# Vinyl chloride, monomer

| CAS number: | 75-01-4 |
| --- | --- |
| Synonyms: | Chloroethene, Chloroethylene, Monochloroethylene, Vinyl chloride |
| Chemical formula: | C2H3Cl |

Workplace exposure standard (amended)

| TWA: | **7 ppb (18.2 µg/m3)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Carc. 1A** |
| IDLH: | **—** |
| **Sampling and analysis:** There is uncertainty regarding quantification of the recommended value with available sampling and/or analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A TWA of 7 ppb (18.2 µg/m3) is recommended to reduce the risk of cancer in exposed workers.

## Discussion and conclusions

Vinyl chloride is used primarily in the manufacture of polyvinyl chloride (PVC). It has also been employed in organic syntheses and in production of vinyl chloride–vinyl acetate copolymers.

The critical effect of exposure is liver cancer.

Vinyl chloride is considered a human carcinogen based on unequivocal results in epidemiological studies. The most convincing evidence comes from two large, multicentre cohort studies, one in Europe and one in North America. These studies focus on workers in plants that manufactured vinyl chloride monomer, polyvinyl chloride or polyvinyl chloride products. Both studies demonstrate a relationship between occupational exposure and liver cancer with the risk increasing strongly with duration of exposure. In the European study, the incidence of liver cancer is related to cumulative exposure in ppm-years. This evidence has been supported by other studies in humans and animals reported in the primary and secondary sources (ACGIH, 2018; DFG, 2019; IARC, 2012). NICNAS (2014) and DFG (2019) cite cancer as the critical effect. Mutagenicity is reported both *in vitro* and *in vivo*. The mechanism of action for carcinogenicity is likely to act *via* a mutagenic mode of action (ACGIH, 2018; DFG, 2019; IARC, 2012; USEPA, 2000). For the purposes of this assessment, vinyl chloride is assumed to be a non-threshold-based genotoxic carcinogen.

The recommended TWA of 7 ppb (18.2 µg/m3) is derived at a minimal cancer risk level through application of an inhalation risk factor derived from a chronic rat inhalation using a pharmacokinetic model (reducing the uncertainty in extrapolating from animals to humans) (US EPA, 2000).

