ETHYLENE OXIDE

CAS number: 75-21-8

Synonyms: Oxirane, EtO

Chemical formula: C_2H_4O

Structural formula:

Workplace exposure standard (amended)

TWA: **0.015 ppb (0.03 µg/m^3)**

STEL: **—**

Peak limitation: **—**

Notations: **Carc. 1B, Sk., DSEN**

IDLH: **—**

Sampling and analysis: *(Below LoD for most analysis methods)*

Recommendation and basis for workplace exposure standard

A TWA of 0.015 ppb (0.03 µg/m^3) is recommended to protect for excess cancers in exposed workers.

Discussion and conclusions

Based on evidence in animals and humans, the carcinogenicity of ethylene oxide is demonstrated to act via a mutagenic mode of action. Therefore, ethylene oxide is considered to be a non-threshold based genotoxic carcinogen (ACGIH, 2001; DFG, 1984; SCOEL, 2012).

The recommended TWA of 0.015 ppb is associated with a minimal cancer risk. The recommended TWA was calculated applying an inhalation slope factor for a total cancer risk based on human data from a large, high-quality, epidemiological study, with exposure estimates for individual workers and assuming an increased early-life susceptibility (US EPA, 2016).

Recommendation for notations

Classified as a category 1B carcinogen according to the Globally Harmonized System of Classification and Labelling on Chemicals (GHS).

Classified as a skin sensitiser but not a respiratory sensitiser according to the GHS.

A skin notation is recommended based on sufficient evidence in humans demonstrating systemic effects following dermal exposure.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	**Year**	***TWA: 1 ppm (1.8 mg/m^3)***
ACGIH	***2001***	***TWA: 1 ppm (1.8 mg/m^3)***
A TWA of 1 ppm is recommended to minimise potential for oncogenic risk and non-neoplastic adverse effects throughout other organs in exposed workers. Summary of data: Human data: • Evidence for human carcinogenicity in two epidemiological studies: leukaemia reported in two industries • Two cases of leukaemia in ≈230 sterilisation plant employees; no exposure concentrations available • Two cases of leukaemia in ≈241 ethylene oxide production plant workers; no exposure concentrations provided. Animal data: • LC_{50}: 835 ppm (female mice, 4 h) • LC_{50}: 960 ppm (male dogs, 4 h) • Positive carcinogenicity in two chronic inhalational studies with rats (both 2 yr in duration) presenting brain tumours and mononuclear cell leukaemia • Demonstrated mutagenic properties in *Salmonella typhimurium, Escherichia coli* an *Neurospora crassa* • Lethal mutagenic outcomes in *Drosophila melanogaster* assays including autosomal deletion mutations in a dose-response relationship. Genotoxic mode of action reported to be alkylating properties of ethylene oxide. Classified a Carc A2: human and animals and reported to be a clastogen in workers. Skin notation assigned based on significant degree of nausea and vomiting in skin exposed workers. Insufficient data available to recommend a sensitisation notation. Insufficient data available to recommend a STEL.		
DFG	***1984***	***NA***
MAK value not established due to carcinogenicity. Summary of additional data: • Carcinogenic in animals • Genotoxicity demonstrated in range of mammalian cell studies • Three cases of leukaemia: 230 persons exposed to an average concentration of 20±10 ml/m^3 with a latency period of >6 and ≤9 yr • H (Skin) notation assigned based on evidence of adverse effects from dermal absorption in various experimental studies and accidental workplace dermal exposure observations.		

Source	Year set	Standard
SCOEL	***2012***	***NA***
No TWA recommended due to carcinogenicity. Summary of additional data: • Provisionally categorised as carcinogenicity-B (genotoxic carcinogen), for which a threshold is not sufficiently supported • Weak alkylating agent with exposures at levels of ≥5 ppm reported to have led to genotoxic damage (cytogenetic signs) in occupationally exposed humans • Skin notation warranted based on systemic toxicity (vomiting and headaches) after local application in human studies • Teratogenicity reported in animals (rats) • As a hapten, ethylene oxide is an active human allergen and case reports describing contact dermatitis caused by reactions to ethylene oxide were noted.		
OARS/AIHA	***NA***	***NA***
No report		
HCOTN	***NA***	***NA***
No report		

Secondary source reports relied upon

Source		Year	Additional information
US EPA	✓	2016	• Characterised as “carcinogenic to humans” by the inhalation route based on the total weight of evidence • Reported clear evidence of genotoxicity and sufficient weight of evidence to support a mutagenic mode of action for carcinogenicity • Inhalation unit risk factor based on human data from a large, high-quality study (excess lymphoid cancer mortality) with exposure estimates for the individual workers and little reported exposure to chemicals other than ethylene oxide.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?	Yes
Is the chemical carcinogenic with a mutagenic mechanism of action?	Insufficient data
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/m^3))	3.0 x 10^{-3}
Calculated TWA value (µg/m^3):	0.03

Notations

Source	Notations
SWA	Carc. 1B, Skin, Sen
HCIS	Carcinogenicity – category 1B, Skin Sensitisation –category 1
EU Annex	NA
ECHA	NA
ACGIH	Carcinogenicity – A2, Skin
DFG	Carcinogenicity – 2, H (Skin),
SCOEL	Carcinogenicity – B, Skin
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

Conclusion:

Adverse effects in human case study:	yes
Dermal LD_{50} ≤1000 mg/kg:	
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%:	

a skin notation is warranted

IDLH

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

Additional information

Molecular weight:	44.05
Conversion factors at 25°C and 101.3 kPa:	1 ppm = Number mg/m^3; 1 mg/m^3 = Number ppm
This chemical is used as a pesticide:	✓
This chemical is a biological product:	☐
This chemical is a by-product of a process:	☐

Molecular weight:	44.05
Conversion factors at 25°C and 101.3 kPa:	1 ppm = Number mg/m^3; 1 mg/m^3 = Number ppm
This chemical is used as a pesticide:	✓
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) (1984) Ethylene oxide – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2012) Recommendation from the Scientific Committee on Occupational Exposure Limits for ethylene oxide. SCOEL/SUM/160.

International Agency for Research on Cancer (IARC) (2008) 1,3-Butadiene, Ethylene Oxide and Vinyl Halides (Vinyl Fluoride, Vinyl Chloride and Vinyl Bromide). IARC Monographs on the evaluation of the carcinogenic risk to humans.

US Environmental Protection Agency (US EPA) (2015) Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide. EPA/635/R-16/350Fc.