# Ethylene dichloride

| CAS number: | 107-06-2 |
| --- | --- |
| Synonyms: | 1,2-Dichloroethane |
| Chemical formula: | C2H4Cl2 |
| Structural formula: | — |

Workplace exposure standard (amended)

| TWA: | **3.1 µg/m3 (0.7 ppb)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Carc. 1B, Sk.** |
| IDLH: | **—** |
| Sampling and analysis: The recommended value is likely to be below the current limit of detection for standard sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A TWA of 3.1 µg/m3 (0.7 ppb) is recommended to minimise the risk of cancer in exposed workers.

Given the data available from the primary sources regarding the carcinogenicity of ethylene dichloride in humans, it is recommended that a review of additional sources be conducted at the next scheduled review.

## Discussion and conclusions

Ethylene dichloride has been used as a degreaser, fumigant, solvent and as an intermediate in the production of vinyl chloride (ACGIH, 2018).

Ethylene dichloride is carcinogenic in animals through multiple routes of exposure and it is assumed to have carcinogenic potential in humans by some sources. ACGIH (2018) classify its carcinogenicity as non-classifiable to humans and SCOEL (2016) note that human carcinogenicity potential is not well characterised. However, DFG (2013) and NICNAS (2013) cite the critical effects in humans as carcinogenicity and genotoxicity. Mutagenicity is demonstrated in both *in vitro* and *in vivo*. The mechanism of action for carcinogenicity may act *via* a mutagenic mode of action (DFG, 2013; NICNAS, 2014; SCOEL 2016; US EPA, 1987). For the purposes of this assessment, ethylene dichloride is assumed to be a non-threshold-based genotoxic carcinogen.

The recommended TWA is derived at a minimal cancer risk level through application of an inhalation slope factor derived from a chronic oral study that identified a dose-dependent and significant increase in incidence of tumours in dosed animals. The study was considered adequate, with a sufficient number of animals treated for less than lifetime and observed until death (US EPA, 1987).

Noting there are inconsistent data and decisions about the carcinogenicity potential of ethylene dichloride in humans, it is recommended that an investigation of additional data sources is undertaken at the next scheduled review.

## Recommendation for notations

Classified as a category 1B 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 based on evidence suggesting rapid dermal absorption and likely adverse systemic effects in animals.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 10 ppm (40 mg/m3) | |
|  |
| ACGIH 2001 TLV-TWA: 10 ppm (40 mg/m3) |
| Summary of data:  TLV-TWA is recommended to protect against effects on the liver and CNS, symptoms include nausea, vomiting and dizziness. Repeated inhalation exposure at 200 ppm in animals resulted in weight loss and liver damage, but no symptoms observed following exposure at 100 ppm in rats.  Derivation of TLV-TWA is not presented.  Human data:   * 3 fatalities following inhalation exposure * liver and kidney damage reported in all 3 and pulmonary oedema in 1 * Other cases involving occupational exposure reported nausea and vomiting as the most common symptoms * 1 study reported symptoms including nausea, vomiting and dizziness in 1/6 workers exposed between 10–37 ppm and notable blood changes in 8/16 workers * Workers primarily exposed at <16 ppm (with few occurrences between 30–50 ppm) experienced adverse effects on the liver and CNS * 100 workers exposed <25 ppm for 5 yr had no significant blood or internal organ changes observed * some complaints regarding the nervous system noted.   Animal data:   * LD50: 770 mg/kg (rats, oral) * Several animal studies determined ethylene dichloride one of the more toxic chlorinated compounds, with body weight loss, pulmonary congestion, liver changes and increased mortality observed at 200 ppm for 7 h/d, 5 d/wk * no adverse effects noted in rats exposed at 100 ppm * Guinea pigs exposed for 226 d at 100 ppm experienced body weight loss and increased liver weight. * various species affected similarly at 200 ppm * high mortality at 400 ppm * Various species experienced high mortality at 500 ppm for 6 h/d, 5 d/wk for 17 wk * Two animal gavage studies for 78 wk (rats, 47 and 95 mg/kg/d; mice, 97 and 195 mg/kg/d in males and 149 and 299 mg/kg/d in females) reported an increased incidence of benign and malignant tumours at multiple sites. * carcinogenicity data with respect to inhalation exposure is limited, thus, an A4 classification assigned * Mutagenic in *S. typhimurium* and *D. melanogaster*,positive genotoxicity results for the induction of chromosomal aberrations and SCE reported. |
| DFG 2013 Not assigned |
| No MAK assigned because substance is considered a genotoxic carcinogen, for which no tolerable level of exposure can be deduced  Summary of additional data:  Human data:   * Exposure at ≈200 ppmfor 7 h, 1,000 ppm for 1 h and 3,000 ppm for 6 min deemed safe * A study involving 360 female workers in a rubber processing factory (in which workers were exposed to ethylene dichloride, gasoline and dichloromethane) reported adverse effects on pregnancy * cases of early births and miscarriages were increased (6.8% vs 2.6% of control group), with detection of ethylene dichloride in breast milk.   Animal data:   * Inhalation exposure at 3,000 ppm (for 7 h) is lethal in animals * autopsies reported pulmonary oedema, liver and kidney damage, occasional necrosis and bleeding in the adrenal cortex * Inhalation exposure at 400 ppm (up to 3 mo) led to mortality and severe liver damage for various animal species * Repeated exposure at 200 ppm (for 7 h/d) increased mortality in rats and guinea pigs * tolerated by rabbits and monkeys, with no symptoms * Several studies determined that exposure at up to 100 mL/m3 was tolerated by rats and guinea pigs without any symptoms * Small animals exposed at 15 mg/m3 for 4 h/d, 6 d/wk for 4 mo resulted in reduced conception rate and increased preimplantation mortality by a factor of 5 * Occlusive dermal application of 2 mL undiluted or a saturated or 1/3 saturated aqueous solution on the shaved skin of the rat for 24 h, reported rapid percutaneous absorption, with likely conversion in the liver to carcinogenic metabolites * during the exposure period the increase was continuous in blood with higher absorption rates than other solvents with dermal notations * Liver DNA single strand breaks reported in mice; induced by single oral and IP doses and *via* high inhalation concentrations. |
| SCOEL 2016 Not assigned |
| Summary of additional data:  Carcinogenic effect and its mode of action could be better characterised. Assumed to be a genotoxic carcinogen for the derivation of a POD for risk assessment.  Human data:   * Inhalation exposure over 2–5 mo caused CNS depression and GIT symptoms including nausea and vomiting (no concentrations provided) * Several cases of workers experiencing seizures and developing brain oedema following inhalation exposure.   Animal data:   * Chronic inhalation studies identified NOAEC of 50 ppm (200 mg/m3 for up to 8 h in rats); * exposure at 100 ppm (400 mg/m3) for 8 h or 200 ppm (800 mg/m3) for 4 h caused degeneration of the olfactory epithelial * Ability to bind DNA in the liver, kidney and lung in rodents *in vivo;* DNA binding observed after inhalation and oral exposures and IP injection * Formation of DNA adducts demonstrated in catfish * Caused point mutations in human and animal cells and bacteria; unscheduled DNA synthesis in human and animal cells; DNA binding in animal cells. |
| OARS/AIHA NA NA |
| No report. |
| HCOTN NA NA |
| No report. |

