ISOPROPYL ETHER

CAS number:	108-20-3
Synonyms:	Diisopropyl ether, 2-isopropoxypropane, isopropyl ether, 2,2´-oxybispropane
Chemical formula:	$C_6H_{14}O$
Structural formula:	—

Workplace exposure standard (interim)

TWA:	**250 ppm (1,040 mg/m^3)**
STEL:	**310 ppm (1,300 mg/m^3)**
Peak limitation:	**—**
Notations:	**—**
IDLH:	**1,400 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 250 ppm (1,040 mg/m^3) is recommended to protect for eye and mucous membrane irritation in exposed workers.

A STEL of 310 ppm (1,300 mg/m^3) is recommended to protect for intoxication and depression in relation to acute exposures in exposed workers.

A review of additional data sources is recommended at the next scheduled review.

Discussion and conclusions

Isopropyl ether is primarily used as a solvent.

Critical effects of exposure are eye and mucous membrane irritation.

Limited human exposure data are available. In humans, exposures at 300 ppm resulted in one in three subjects reporting an unpleasant odour. Exposure at 800 ppm resulted in eye and nose irritation (ACGIH 2018). DFG (2005) derived MAK partially from the NOAEC of 480 ppm in rats for local and systemic effects; the next highest concentration of 3,300 ppm only increased liver and kidney weights. Therefore, given the concentration gap of about 10 fold and minor symptoms between the NOAEC and LOAEC in this study, it is not considered sufficient evidence to lower the TWA.

Given the absence of available long-term exposure data, an interim TWA of 250 ppm is recommended to limit irritant effects based on the recommendation by ACGIH (2018). Evidence of irritation in humans following short-term exposures supports the recommendation of a STEL at 310 ppm. A review of additional data sources is recommended at the next scheduled review to address the absence of chronic toxicological data.

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.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 250 ppm (1,040 mg/m^3); STEL: 310 ppm (1,300 mg/m^3)***
ACGIH	***2001***	***TLV-TWA: 250 ppm (1,040 mg/m^3); TVL-STEL: 310 ppm (1,300 mg/m^3)***

TLV-TWA recommended to minimise the risk of eye and mucous membrane irritation in exposed workers (derivation of TLV-TWA not stated).

Summary of data:

Human data:

- Exposure at 500 ppm for 15 min (inhalation) not considered irritating:
  - 1/3 subjects reported an unpleasant odour at 300 ppm
  - 800 ppm for 5 min resulted in eye and nose irritation
- Odour reported as more irritating than ethyl ether.

Animal data:

- LD_{50}: 4.6–11.4 g/kg (rats, oral)
- Acute oral exposure symptoms include intoxication, respiratory failure caused by depressant action and fatality
- Exposure at 10,000 ppm (monkeys, rabbits, guinea pigs, 1 h, 20 d, inhalation) symptoms included intoxication and depression
- Exposure at 1,000 ppm (monkeys, rabbits, guinea pigs, 3 h, 20 d, inhalation) produce no deleterious effects
- Dermal exposure reported to cause dermatitis.

Insufficient data to recommend a skin, sensitiser or carcinogen notation.

DFG	***2005***	***MAK: 200 ppm (850 mg/m^3)***

Derivation of MAK based on a NOEL of 480 ppm for local and for systemic effects and reports of an unpleasant odour at 300 ppm in humans.

Summary of additional data:

- LC_{50}: 36,000 ppm (mice, 15 min)
- Exposure at 480, 3,300 and 7100 ppm (rats, 6 h/d, 5 d/wk, 90 d, inhalation):
  - no change in body weight, clinico-chemical parameters, number of sperms and spermatids, liver and kidney weights, histopathological effects in any of the group
  - the next highest concentration of 3,300 ppm only increased liver and kidney weights in males
  - NOEL 480 ppm for liver and kidney effects
- NOAEL: >7,060 ppm (rats, 90 d, inhalation) for neurotoxic effects
- NOAEL: 430 ppm (rats, 6 h/d, gestation day 6–15, inhalation) for maternal and developmental toxicity, only one usual finding was reported at 3,095 ppm which could be considered a skeletal variation
- Negative results in mutagenic assays.

Source	Year set	Standard
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
ECHA	✓	2011	• LD_{50}: <2,000 mg/kg (rabbit, dermal) • Negative results in skin sensitiser study.
US NIOSH	✓	1994	• LC_{50}: 28,486 ppm (rabbit).

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? No

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

Notations

Source	Notations
SWA	NA
HCIS	NA
NICNAS	NA
EU Annex	NA
ECHA	NA
ACGIH	NA
DFG	NA
SCOEL	NA
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	
Adverse effects in human case study:	no
Dermal LD_{50} ≤1000 mg/kg:	no
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 not warranted

IDLH

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

Additional information

Molecular weight:	102.18
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:	☐
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) (2005) Diisopropyl ether – MAK value documentation.

European Chemicals Agency (ECHA) (2011) Diisopropyl ether – REACH assessment.

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