

ETHYL ETHER

CAS number: 60-29-7

Synonyms: Diethyl ether, diethyl oxide, ether

Chemical formula: $C_4H_{10}O$

Structural formula: —

Workplace exposure standard (retained)

TWA: 400 ppm (1,210 mg/m³)

STEL: 500 ppm (1,520 mg/m³)

Peak limitation: —

Notations: —

IDLH: 1,900 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 400 ppm (1,210 mg/m³) is recommended to protect for nasal irritation, chronic headaches or cognitive disturbance in exposed workers.

A STEL of 500 ppm (1,520 mg/m³) is recommended to protect for acute nasal irritation and CNS effects in exposed workers.

Discussion and conclusions

Ethyl ether is used as a solvent and formerly as an anaesthetic. Critical effects are nasal irritation, to which a tolerance may be acquired as noted in comparisons of workplace exposure data with acute volunteer exposure studies (ACGIH, 2018; DFG, 1999). Concentrations above 19,000 ppm have anaesthetic effects in humans (ACGIH, 2018). Chronic exposure above 500 ppm causes loss of appetite, headaches, dizziness and cognitive disturbance in workers (ACGIH, 2018).

The current TWA of 400 ppm is retained based on human exposure data indicating that systemically available substance causes no adverse effects at this concentration and reports that workplace concentrations below 500 ppm are not injurious or uncomfortable to acclimated workers (ACGIH, 2018). The current STEL of 500 ppm is also retained based on the absence of irritation at concentrations less than 500 ppm reported in different studies (ACGIH, 2018) and is expected to be protective of dizziness that may be experienced in some individuals above 2,000 ppm (ACGIH, 2018). From the available information, narcosis or anaesthesia are not expected to occur below 10% of the lower explosive limit, which determines the IDLH for ethyl ether (ACGIH, 2018; NIOSH, 1994).

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 not warranted based on the available evidence.

DRAFT

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 400 ppm (1,210 mg/m³); STEL: 500 ppm (1,520 mg/m³)
ACGIH	2001	TLV-TWA: 400 ppm (1,210 mg/m³); TLV-STEL: 500 ppm (1,520 mg/m³)
<p>TLV-TWA intended to protect for eye, nasal and respiratory tract irritation and narcosis that can lead to general anaesthesia. Chronic exposure causes loss of appetite, headache, cognitive disturbance and exhaustion. Insufficient data to recommend notations for carcinogenicity, skin absorption, or sensitisation.</p> <p>Summary of data:</p> <p>TLV-TWA and TLV-STEL derived from weight of evidence from volunteer and workplace data that indicate habituation to initial irritation effects may occur following prolonged exposure.</p> <p>Human data:</p> <ul style="list-style-type: none"> • General anaesthesia at 100,000–150,000 ppm, but may be lethal due to respiratory arrest <ul style="list-style-type: none"> ◦ anaesthesia maintained at 50,000 ppm, lowest anaesthetic limit: 19,000 ppm ◦ abnormal liver function reported in patients given ethyl ether as an anaesthetic • Tolerance/habituation may be acquired over repeated exposure • Albuminuria reported in chronically exposed workers • Repeat skin exposure may cause drying/cracking of skin due to defatting; irritation to eyes and mucous membranes occurs on contact with liquid or saturated vapours • Complaints of nasal irritation at 200 ppm in volunteers; 300 ppm considered objectionable for working conditions (no further information provided) • Exposure at 400 ppm calculated to deliver effective dose of 1.25 g in an individual of average weight and result in a blood concentration that is not associated with signs of intoxication (no further details provided) <ul style="list-style-type: none"> ◦ exposure to 2,000 ppm would deliver 6.25 g and cause dizziness in some individuals (no further information provided) • Cited study reports that concentrations >500 ppm would lead to unsatisfactory exposure • Concentrations of 500–1,000 ppm cause no observable injury to health, but 500 ppm is justifiable to avoid irritation and complaint • No carcinogenicity or genotoxicity data presented. <p>Animal data:</p> <ul style="list-style-type: none"> • None presented. 		

