# Propylene dichloride

| CAS number: | 78-87-5 |
| --- | --- |
| Synonyms: | 1,2-Dichloropropane |
| Chemical formula: | C3H6Cl2 |

Workplace exposure standard (interim)

| TWA: | **10 ppm (46 mg/m3)** |
| --- | --- |
| STEL: | **—** |
| Peak limitation: | **—** |
| Notations: | **Carc. 1B, Sk.** |
| IDLH: | **400 ppm** |
| **Sampling and analysis:** The recommended value is quantifiable through available sampling and analysis techniques. | |

## Recommendation and basis for workplace exposure standard

An interim TWA of 10 ppm (46 mg/m3) is recommended to protect for irritation and potential liver damage and cancer in exposed workers.

Given the limited data available from the primary sources, it is recommended that a review of additional sources be conducted at the next scheduled review.

## Discussion and conclusions

Propylene dichloride is used as a solvent in dry cleaning, paint removers and petrol production.

Critical effects of exposure are respiratory tract and liver damage, respiratory tract irritation and potential bile duct carcinogenicity.

Several case studies associated with occupational exposure indicated increased risk of bile duct cancers; but are confounded by mixed exposures (NICNAS, 2017; IARC, 2017). Average time-weighted exposures estimated in these workplaces were above 60 ppm (IARC, 2017). Chronic inhalation induces nasal tumours in rats at 500 ppm and bronchoalveolar tumours in mice at 32 ppm (IARC, 2017). Equivocal genotoxicity reported *in vitro* and *in vivo* (ACGIH, 2018; DFG, 1998; IARC, 2017). A NOAEC of 15 ppm for nasal tissue damage and irritation with a corresponding LOAEC of 50 ppm is reported in rats. NOAEC for this endpoint in mice or haematological changes in rabbits are considerably higher at 150 ppm (ACGIH, 2018; US EPA, 1991).

A threshold for carcinogenicity is not determined in the available dataset. However, workplace exposures of 60 ppm and above are associated with increased incidences of biliary cancers.

The TWA of 10 ppm by ACGIH (2014) is recommended to be adopted in the interim. This TWA is expected to be protective of irritation and potential systemic effects and minimise the risk of cancer in exposed workers.

Given the equivocal evidence for genotoxicity in humans (ACGIH, 2014; DFG, 1993), further assessment of additional sources is recommended during subsequent reviews to assess the suitability of the interim TWA.

## 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. There is evidence of positive patch test results and dermal sensitisation in animals in primary sources (ACGIH, 2014; DFG, 1993). However, it is not considered a skin sensitiser by NICNAS (2017) based on negative results in standard LLNA test. Further review of additional data sources is recommended to investigate skin sensitiser notation.

A skin notation is warranted as evidence indicates contact dermatitis in humans and reports of systemic effects in animals.

