PROPYLENE IMINE

CAS number: 75-55-8

Synonyms: 2-Methylaziridine, propylenimine

Chemical formula: C_3H_7N

Structural formula: —

Workplace exposure standard (amended)

TWA: **0.2 ppm (0.5 mg/m^3)**

STEL: **—**

Peak limitation: **—**

Notations: **Sk.**

IDLH: **100 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 0.2 ppm (0.5 mg/m^3) is recommended to protect for upper respiratory tract irritation and kidney damage in exposed workers.

The available data do not warrant a STEL.

Given the limited data about the carcinogenic potential in humans, a review of additional data sources is recommended at the next scheduled review.

Discussion and conclusions

Propylene imine is used as a chemical intermediate in the manufacture of a variety of paper, textile, rubber and pharmaceutical chemicals.

Critical effects of exposure are upper respiratory tract irritation and kidney damage.

No human data are available. Toxic properties are homologous to those of ethyleneimine (EI) with irritation of skin, eye and upper respiratory tract. Nausea is reported as a symptom of acute exposure. Lethality is reported following two-hour exposures and not half hour exposures in guinea pigs at 500 ppm. ACGIH (2018) report acute exposure guideline levels (AEGL-2) for the prevention of disability and impairment of escape capability at 83 ppm for ten minutes and 1.2 ppm for eight hours. These levels are based on a NOAEC in guinea pigs of 500 ppm for 30 minutes. No further data are provided. In a sub-chronic study, rats given intraperitoneal injections of 8 mg/kg/day developed minor kidney damage. ACGIH (2018) reported that the 8 mg/kg/day dose is the equivalent to an eight-hour inhalation exposure of approximately 20 ppm (ACGIH, 2018). Evidence in animals suggests carcinogenicity (ACGIH, 2018; IARC, 1999). HCOTN (1999) and DFG (2012) note it is a genotoxic carcinogen. However, there is a lack of data to confidently confirm this effect in humans by inhalation. Therefore, it is unclear if a non-threshold mechanism for cancer is a critical effect in recommending a TWA.

Given the limited available data and due to its carcinogenic potential in animals, a TWA of 0.2 ppm (0.5 mg/m^3) by ACGIH (2018) is recommended. This concentration is cited as protective of upper respiratory tract irritation and effects in kidneys. As there are uncertainties about the carcinogenic potential in humans, a review of additional data sources is recommended at the next scheduled review.

The available data from acute exposures in animals do not warrant a STEL.

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 of dermal uptake and systemic effects in animals.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 2 ppm (4.7 mg/m^3)***
ACGIH	***2009***	***TLV-TWA: 0.2 ppm (0.5 mg/m^3); TLV-STEL: 0.4 ppm (1 mg/m^3)***

TLV-TWA and TLV-STEL recommended to minimise the potential for upper respiratory tract irritation and kidney damage.

Summary of data:

- TLV-TWA and TLV-STEL based on:
  - similarity in toxicology of homologue EI (TLV-TWA 5 ppm) and 1/4 to 1/8 as potent based on a very limited inhalation study in rats
  - rats dosed *via* IP injections showed minor kidney damage following a dose of 8 mg/kg/d; assuming 100% absorption, this is the equivalent of an 8 h inhalation exposure of ≈20 ppm; no further information.

Human data:

- No human data presented
- Acute toxic properties similar to those of EI:
  - irritation of skin, eye and upper respiratory tract, nausea, vomiting, headache, dizziness and shortness of breath
- Acute exposure guideline levels (AEGL-2):
  - prevention of disability and impairment of escape capability
  - 83 (10 min), 25 (30 min), 12 (1 h), 2.5 (4 h) and 1.2 (8 h) ppm
  - based on NOAEC in guinea pigs of 500 ppm (30 min); no further information.