Source	Year set	Standard
DFG	1964	MAK: 400 ppm (1,200 mg/m³)
<p>Summary of additional data:</p> <p>MAK established in 1964 retained based on animal inhalation studies that do not suggest systemic toxicity below 1,000 ppm. Human exposure studies reporting irritation effects, also cited in ACGIH (2018), considered inadequately documented for derivation of a MAK.</p> <p>Human data:</p> <ul style="list-style-type: none"> • Mucosal irritation observed when used as an anaesthetic at 19,000–200,000 ppm <ul style="list-style-type: none"> ◦ anaesthesia can take up to 15 min at 100,000–200,000 ppm • Acute lethal oral dose: 20,000–50,000 mg • Mucosal irritation at 200 ppm in volunteer study (n=10, 3–5 min); 300 ppm intolerable for workplace, 100 ppm considered acceptable <ul style="list-style-type: none"> ◦ not considered for agency's assessment due to insufficient documentation and exposure duration • No evidence for sensitising potential based on weight of evidence of workplace reports of dermal exposures • Inadequately conducted epidemiological studies report slight increase in abortions in women exposed to anaesthetic concentrations in hospitals during pregnancy. <p>Animal data:</p> <ul style="list-style-type: none"> • LD₅₀: >14,200 mg/kg (rabbits, dermal) • LC₅₀: 31,300–65,000 ppm (rats, 1.5 h); 73,000 ppm (rats, 2.5 h) • LD₅₀: 1,215–2,540 mg/kg (rats, oral) • No adverse changes to body weight, haematological parameters, or histopathology at 2,000 ppm in repeat inhalation study (rats, rabbits, guinea pigs, 7 h/d, 5 d/wk, 35 d); <ul style="list-style-type: none"> ◦ relative liver weights were increased in rabbits, but decreased in rats, cited study notes these changes may not have been treatment-related ◦ no signs of irritation in any treated animals • Separate repeat inhalation study at 1,000 ppm and 10,000 ppm (rats, mice, guinea pigs, 22 h/d, 35 d); <ul style="list-style-type: none"> ◦ no adverse effects in rats at both concentrations ◦ slight delay in weight gain in guinea pigs at 1,000 ppm; body weight loss and mortality in 10,000 ppm group, autopsy found enlarged livers without lesions ◦ increased body weight gain in mice and increased liver weight in male mice at 1,000 ppm; mortality at 10,000 ppm and increased liver weights in both sexes ◦ occasional changes in organ weights not considered substance-related effects • Repeat gavage study with exposure groups 500, 2,000 and 3,500 mg/kg/d (rats, 90 d); <ul style="list-style-type: none"> ◦ NOAEL: 500 mg/kg/d ◦ mortality of both sexes, delay in body weight gain in males and increased liver weight in females of 2,000 mg/kg/d group • No irritation to skin as non-occlusive patch; mild irritation when applied as liquid to eyes (rabbits) • Evidence for non-specific teratogenicity at anaesthetic concentrations (5–10% v/v) not considered relevant to workplace exposures; toxic reproductive effects are not expected from metabolites • Non-mutagenic <i>in vitro</i>. 		

Source	Year set	Standard
SCOEL	1991 TWA: 100 ppm (308 mg/m ³); STEL: 200 ppm (616 mg/m ³)	
Summary of additional data:		
<ul style="list-style-type: none">TWA and STEL based on NOAEL of 100 ppm and LOAEL of 200 ppm for irritation effects in volunteer study (n=10, 3–5 min, cited by ACGIH, 2018 and DFG, 1999).TWA expected to be protective of systemic effects noted in 90-d gavage study above NOAEL of 500 mg/kg/d \approx1,000 ppmNo evidence for genotoxicity <i>in vitro</i> or <i>in vivo</i>.		
OARS/AIHA	NA	NA
No report.		
HCOTN	NA	NA
No report.		

Secondary source reports relied upon

Source	Year	Additional information
HSE	✓ 2002	• TWA: 100 ppm (308 mg/m ³); STEL: 200 ppm (616 mg/m ³).
Nordic Council	✓ 1992	• Case of accidental fatal dermal exposure from occlusive patch on scalp as seborrhoeic dermatitis treatment (no further information).
US EPA	✓ 1990	• Repeat gavage study cited in DFG (1999) and SCOEL (1991) used as principal study to derive oral reference dose.
US NIOSH	✓ 1994	• IDLH based on 10% of the lower explosive limit of (1.9%).

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?	No
Is the chemical carcinogenic with a mutagenic mechanism of action?	Insufficient data

The chemical is not a non-threshold based genotoxic carcinogen.

Notations

Source	Notations
SWA	—
HCIS	—
NICNAS	NA
EU Annex	NA
ECHA	—
ACGIH	—
DFG	—

Source	Notations
SCOEL	—
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
<p>Adverse effects in human case study:</p> <p>Dermal LD₅₀ ≤ 1000 mg/kg: no</p> <p>Dermal repeat-dose NOAEL ≤ 200 mg/kg:</p> <p>Dermal LD₅₀/Inhalation LD₅₀ < 10:</p> <p><i>In vivo</i> dermal absorption rate > 10%: no</p> <p>Estimated dermal exposure at WES > 10%:</p>
a skin notation is not warranted

IDLH

Is there a suitable IDLH value available? Yes, based on LEL

Additional information

Molecular weight:	74.12
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 3.03 mg/m ³ ; 1 mg/m ³ = 0.330 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 <input type="checkbox"/> DFG <input type="checkbox"/> 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) (1999) Diethyl ether – MAK value documentation.

European Chemicals Agency (ECHA) (2019) Ethyl ether – REACH assessment.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (1991) Recommendation from the Scientific Committee on Occupational Exposure Limits for Diethyl ether. SCOEL/SUM/15B.

Nordic Expert Group for Criteria Documentation of Health Risks of Chemicals (1992) Ethyl ether. NR 1992:30.

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

US Environmental Protection Authority (US EPA) (1990) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Ethyl ether.

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

DRAFT