

## PROPYLENE OXIDE

**CAS number:** 75-56-9

**Synonyms:** 1,2-Epoxypropane, 2,3-epoxypropane, methyl ethylene oxide, methyloxacyclopropane, methyloxirane, propene oxide, 1,2-propylene oxide

**Chemical formula:** C<sub>3</sub>H<sub>6</sub>O

**Structural formula:** —

### Workplace exposure standard (amended)

**TWA:** 2 ppm (4.8 mg/m<sup>3</sup>)

**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

A TWA of 2 ppm (4.8 mg/m<sup>3</sup>) is recommended to protect for irritation of the respiratory tract, damage of the nasal epithelium and nasal cancer in exposed workers.

### Discussion and conclusions

Propylene oxide is used as an intermediate for polyether polyols, which are used mainly in the manufacture of polyurethanes. It is also used in paint, lacquer and varnish production, in process regulators, synthetic lubricants and fuel additives and in cleaning agents.

Critical effects of exposure are irritation of the upper respiratory tract, mucous membrane and eyes, damage to nasal epithelium and local carcinogenic effects at the site of contact. It is corrosive to the eye as a vapour.

Propylene oxide is a demonstrated nasal carcinogen in rats and mice at concentrations that cause regenerative hyperplasia of the nasal epithelium. Avoiding these proliferative changes in the nasal epithelium is expected to prevent the formation of tumours, indicating that a practical threshold exists (ACGIH, 2018; DFG, 2012; SCOEL, 2010). A NOAEC of 50 ppm for cytotoxic and proliferative changes in nasal mucosa is identified in rats. A different study reports non-neoplastic effects on the nasal mucosa of rats after chronic exposures at 30 ppm (LOAEC) (ACGIH, 2018; DFG, 2012; SCOEL, 2010). A Benchmark Dose Lower Confidence Limit (BMDL<sub>05</sub>) of 11 ppm is calculated in this study (DFG, 2012). No evidence of carcinogenicity in humans is available (ACGIH, 2018; DFG, 2012; SCOEL, 2010).

Based on the assumption that prevention of proliferative changes will reduce the cancer risk and the calculated BMDL<sub>05</sub> of 11 ppm, the TWA of 2 ppm derived by ACGIH (2018) and DFG (2012) is recommended.

## **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. The evidence suggests propylene oxide has skin sensitising potential and a review of this classification is recommended.

A skin notation is recommended based on evidence of systemic effects in humans.

DRAFT

## APPENDIX

### Primary sources with reports

Source	Year set	Standard
<b>SWA</b>	<b>1991</b>	<b>TWA: 20 ppm (48 mg/m<sup>3</sup>)</b>
<b>ACGIH</b>	<b>2014</b>	<b>TLV-TWA: 2 ppm (4.8 mg/m<sup>3</sup>)</b>
<p>TLV-TWA recommended to minimise the potential for skin sensitisation, irritation of the eyes, mucous membranes and skin and increased cell proliferation, thus reducing the cancer risk.</p> <p>Summary of data:</p> <p>TLV-TWA of 2 ppm based on:</p> <ul style="list-style-type: none"> <li>rodent nasal carcinogenicity at concentrations associated with irritation and epithelial regenerative hyperplasia: <ul style="list-style-type: none"> <li>NOAEL of 50 ppm for rats based on cytotoxic and proliferative changes in nasal mucosa which are stages in tumour development</li> </ul> </li> <li>non-neoplastic effects on the nasal mucosa seen in rats after chronic exposures at 30 ppm</li> <li>considered less potent than EtO (TLV-TWA 2018 of 1 ppm; suspected human carcinogen): <ul style="list-style-type: none"> <li>both contain the three-membered oxirane ring reactive towards nucleophilic centres like DNA and proteins</li> </ul> </li> <li>consideration of the preferred values of 1, 2 and 5.</li> <li>no specific derivation presented.</li> </ul> <p>Human data:</p> <ul style="list-style-type: none"> <li>Corneal burns from exposure to vapour and dermatitis from contact with liquid reported</li> <li>Reduced capacity to repair DNA damage associated with TWA 0.6–12 ppm. No further information</li> <li>Case report of hand eczema after 8 mo working with chemical; patch test positive</li> <li>Histopathology laboratory assistant developed dermatitis on both hands after handling</li> <li>Nested case-control study; exposure either ever or never, no concentration: <ul style="list-style-type: none"> <li>Elevated, but not statistically significant, odds ratios for men exposed were found for non-lymphatic leukaemia (OR= 1.3), multiple myeloma (OR= 3.4) and NHL. No information on possible confounders</li> </ul> </li> <li>No biologically significant increases in chromosomal aberrations of peripheral lymphocytes collected from two different groups of workers employed in propylene oxide manufacture: <ul style="list-style-type: none"> <li>ambient TWA &lt;50 mg/m<sup>3</sup>.</li> </ul> </li> </ul> <p>Animal data:</p> <ul style="list-style-type: none"> <li>Rats exposed <i>via</i> inhalation at 0, 30, 100 or 300 ppm for 6 h/d, 5 d/wk for 28 mo: <ul style="list-style-type: none"> <li>significant increase in non-neoplastic degenerative change of the olfactory epithelium at ≥30 ppm</li> <li>LOAEC: 30 ppm, based on extra-thoracic respiratory tract effects</li> <li>increased mortality at 300 ppm by wk 115</li> <li>total number of malignant tumours increased significantly at 300 ppm</li> </ul> </li> <li>Male rats exposed <i>via</i> inhalation at 0, 10, 20, 50, 150 or 525 ppm for up to 4 wk; followed by 4 wk recovery: <ul style="list-style-type: none"> <li>cell proliferation examined end of wk 1, wk 4 and post-exposure weeks 1 and 4</li> <li>non-neoplastic changes absent in animals exposed at ≤50 ppm</li> </ul> </li> </ul>		