# Appendix

### Primary sources with reports

| Source Year set Standard |
| --- |
| SWA 1991 TWA: 75 ppm (347 mg/m3); STEL: 110 ppm (508 mg/m3) | |
|  |
| ACGIH 2014 TLV-TWA: 10 ppm (46 mg/m3) |
| TLV-TWA intended to protect for respiratory tract damage and, at higher concentrations, liver damage as observed in animals.  Summary of data:   * TLV-TWA based on lowest NOAEC of 15 ppm for slight nasal tissue damage in rats; ACGIH notes this value is likely to be conservative since these endpoints only observed at 150 ppm in other species. * Not classifiable as a carcinogen in humans based on negative or equivocal evidence for carcinogenicity in chronic oral dose studies with rats and mice. * Skin notation not warranted, dermal sensitiser notation recommended based on animal studies and positive patch test results in humans.   Human data:   * Liver and kidney main target organs from occupational exposures to 60–98% solutions * 10 cases of allergic dermatitis on hands of engineering workers occupationally exposed to 10–40% solutions: * positive patch test results when challenged with ≥2% solution compared to 120 controls * Positive patch test results in 2 workers with dermatitis exposed to aerosols for 4–6 yr: * aerosols contained 7.4–12.7% propylene dichloride.   Animal data:   * LC50: 3,000 ppm (rats, 8 h); 720 ppm (mice, 10 h) * Dermal LD50: 10,141 mg/kg (rabbits), 2,340 mg/kg (rats); oral LD50: 487 mg/kg (rats) * Positive dermal sensitisation in a Magnusson and Kligman maximisation test (guinea pigs) * No histopathological changes in liver at 400 ppm in sub-chronic inhalation study (rats, guinea pigs, dogs, 7 h/d, 5 d/wk, 128–140 d); mortality and hepatomas in mice at this dose * NOAEC: 15 ppm for nasal tissue damage in sub-chronic inhalation study with dose groups 0, 15, 50, and 150 ppm (rats, 6 h/d, 5 d/wk, 13 wk); effects were minimal above 50 ppm:   + no effects observed in mice under same exposure regime (mice, 6 h/d, 5 d/wk, 13 wk); NOAEC: 150 ppm   + no irritational effects in rabbits up to 1,000 ppm, haematological changes at 150 ppm (lowest tested dose) in males (rabbits, 6 h/d, 5 d/wk, 13 wk) * NOAEL: 100 mg/kg/d for histopathological liver damage determined from subchronic gavage studies (mice, rats, 5 d/wk, 13 wk); LOAEL: 250 mg/kg/d:   + agency notes 100 mg/kg/d in rodents equates to an inhalational dose ≈150 ppm in humans assuming 100% absorption, 70 kg body weight, and 10 m3 respiratory volume * Slight increased incidence of mammary gland tumours and reduced body weight and survival at 250 mg/kg/d (females) in chronic oral dose study with dose groups 0, 62/125, and 125/250 mg/kg/d (males/females) (rats, 5 d/wk, 2 yr): * no carcinogenicity in males * evidence for carcinogenicity in females considered equivocal by cited article (NTP) * Hepatocellular adenomas coincident with hepatic necrosis and non-significant incidence of carcinomas in chronic oral dose study with dose groups 0, 125, 250 mg/kg/d (mice, 5 d/wk, 2 yr): * cited article (NTP) concluded limited evidence for carcinogenicity in animals * Mutagenic *in vitro* in bacteria, but not *in vivo* in dominant lethal mutation assays with *Drosophila melanogaster* and rats.   Insufficient data to recommend a TLV-STEL or respiratory sensitiser notation. |
| DFG 1993 Not assigned |
| Summary of additional data:  MAK not assigned due to genotoxic potential and carcinogenic activity observed in animals. Carcinogenicity – group 3b assigned due to evidence for carcinogenic activity in rats and mice.  Human data:   * Equivocal sensitisation data in human patch test studies:   + positive patch-test reactions using 1, 2, 5, 10, and 20% solutions in petrolatum   (n=6–10/dose, 48 h)   * + overall negative results at these concentrations in second patch test (n=120, no details on duration); 2 positive reactions at 20%.   Animal data:   * Increased incidence of hepatic tumours in chronic gavage study at 125 and 250 mg/kg/d (mice, 5 d/wk, 2 yr, also cited in ACGIH, 2018); * study used to support carcinogenicity notation * Evidence for mutagenicity is equivocal based on several *in vitro* studies in bacteria and mammalian cell lines, and *in vivo* in a recessive lethal mutation assay with *Drosophila melanogaster*.   Insufficient data to assign notations for skin absorption or sensitisation. |