### Secondary source reports relied upon

| Source |  | Year | Additional information |
| --- | --- | --- | --- |
| NICNAS |  | 2013 | * Main critical effects to human health are carcinogenicity and mutagenicity * 1 case reported 14/26 workers experienced headaches, concentration and memory problems, dizziness, nausea and irritation of skin and mucous membranes upon exposure through fumigation of freight containers * LD50: 4,270–5,600 mg/kg (rabbits, dermal) * 4 h LC50 in rats estimated at 8,000 mg/m3; 6 h LC50 in mice estimated at 1,080 mg/m3 * 2 animal studies demonstrated increased incidence of tumours (liver, kidney, mammary gland) following inhalation exposure at ≥10 ppm, for >104 wk * human carcinogenicity data remains inconclusive * No evidence of reproductive/developmental effects following exposure in animals. |
| IARC |  | 1999 | * Available human cancer studies inconclusive, difficultly linking mortality or cancer incidence specifically to ethylene dichloride exposure * Significant increase in liver sarcomas in male mice and hepatocellular, bronchiolar-alveolar and mammary gland adenomas in female mice when exposed to whole-body inhalation at 90 ppm for 6 h/d, 5 d/wk, 104 wk. |
| US EPA |  | 1987 | * Classification — B2; probable human carcinogen; based on the induction of several tumour types in rats and mice treated by gavage and lung papillomas in mice after topical application * Oral CSF: 9.1 x 10-2 per mg/kg/d * IUR: 2.6 x 10-5 per µg/m3: * 1x10-6 – 0.04 µg/m3 * 1x10-5 – 0.4 µg/m3 * 1x10-4 – 4.0 µg/m3 * Dose-dependent and significant increase in incidence of haemangiosarcoma in exposed animals. |
| OECD |  | 2002 | * NOAEL (rats, 4 h inhalation): 1,400 mg/m3 * Increased incidence of cancer in exposed animals after oral exposure, but not after inhalation with concentrations up to 150 ppm (600 mg/m3) * Evidence of genotoxicity in bacterial and mammalian *in vitro* test systems. |
| US NIOSH |  | 2014 | * TWA of 1 ppm (4 mg/m3) and STEL of 2 ppm (8 mg/m3) to protect for carcinogenic effects. |

### 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)) | 2.6 x 10-5 |
| Calculated TWA value (µg/m3) | 3.1 |

## Notations

| Source | Notations |
| --- | --- |
| SWA | Carc. 1B |
| HCIS | Carcinogenicity – category 1B |
| NICNAS | Carc. Cat 2 |
| EU Annex | NA |
| ECHA | Carc. 1B |
| ACGIH | Carcinogenicity – A4 |
| DFG | Carcinogenicity – 2, 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 |
| --- |
| |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | | **Conclusion:** |  |  |  |  |  |  | |  |  | 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%: |  |  |  |  | |  |  |  |  | **a skin notation is not warranted** | | | |  |  |  |  |  |  |  | |

### IDLH

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

## Additional information

| Molecular weight: | 98.96 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 4.05 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 |
| --- | --- |
| 1991 | TWA: 10 ppm (40 mg/m3) |

## 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). (2013). 1,2-Dichloroethane – MAK value documentation.

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EU Scientific Committee on Occupational Exposure Limits (SCOEL). (2016). Recommendation from the Scientific Committee on Occupational Exposure Limits for Ethylene dichloride. SCOEL/REC/302.

International Agency for Research on Cancer (IARC). (1999). 1,2-Dichloroethane. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS). (2013). Ethane, 1,2-dichloro: Human health tier II assessment – IMAP report.

Organization for Economic Co-operation and Development (OECD). (2002). SIDS Initial Assessment Profile. SIAM 15, 22-25.

US Environmental Protection Agency (US EPA). (1987). Integrated Risk Information System (IRIS) – 1,2 Dichloroethane; CASRN 107-06-2.

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