Source	Year set	Standard
		<ul style="list-style-type: none"> <li>○ NOAEC: 50 ppm</li> <li>• Mice and rats exposed <i>via</i> inhalation at 0, 200 or 400 ppm for 6 h/d, 5 d/wk for 103 wk: <ul style="list-style-type: none"> <li>○ some evidence of carcinogenicity in rats at 400 ppm, based on increased incidence of papillary adenomas of the nasal turbinates</li> <li>○ clear evidence of carcinogenicity in mice at 400 ppm, based on 10/50 males and 5/50 females developing haemangiomas or haemangiosarcomas of the nasal sub-mucosa</li> <li>○ concomitant suppurative inflammation, regenerative hyperplasia and squamous metaplasia of the rat nasal epithelium and provoked inflammation of these tissues in mice.</li> </ul> </li> </ul> <p>Genotoxicity:</p> <ul style="list-style-type: none"> <li>• Mutagenic in cultured mouse L5178Y lymphoma cells</li> <li>• Base-pair substitution in <i>S. typhimurium</i> strains TA1535 and TA100; <i>E. coli</i> and <i>B. subtilis</i></li> <li>• Depending on the <i>in vitro</i> assay, 5–10 times less potent than EtO</li> <li>• 9 times less potent an alkylating agent <i>in vivo</i> than EtO.</li> </ul> <p>DSEN notation warranted based on skin sensitisation evidence in workers. Insufficient data to recommend a respiratory sensitiser or skin notation or TLV-STEL.</p>
<b>DFG</b>	<b>2012</b>	<b>MAK: 2 ppm (4.8 mg/m<sup>3</sup>)</b>
		<p>MAK recommended to protect for carcinogenic and cytotoxic effects in the nasal epithelium.</p> <p>Summary of additional data:</p> <ul style="list-style-type: none"> <li>• If cell proliferation is avoided in nasal epithelium, formation of tumours not expected</li> <li>• MAK based on following: <ul style="list-style-type: none"> <li>○ NOAEC of 50 ppm in rats (cited by ACGIH, 2018)</li> <li>○ LOAEC of 30 ppm in rats (cited by ACGIH, 2018); BMDL<sub>05</sub> of 11 ppm calculated from this study</li> <li>○ starting with the BMDL<sub>05</sub> of 11 ppm a correction factor of 3 is applied to account respiratory volume difference between rats and humans</li> <li>○ additional factor of 6/8 to account difference in study exposure duration 6 h to workday 8 h</li> <li>○ results in 2.75 ppm; rounded to a TWA of 2 ppm</li> </ul> </li> <li>• NOAEC for toxic effects on prenatal development at 300 ppm for rats and 500 ppm for rabbits; maternally toxic in rats at 500 ppm.</li> </ul>
<b>SCOEL</b>	<b>2010</b>	<b>TWA: 1 ppm (2.41 mg/m<sup>3</sup>)</b>
		<p>Primary effect of concern is local carcinogenicity with the nasal epithelium as demonstrated in rats</p> <p>Summary of additional data:</p> <ul style="list-style-type: none"> <li>• No evidence of carcinogenicity in humans</li> <li>• Methyl homologue of EtO</li> <li>• Primary target of both toxicity and carcinogenicity is at the port of entry; characterised by a practical threshold</li> <li>• Mode of action of rodent nasal carcinogenesis due to contributions of several factors besides genotoxicity including glutathione depletion in nasal respiratory mucosa: <ul style="list-style-type: none"> <li>○ glutathione an important scavenging function in detoxification</li> </ul> </li> <li>• NOAEC of 50 ppm in rats (cited by ACGIH, 2018)</li> <li>• No specific derivation description but TWA of 1 ppm based on following:</li> </ul>