| 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 |  | 2017 | * Not considered a skin sensitiser based on negative results in standard LLNA with mice and modelled data that do not predict sensitisation in humans and guinea pigs * Carcinogenic in standardised animal studies and may induce bile duct cancers in humans * Increased incidence of cholangiocarcinoma in Japanese printing workers (also cited in IARC, 2017), also demonstrated in other countries; however, exposure estimates not included * Human carcinogenicity data are limited, no epidemiological studies available to assess the impact of confounders in available workplace data * Not clastogenic based on weight of evidence from *in* *vitro* and *in* *vivo* genotoxicity studies * Equivocal evidence for mutagenicity:   + point mutations *in vitro* in bacteria and *in* *vivo* in comet assay following inhalation at 150–600 ppm (mice, 6 wk, no further details provided)   + no excess micronucleus formation *in vivo* at inhalational dose 150–600 ppm (mice, 6 wk, no further details provided)   + no significant increase in mutation rates of human bile duct tumour cells exposed at cytotoxic concentrations in single and repeat dose experiments (no further exposure details provided). |
| IARC |  | 2017 | * 17 cases of biliary cancer reported in case studies of printing press workers in Japan exposed to solvent mixtures (n=100):   + estimated 8-h average exposure of these workers was 60–210 ppm and 130–160 ppm dichloromethane   + carcinogenic action of dichloromethane cannot be separated from the information available from these studies; however, IARC considers evidence sufficient to classify propylene dichloride as a human carcinogen * Dose-dependent increased incidence of bronchoalveolar (females) and Harderian gland (males) tumours in chronic inhalation study with dose groups 0, 32, 80, and 200 ppm (mice, 6 h/d, 5 d/wk, 104 wk); dose-dependent increase of nasal epithelial lesions in females * Increased incidence of nasal cavity tumours at 500 ppm in chronic inhalation study with dose groups 0, 80, 200, 500 ppm (rats, 6 h/d, 5 d/wk, 104 wk); no tumours detected in other dose groups * Metabolism *via* glutathione, as observed with other chlorinated solvents, plausibly forms genotoxic metabolites, but not direct evidence available * Available *in* *vitro* and *in* *vivo* genotoxicity data are equivocal and limited; no human *in vivo* genotoxicity data are available * Sufficient evidence in humans and animals to classify substance as carcinogenic in humans (Group 1). |
| US EPA |  | 1991 | * Inhalation RfD principally based on 13 wk inhalation experiments with rats, mice, and rabbits (studies also cited in ACGIH, 2018):   + slight epithelial hyperplasia in nasal cavity at 15 ppm (2/9 female rats) regarded as LOAEC for these studies and used to derive inhalation RfD   + concludes that mice and rabbits are 10 and 1,000 times less sensitive to these nasal effects than rats, respectively * Carcinogenic potential not evaluated. |
| US NIOSH |  | 1994 | * IDLH based on inhalation toxicity data in animals. |

### 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 | — |
| HCIS | Carcinogenicity – category 1B |
| NICNAS | Carc. Cat. 1B |
| EU Annex | Carcinogenicity – category 1B |
| ECHA | Carc. 1B |
| ACGIH | Carcinogenicity – A4, DSEN |
| DFG | Carcinogenicity – 3B |
| 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

| Calculation |
| --- |
| |  |  |  |  | | --- | --- | --- | --- | | Adverse effects in human case study: | yes | 4.00 |  | | Dermal LD50 ≤1000 mg/kg: |  |  |  | | 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: | 112.98 |
| --- | --- |
| Conversion factors at 25°C and 101.3 kPa: | 1 ppm = 4.62 mg/m3; 1 mg/m3 = 0.216 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) (1998) 1,2-Dichloropropane – MAK value documentation.

European Chemicals Agency (ECHA) (2019) Propylene dichloride – REACH assessment.

International Agency for Research on Cancer (IARC) (2017) 1,2-Dichloropropane. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2017) Propane, 1,2-dichloro: Human health tier II assessment – IMAP report.

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

US Environmental Protection Authority (US EPA) (1991) Integrated Risk Information System (IRIS) Chemical Assessment Summary – 1,2-Dichloropropane.