# Ethylene chlorohydrin

| CAS number: | 107-07-3 |
| --- | --- |
| Synonyms: | Glycol chlorohydrin, 2-chloroethanol |
| Chemical formula: | C2H5ClO |

Workplace exposure standard (retained)

| TWA: | **—** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **1 ppm (3.3 mg/m3)** |
| Notations: | **Sk.** |
| IDLH: | **7 ppm** |
| **Sampling and analysis:** The recommended value is quantifiable through available sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

A peak limitation of 1 ppm (3.3 mg/m3) is recommended to protect for systemic central nervous system (CNS) effects and liver toxicity in exposed workers.

## Discussion and conclusions

Ethylene chlorohydrin is used as a solvent and in the manufacture of ethylene glycol and ethylene oxide.

Critical effects are primarily adverse CNS, cardiovascular, liver and kidney effects and possibly irritation effects to the eyes, skin and respiratory tract.

Human exposure data are limited to poorly documented accidental acute exposure data (ACGIH, 2018; DFG 2019). Reversible dizziness, nausea, low blood pressure, mild albuminuria and skin erythema are reported in exposed workers at a concentration of approximately 18 ppm (DFG, 2019). Animal exposure data indicate that a steep dose-response relationship exists as demonstrated by liver damage. Increased mortality is observed in rats exposed at 67.5 mg/kg/day in a repeat feeding study with a corresponding NOAEL of 45 mg/kg/day (ACGIH, 2018).

Based on a weight of evidence approach that is aligned with the evaluation of the ACGIH (2018), the current peak limitation of 1 ppm is retained and expected to be protective of systemic CNS effects and severe liver toxicity observed in animals and humans.

A TWA is not recommended due to the severity of reported toxic endpoints at relatively low doses and evidence for cumulative toxicity observed in a repeat dose study with rats, which has not been suitably characterised in humans (ACGIH, 2018).

