is close to the sub-chronic NOAEC in animals (no further details provided).  Substance is gaseous at physiological temperature, skin notation therefore not considered relevant in occupational setting.  Human data:   * No significant signs of changes in haematology, clinical chemistry, or mortality in workplace study (n=178) at average exposures of <5–75 ppm; agency considers sample size too small to be conclusive.   Animal data:   * NOAEC: 25 ppm for liver and kidney damage (not specified), LOAEC: 47.3 ppm in sub-chronic inhalation study (rats, guinea pigs, rabbits, dogs, monkeys, 24 h/d, 7 d/wk, 90 d) * Dose-dependent fatty infiltration of liver cells at 25 and 75 ppm in chronic inhalation study (rats, 6 h/d, 5 d/wk, 1.5 yr); effects at 25 ppm slight, severity did not progress between 6–12 mo and reversible within 6 mo after exposure cessation:   + used as POD for TWA derivation * Mutagenic *in vitro* in bacteria with metabolic activation, but not in mammalian cells; non-mutagenic *in vivo.* |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2016 | * Not considered genotoxic based on the available *in vitro* and *in vivo* genotoxicity studies * Limited evidence for carcinogenicity (category 3) * Renal tubule cancer (males only) and reduced survival at 6.25–25 ppm in chronic inhalation study (mice, 6 h/d, 5 d/wk, 2 yr); increased incidence of haemangioma in all organs (females only), liver cell adenoma and alveolar/bronchiolar carcinoma at 12.5 ppm (females) and liver cell carcinoma at 25 ppm (females):   + dose-dependent degeneration of olfactory epithelium in all exposed groups and sexes * Increased incidence of alveolar epithelium hyperplasia, nasal epithelium degeneration, fatty liver degeneration and dose-dependent malignant mesothelioma at 25, 50 and 100 ppm in chronic inhalation study (rats, 6 h/d, 5 d/wk, 2 yr). |
| IARC |  | 2019 | * Moderate evidence for genotoxicity, no data available for human exposures, not genotoxic in small number of *in vivo* studies, but mutagenic *in vitro* in the presence of metabolic activation in mammalian cells and bacteria * Inconsistency between toxic effects and incidence of liver, lung and nose in chronic inhalation studies with mice and rats (also presented in NICNAS 2016):   + liver inflammation observed in males and females (rats), tumour induction only detected in females (mice)   + nasal epithelium degeneration occurred in males and females (rats), tumours only observed in males * Inadequate evidence for carcinogenicity in humans * Sufficient evidence for carcinogenicity in animals * Overall, substance is possibly carcinogenic to humans (Group 2B):   + agency notes a higher classification (Group 2A) is disputed by a minority of its evaluators due to similarity of the substance to vinyl chloride. |
| US EPA |  | 2002 | * Weight of evidence not sufficient to justify deriving an inhalation unit risk for carcinogenicity in humans. |

### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | Insufficient data |
| --- | --- |
| Is the chemical carcinogenic with a mutagenic mechanism of action? | Insufficient data |
| **Insufficient data are available to determine if the chemical is a non-threshold based genotoxic carcinogen.** | |

## Notations

| Source | Notations |
| --- | --- |
| SWA | Carc. 2 |
| HCIS | Carcinogenicity – category 2 |
| NICNAS | Carc. Cat 3 |
| EU Annex | Carcinogenicity – category 2 |
| ECHA | Carc. 2 |
| ACGIH | Carcinogenicity – A4 |
| DFG | Carcinogenicity 3B |
| SCOEL | — |
| 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: | 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%: | no | -2.00 |  | |  |  | -2 | **a skin notation is not warranted** | |

### IDLH

| Is there a suitable IDLH value available? | No |
| --- | --- |

## Additional information

| Molecular weight: | 96.94 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 3.97 mg/m3; 1 mg/m3 = 0.25 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) (1985) Vinylidene chloride – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2008) Recommendation from the Scientific Committee on Occupational Exposure Limits for Vinylidene Chloride. SCOEL/SUM/132.

European Chemicals Agency (ECHA) (2019) Vinylidene chloride – REACH assessment.

International Agency for Research on Cancer (IARC) (2019) Some Chemicals that cause tumours of the urinary tract in rodents, Volume 119. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2016) Ethene, 1,1-dichloro: Human health tier II assessment – IMAP report.

US Environmental Protection Authority (US EPA) (2002) Integrated Risk Information System (IRIS) Chemical Assessment Summary – 1,1-Dichloroethylene (1,1-DCE).