Source	Year set	Standard
		<ul style="list-style-type: none"> <li>minimal local glutathione depletion in the nasal tissue of the rats at 5 ppm</li> <li>SCE not distinguishable in workers at &lt;2 ppm from those of non-exposed controls</li> <li>LOAEC of 30 ppm in rats (cited by ACGIH, 2018).</li> </ul>
<b>OARS/AIHA</b>	<b>NA</b>	<b>NA</b>
No report.		
<b>HCOTN</b>	<b>NA</b>	<b>NA</b>
No report.		

## Secondary source reports relied upon

Source	Year	Additional information
NICNAS	✓ 2013	<ul style="list-style-type: none"> <li>Mutagenic in spot tests in <i>E. coli</i> strains WP2, CM891, CM871.</li> </ul>
IARC	✓ 1994	<ul style="list-style-type: none"> <li>DNA adducts formed in various organs of mice, rats and dogs: <ul style="list-style-type: none"> <li>binding in mouse liver DNA was about 1/20 of EtO</li> </ul> </li> <li>Inadequate evidence in humans for carcinogenicity: <ul style="list-style-type: none"> <li>sufficient evidence in experimental animals</li> </ul> </li> <li>Possibly carcinogenic to humans - Group 2B.</li> </ul>
US EPA	✓ 1990	<ul style="list-style-type: none"> <li>Retrospective cohort study of 602 employees in 8 production plants, with exposure to propylene oxide and EtO and other chemicals, including dichloropropane and epichlorohydrin: <ul style="list-style-type: none"> <li>mortality in each cancer category not significantly higher than expected</li> </ul> </li> <li>Increased incidence of benign and malignant tumours at site of exposure in two species of animals, when exposed by subcutaneous injection, by inhalation and by gavage</li> <li>Probable human carcinogen.</li> </ul>

## Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?

Yes

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. 1B
HCIS	Carcinogenicity – category 1B
NICNAS	Carc. Cat 2
EU Annex	NA



Source	Notations
ECHA	Carc. 1B
ACGIH	Carcinogenicity – A3, DSEN
DFG	Carcinogenicity – 4, Sh (dermal sensitiser)
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:

yes

Dermal LD<sub>50</sub> ≤ 1000 mg/kg:

Dermal repeat-dose NOAEL ≤ 200 mg/kg:

Dermal LD<sub>50</sub>/Inhalation LD<sub>50</sub> < 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:	58.07
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 2.38 mg/m <sup>3</sup> ; 1 mg/m <sup>3</sup> = 0.42 ppm
This chemical is used as a pesticide:	<input type="checkbox"/>
This chemical is a biological product:	<input type="checkbox"/>
This chemical is a by-product of a process:	<input type="checkbox"/>
A biological exposure index has been recommended by these agencies:	<input type="checkbox"/> ACGIH    ✓ DFG    ✓ SCOEL

## Workplace exposure standard history

Year	Standard
<a href="#">Click here to enter year</a>	

## References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7<sup>th</sup> Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the [TLVs® and BEIs® Guidelines section](#) on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (2013) 1,2-Epoxypropane – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2010) Recommendation from the Scientific Committee on Occupational Exposure Limits for propylene oxide. SCOEL/SUM/161.

International Agency for Research on Cancer (IARC) (1994) Propylene oxide. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2013) Methyloxirane (R-, S- and (R,S)-): 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 oxide.

US EPA (1990) - Integrated Risk Information System (IRIS) Propylene oxide; CASRN 75-56-9