## Recommendation for notations

Not classified as a 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 of dermal absorption and adverse systemic effects in animals.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 Peak limitation: 1 ppm (3.3 mg/m3) | |
|  |
| ACGIH 2004 TLV-CEILING: 1 ppm (3.3 mg/m3) |
| TLV-Ceiling intended to protect for systemic central nervous, cardiovascular, liver and kidney effects and irritation to the eyes, skin and respiratory tract, nausea and abdominal pain.  Summary of data:  TLV-Ceiling derivation not presented.  Human data:   * Odour threshold: 0.4 ppm * Accidental ingestion of ≈1–20 mL fatal in 2 cases * Fatal at 300 ppm for ≈2 h in 1 case * Several cases of nausea, vomiting, and irritation of eyes, nose, and lungs at ≈300–500 ppm in industrial accident (unspecified duration)   + one fatality at this concentration with severe liver and brain damage reported.   Animal data:   * Oral LD50: 72 mg/kg (rats); ip LD50: 56 mg/kg (rats):   + acute lethality caused by respiratory depression without overt organ pathology   + liver protein and glutathione depletion at single oral dose 10–50 mg/kg (rats) * LD50: 205 mg/kg (guinea pigs, dermal); single dose NOAEL: 81 mg/kg * Lethal at 900–1,000 ppm (rats, 15 min) and at 700–800 ppm (unspecified species, 2–8 h) * Repeat gavage studies with treatment range: ≈30–67.5 mg/kg/d (rats, dogs, monkeys, 90 d) reported:   + NOAEL: 45 mg/kg/d (rats, monkeys); severe vomiting in dogs at this level   + reduced bw gain at 62.5 mg/kg/d (monkeys); some deaths and depressed growth rates at 67.5 mg/kg/d (rats) * Repeat IP injection study (rats, 1 mo) suggests cumulative effect based on NOAEL: 6.4 mg/kg (7 d/wk) versus NOAEL: 12.8 mg/kg (3 d/wk) * Repeat inhalation study with treatment range 0.0033–0.23 ppm (unspecified species and exposure duration, 4 mo) reported:   + NOAEL: 0.0033 ppm   + LOAEL: 0.017 ppm for changes in urine nitrogen levels and slight CNS inhibition (no further information available) * No evidence of carcinogenicity in chronic dermal application studies (rats, mice, 2 yr); treatment groups: 50–100 mg/kg/d (rats), 7.5–15 mg/kg/d (mice) * Dose-related incidence of defective embryos (chickens); no malformations observed in mice administered orally or by inhalation (no further information provided) * Mutagenic potential is equivocal from *in vitro* and *in vivo* studies, but suggests DNA damaging ability; increased chromosomal aberrations in bone marrow at inhalational exposure >0.22 ppm (rats, duration not specified) * No ADME data presented.   Low dermal LD50 values reported in animals warrant a skin notation. Chronic dermal application in animal studies yielded negative results for carcinogenicity. |
| DFG 2018 MAK: 2 ppm (6.7 mg/m3) |
| Summary of additional data:  Previous MAK of 2 ppm retained based on reports of systemic effects in workers exposed to mixture of ethylene chlorohydrin and 1,2-dichloroethane at >18 ppm, and irritation effects reported at 300–500 ppm. Considered protective of systemic effects observed in repeat gavage study in rats with NOAEL of 45 mg/kg/d, representing a worst-case exposure route.  Skin notation is retained due to low dermal LD50 values in animals and reports of dermal toxicity in the workplace.  Negative result in animal skin sensitisation study suggests sensitiser notation is not warranted.  Not classified as a carcinogen based on results of chronic animal studies.  Human data:   * Calculated dermal LD50: <5 mL * Accidental exposure of ¼ of the body surface for 0.5 h caused nausea, vomiting and severe psychotic syndrome followed by unconsciousness, pulmonary oedema and incipient central respiratory paralysis   + histopathological and clinical-chemical liver and kidney damage were detected   + symptoms resolved within 5 d * Accidental industrial exposure to average concentration of 18 ppm of ethylene chlorohydrin and 1,2-dichloroethane (unknown duration) caused nausea, dizziness, low blood pressure, mild narcosis, mild albuminuria, skin erythema   + all effects were reversible * No skin irritation in volunteer patch test at 0.05–1.1% (n=12, 1–8 h)   + 1 volunteer showed mild erythema and oedema at 0.05% * Retrospective cohort study (n=61) of production plant workers showed increased incidence of fatigue and anorexia at average concentration of 1.2 ppm (4 mg/m3)   + effects may have been caused by peak exposures   + study considered inadequate for evaluation due to mixed exposures and small cohort size * Several other case control and cohort studies not considered for evaluation due to mixed exposure confounders.   Animal data:   * LC50: 16–62 ppm (rats, 4 h); 117 ppm (mice, 4 h); 918 ppm (guinea pigs, 4 h) * Irreversible irritation in eyes at 60 mg (rabbits, neat); 8 d observation period * Repeat feeding study with treatment range: 15–22.5 mg/kg (dogs, 15 wk) reported:   + NOAEL: 15 mg/kg; vomiting and dose-dependent haemoglobin fluctuations at ≥22.5 mg/kg/d * Developmental study by repeat gavage, treatment range: 50–100 mg/kg/d (mice, GD 6–16):   + maternal and foetal NOAEL: 50 mg/kg/d   + maternal and foetal LOAEL: 100 mg/kg/d for reduced bw gain (maternal) and reduced liver weights (foetal) * Target organs are liver, kidney and pancreas (rats, mice), and lungs and heart (rats) * 5–50 mg/kg dose excreted 77–80% in urine, 2–4% in faeces, and 1–2% in exhaled CO2 (rats) within 24 h; peak blood concentrations reached after 1–2 h of dosage, half-life ≈4 h * Dermal absorption of ≈25% inferred from LOAEL for mortality in repeat dermal application studies (rats) compared with oral uptake studies assuming ≈100% oral absorption * Substance is rapidly eliminated *in vivo* evidenced by unchanged tumour incidences in carcinogenicity studies in rats and mice * Weakly mutagenic *in vitro* in the presence of metabolic activation, not affirmed in *in vivo* systems (mice). |
| 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 |
| --- | --- | --- | --- |
| HSE |  | 2002 | * 15 min STEL: 1 ppm (3.3 mg/m3). |
| ECHA |  | 2019 | * Decreased bw gain, adverse CNS effects, haematological and urological changes, and increased liver weight reported at 3 ppm in inhalational study with treatment range: 0.3–3 ppm (rats, duration not specified, 5 d/wk, 1 mo); agency considers this study to be inadequately documented. |
| US NIOSH |  | 1994 | * IDLH based on acute inhalation toxicity data in animals. |

### 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 | Skin |
| HCIS | — |
| NICNAS | NA |
| EU Annex | — |
| ECHA | — |
| ACGIH | Carcinogenicity – A4, Skin |
| DFG | H (skin) |
| SCOEL | NA |
| HCOTN | NA |
| IARC | NA |
| 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: | yes | 4.00 |  | | Dermal LD50 ≤1000 mg/kg: | yes | 3.00 |  | | Dermal repeat-dose NOAEL ≤200 mg/kg: | no | -3.00 |  | | Dermal LD50/Inhalation LD50 <10: | no | -3.00 |  | | *In vivo* dermal absorption rate >10%: | yes | 3.00 |  | | Estimated dermal exposure at WES >10%: |  |  |  | |  |  | 0 | **a skin notation is warranted** | |

### IDLH

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

## Additional information

| Molecular weight: | 80.52 |
| --- | --- |
| 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) (2019) 2-Chloroethanol – MAK value documentation, German language edition.

Deutsche Forschungsgemeinschaft (DFG) (1983) 2-Chloroethanol – MAK value documentation, German language edition.

European Chemicals Agency (ECHA) (2019) Ethylene chlorohydrin – REACH assessment.

UK Health and Safety Executive (HSE) (2002) EH40/2005 Workplace exposure limits.

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