## Recommendation for notations

Classified as a carcinogen category 1A 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.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 5 ppm (13 mg/m3) | |
|  |
| ACGIH 2001 TLV-TWA: 1 ppm (2.6 mg/m3) |
| TLV-TWA recommended to minimise the potential for liver cancer, particularly angiosarcoma.  Summary of data:   * TLV-TWA based on identification of approximate 6.5 ppm LOEL from a strong epidemiological study and demonstrated effectiveness of a 1 ppm OEL in preventing occurrence of angiosarcoma in exposed workers * No cases of liver angiosarcoma observed in individuals first exposed since 1974 when the vinyl chloride industry began complying with the U.S. OSHA PEL of 1 ppm.   Human data:   * Chronic exposure to lower levels (100–1,000 ppm) associated with a spectrum of symptoms collectively termed "vinyl chloride disease," which includes Raynaud's syndrome and acroosteolysis * Cancer of the liver (particularly angiosarcoma) causally related to occupational exposure and widely recognised as the most sensitive endpoint of toxicity among humans; the toxic effect of greatest concern is liver cancer * This European study contains a detailed account of the relationship between estimated occupational exposures and subsequent angiosarcoma: * a collaborative, multicentre cohort study of exposed workers coordinated by IARC with a total of 12,706 subjects from 19 factories in Sweden, Italy, UK and Norway * only employees ≥1 yr of exposure included in the study * average length of follow-up was 17 yr but ranged from 10–25 yr * systematic and occasional air measurements provided basis for past exposures and indication of variability between job titles * cumulative exposure in ppm-yr calculated; accomplished through multiplying exposure level from job-exposure matrices by duration of employment * observed mortality compared to expected mortality based on national mortality rates specific for age and 5-yr calendar periods * for all workers exposed ≥1 yr, a statistically significant excess in cancer of the liver (SMR, 286; 95% CI, 183–425) and cancer of an unspecified site (SMR, 187; 95% CI, 120–278) observed * 16 cases of liver angiosarcoma among 24 deaths coded as liver cancer * incidence of liver cancer and liver angiosarcoma significantly increased among exposed workers; clearly related to time since first exposure; duration of employment; and estimated ranked and quantitative exposures * multi-variate analysis among exposure groups demonstrated two variables: years since first exposure and cumulative exposure; which had a statistically significant effect on risk of liver cancer mortality * cumulative exposures clearly related to increases in relative liver cancer risk in a dose-related manner; cumulative exposures of <500 ppm-yr, 500–1,999 ppm-yr, 2,000–5,999 ppm-yr, 6,000–9,999 ppm-yr and >10,000 ppm-yr associated with RR of 1, 1.2, 4.6, 12.2 and 17.1 for liver cancer, respectively * 24 incidences of liver angiosarcoma identified; analysis of cases indicated cumulative exposures of <2,000 ppm-yr, 2,000–5,999 ppm-yr, 6,000–9,999 ppm-yr and >10,000 ppm-yr associated with RR of 1, 6.8, 24.7 and 45.4 for liver angiosarcoma, respectively * a cumulative exposure of 288 ppm-yr is equivalent to 6.5 ppm for 45 yr; regarded as the lowest cancer-causing dose of vinyl chloride so far demonstrated * US multicentre study: * 10,743 men who worked in 37 plants that manufactured either vinyl chloride monomer, polyvinyl chloride, both vinyl chloride monomer and polyvinyl chloride, or homo- or copolymers with or without vinyl or polyvinyl chloride * worked for least 1 yr with average duration of exposure of 16 yr * Standard Mortality Ratios were determined for 28 different types or classes of cancer and other non-malignant causes of death * observed numbers for all cancers and cancers of the liver, gall bladder, brain, and lympho- and reticulosarcomas exceeded the expected number * Quantitative risk assessments undertaken by deriving measures of dose in terms of metabolised vinyl chloride (or vinyl chloride DNA adduct formation) and using rat or human incidence data to project dose-response relationships into the low dose range; all estimates based on extrapolation of vinyl chloride angiosarcoma dose-response to low doses using quantitative models result in estimates of risk which by far exceed risk at comparable levels actually observed in human populations.   Animal data:   * A comprehensive series of animal studies summarised in a cited reference: * studies included a variety of doses administered to rats, mice or hamsters via inhalation, ingestion and intraperitoneal or subcutaneous injections using an assortment of dosing schedules * ≈7,000 animals were evaluated in total * in one group of inhalation studies, rats exposed 4 h/d, 5 d/wk for 52 wk at concentrations ranging from 1–30,000 ppm; statistically significant increases in the following tumours observed: mammary gland carcinomas at 5 ppm; liver angiosarcoma in females at 50 ppm and at 200 ppm in males; nephroblastoma in males at 100 ppm and at 250 ppm in females; 1/119 rats in the 10 ppm group and 5/120 rats in the 25 ppm group also had liver angiosarcoma (not statistically significant, a causal relationship to vinyl chloride assumed since angiosarcoma is extremely rare) * concluded the only concentrations not associated with increases of angiosarcoma were 1 and 5 ppm * Significantly increased incidence of liver haemangiosarcomas in rats and mice exposed for 6-12 mo at ≈250 ppm and in male rats exposed 6 h/d, 6 d/wk for 12 mo at 100 ppm and then sacrificed at 18 months.   Genotoxicity   * Mutagenic to *S. typhimurium* in the presence of hepatic mixed function oxidase enzymes * Metabolites, 2-chloroethylene oxide and 2-chloroacetaldehyde, direct-acting mutagens in *S. typhimurium* and in *E. coli* * S9 preparations from human liver specimens active in converting vinyl chloride into mutagens in *S. typhimurium* strains TA1530 or TA100. |
| DFG 2019 Not assigned |
| No MAK assigned due to genotoxicity and carcinogenicity.  Summary of additional data:   * Liver angiosarcoma diagnosed in 2008 in worker exposed between 1957 and 1965; supports findings on the long latency of angiosarcoma following exposure * In an embedded case-control study, 38 lung cancer patients from a cohort of 1,658 vinyl chloride workers were compared to 224 cancer-free controls; a 20% increase in lung cancer risk was identified for each additional year as an exposed worker; dose-response relationship not established * 691 male and 588 female subjects with histologically diagnosed renal cell carcinoma, evaluation of data from questionnaires revealed an increased OR of 2.0 (95% CI:   1.2–3.3) for the subjects exposed   * Refers to multicentre study from Italy, Norway, Sweden and the UK cited by ACGIH (2018) * In a meta-analysis of 8 independent multicentre studies from the USA, Canada, Europe, the former USSR, China and Taiwan, cancer mortality recorded by a total of 43,810 workers from more than 90 vinyl chloride factories; authors conclude workers not only have known increased risk of angiosarcoma of the liver, but also increased risk of hepatocellular carcinoma and soft tissue sarcoma * DFG concludes carcinogenic in humans and mainly induces angiosarcomas of the liver, but is also very likely to cause hepatocellular tumours * Reported to induce liver tumours, breast carcinomas, brain tumours and nephroblastomas as well as tumours in lungs, forestomach and cymbal gland in rats, mice and hamsters after oral administration from 1.3 mg/kg and inhalation exposure from 25 ppm * Mutagenic in bacteria and yeast; metabolic activation is necessary to achieve a mutagenic effect or to achieve a maximum effect; base pair substitutions are common * After inhalation, mutagenic and clastogenic in soma cells. Numerous indicator tests have shown DNA alkylation in rats and mice, DNA damage in mice and the known etheno-DNA adducts in rats. |
| SCOEL NA NA |
| No report. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2014 | * Critical effect is carcinogenicity * Numerous*in vitro* (with and without metabolic activation) and*in vivo* genotoxicity studies on the chemical showing DNA damage (no further information) * OEL of 5 ppm may not provide sufficient protection for workers with long-term repeated exposure * NOAEC in rats, rabbits, guinea pigs or dogs is 50 ppm for 6 mo (no further information) |
| IARC |  | 2012 | * Considered carcinogenic to humans; refers to multicentre cohort studies cited by ACGIH (2018) and DFG (2019) * Induces unscheduled DNA synthesis in mice, rats and hamsters *in vivo* * In rats, DNA adducts found in various organs after exposure by inhalation * Strong evidence that carcinogenicity operates by a genotoxic mechanism involving metabolic activation to reactive metabolites, binding of the metabolites to DNA and pro-mutagenic action of these adducts leading to mutations in proto-oncogenes and tumour-suppressor genes. |
| US EPA |  | 2000 | * Considered human carcinogen based on sufficient data from several independent retrospective and prospective cohort studies demonstrating statistically significant elevated risk of liver cancer, specifically angiosarcomas, from exposure * Concludes carcinogenic in rodents by both oral and inhalation routes and some data indicate it produces tumours when does by subcutaneous methods * Several lines of evidence indicate metabolites are genotoxic, interacting directly with DNA (no further details) * Provides an Inhalation Unit Risk of 4.4x10-6 (risk per µg/m3) for continuous lifetime exposure during adulthood; based on rat inhalation study cited by ACGIH (2018): * rats exposed 4 h/d, 5 d/wk for 52 wk at concentrations ranging from 1–30,000 ppm; mice and hamsters to   50–30,000 ppm for 30 wk, followed by observation period   * statistically significant increase in tumour incidence, including liver angiosarcoma, observed in all three species at 50 ppm * human equivalent concentrations derived using a PBPK model * Although human studies preferable for deriving human cancer risk estimates, exposure data from most epidemiology studies inadequate to derive risk estimates; because vinyl chloride metabolism becomes nonlinear at high exposure concentrations, cumulative exposure (provided in cited epidemiological studies) not sufficient for quantitating risk. |