Animal data:

- $LD_{50:}$ 34 mg/kg (guinea pigs, dermal)
- Rats inhaling 500 ppm for 2 h survived:
  - 5/6 died following 4 h at 500 ppm
  - guinea pigs inhaling 500 ppm for 30 min survived, 3/5 died following 2 h exposure
- Sub-chronic study in rats given single IP injections of 8, 16 or 24 mg/kg; kidney function observations included:
  - at 8 mg/kg/d, a small rise in N-acetyl-beta-D-glucosaminidase (NAG) seen with minor histologic changes and no change in urine volume
  - 16 mg/kg/d produced more significant enzyme changes, peaking at 3 d post-injection and returning to normal by d 12
- 45 tumours in 37/52 rats given oral intubation of 10 mg/kg/d by gavage, 2/wk for 60 wk:
  - authors concluded potent carcinogen in rats, affecting a wide variety of organs; no further information
- Positive genotoxicity in *S. typhimiurium* strain TA100, TA1535 and not TA1538
- Mutagenic activity reported in *E. coli* and *Saccharomyces cerevisiae* D3.

DFG	***2012***	***Not assigned***

No MAK recommended due to carcinogenic potential as evidenced in rats.

Summary of additional data:

Source	Year set	Standard
• 26 male and 26 female rats/dose group; 10 or 20 mg/kg/d by gavage 2/wk for 60 wk: o high dose stopped after 28 wk due to mortality o at both doses breast adenocarcinomas occurred in the females and gliomas in both sexes o male and female rats developed squamous cell carcinoma in the ear canal and granulocytic leukaemia o intestinal tumours in males • Considered a genotoxic carcinogen and categorised in category 2 carcinogen.		
SCOEL	***NA***	***NA***
No report.		
OARS/AIHA	***NA***	***NA***
No report.		
HCOTN	***1999***	***NA***
Considered carcinogenic; estimated additional lifetime cancer risk: • 4 x 10^{-5} for 40 yr of occupational exposure to 0.6 µg/m^3 • 4 x 10^{-3} for 40 yr of occupational exposure to 60 µg/m^3. Summary of additional data: • States EU classification as genotoxic carcinogen; uses information from reviews by ACGIH and IARC; no further information • No epidemiological data • Uses rat gavage study data as cited by DFG (2012); total incidence of rats with a mixture of tumours was 37/52 for 10 mg/kg/d and linear model to estimate additional lifetime risk of cancer • 4 x 10^{-5} for 40 yr of occupational exposure to 0.6 µg/m^3 • 4 x 10^{-3} for 40 yr of occupational exposure to 60 µg/m^3.		

Secondary source reports relied upon

Source		Year	Additional information
NICNAS	✓	2014	• No additional data.
IARC	✓	1999	• Carcinogenic in rats following oral administration, the only species and route tested, producing a variety of malignant tumours: o considered sufficient evidence for the carcinogenicity in experimental animals • Possibly carcinogenic to humans (Group 2 B).
NTP	✓	ND	• Reasonably anticipated to be a human carcinogen based on sufficient evidence of carcinogenicity from studies in experimental animals; cites same study as ACGIH and DFG • No further information.

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	Carc. 1B, Skin
HCIS	Carcinogenicity – category 1B
NICNAS	Carc. Cat 2
EU Annex	NA
ECHA	Carc. 1B
ACGIH	Carcinogenicity – A3, Skin
DFG	Carcinogenicity – 2, H (skin)
SCOEL	NA
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:	
Dermal LD_{50} ≤1000 mg/kg:	yes
Dermal repeat-dose NOAEL ≤200 mg/kg:	
Dermal LD_{50}/Inhalation LD_{50} <10:	
In vivo dermal absorption rate >10%:	
Estimated dermal exposure at WES >10%:	
	consider assigning a skin notation

IDLH

Is there a suitable IDLH value available?	Yes

Additional information

Molecular weight:	57.09
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 2.24 mg/m^3; 1 mg/m^3 = 0.44 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* on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (2006) Propylenimin – MAK value documentation.

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

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2014) Aziridines: Human health tier II assessment – IMAP report.

National Toxicology Program (NTP) (ND) Report on Carcinogens, Fourteenth Edition 2-Methylaziridine CAS No. 75-55-8

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