### Carcinogenicity — non-threshold based genotoxic carcinogens

| Is the chemical mutagenic? | Yes |
| --- | --- |
| Is the chemical carcinogenic with a mutagenic mechanism of action? | Yes |
| **The chemical is a non-threshold based genotoxic carcinogen.** |  |
| Is a cancer slope factor or inhalation unit risk value available? | Yes |
| Inhalation unit risk value (1/(µg/m³)) | 4.4x10-6 |
| Calculated TWA value (µg/m3) | 18.2 (7 ppb) |

## Notations

| Source | Notations |
| --- | --- |
| SWA | Carc. 1A |
| HCIS | Carcinogenicity – category 1A |
| NICNAS | NA |
| EU Annex | NA |
| ECHA | Carc. 1A |
| ACGIH | Carcinogenicity – A1 |
| DFG | NA |
| SCOEL | NA |
| 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

Insufficient evidence to recommend a skin notation.

### IDLH

| Is there a suitable IDLH value available? | No, the chemical is a genotoxic carcinogen |
| --- | --- |

## Additional information

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| --- | --- |
| Molecular weight: | 62.49 |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 2.56 mg/m3; 1 mg/m3 = 0.39 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) (2019) Vinylchlorid – MAK value documentation I n German language

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

International Agency for Research on Cancer (IARC) (2012) Vinyl chloride. IARC Monographs on the evaluation of the carcinogenic risk to humans.

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US Environmental Protection Authority (US EPA) (2000) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Vinyl chloride.