

ISOPROPOXYETHANOL

CAS number: 109-59-1

Synonyms: Ethylene glycol monoisopropyl ether, IPE, isopropyl cellosolve, isopropyl glycol

Chemical formula: $C_5H_{12}O_2$

Structural formula: —

Workplace exposure standard (amended)

TWA: 10 ppm (43 mg/m³)

STEL: —

Peak limitation: —

Notations: Sk.

IDLH: —

Sampling and analysis: The recommended value is quantifiable through available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 10 ppm (43 mg/m³) is recommended to protect for adverse haemolytic (blood cell) effects in exposed workers.

Discussion and conclusions

Isopropoxyethanol is used as a solvent for latex paints, resin coatings, and textile dyes.

Critical effects of exposure are haemolytic disorders including erythrocyte osmotic fragility, haemoglobinuria and anaemia as observed in animals. No substance-specific human exposure data are available. A NOAEL of 30 ppm for haemolytic endpoints is presented in rats with a corresponding LOAEL of 100 ppm (DFG, 2018). Rats are more susceptible to these endpoints than humans (ACGIH, 2018; DFG, 2018, ECHA, 2019).

The TWA of 10 ppm is based on the NOAEL of 30 ppm in rats reported from a sub chronic inhalation study (DFG, 2018). This NOAEL has been halved to account for translation between animals and humans and rounded down as presented by DFG (2018). This approach is considered appropriate noting that rats are more sensitive than humans to haemolytic endpoints.

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 recommended based on *in vitro* studies with human skin that indicate an appreciable amount of the substance may be absorbed relative to the inhalational burden if the TWA is observed. This is supported by a relatively low acute dermal LD₅₀ in rabbits (DFG, 2018).

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 25 ppm (106 mg/m³)
ACGIH	2001	TLV-TWA: 25 ppm (106 mg/m³)
TLV-TWA intended to minimise potential for blood disorders including erythrocyte osmotic fragility, haemoglobinuria and anaemia. Summary of data: TLV-TWA derivation not presented, but expected to be protective of haemolytic effects in exposed workers based on available studies with rats. Human data: - Less susceptible than rats to haemolytic action of glycol ethers (no further information provided). Animal data: - Metabolised to the corresponding carboxylic acid (no further information provided) - No adverse effects noted at 32 ppm in acute inhalation study (rats, 4 h); significant erythrocyte osmotic fragility at 62 ppm, 2-butoxyethanol showed the same toxicity - Haemoglobinuria, anaemia and pulmonary congestion at 1,000 ppm in repeat inhalation study (rats, 6 h, 15 exposures) - effects transient at 300 ppm - NOAEL: 100 ppm - No overt signs of toxicity at 200, 50, or 25 ppm in subchronic inhalation study (4 species including dogs, 6 h/d, 26 wk); changes to haematological parameters, including erythrocyte osmotic fragility, dose dependent in some species but minimal at 25 ppm (no further details provided). Insufficient data to recommend a TLV-STEL or notations for carcinogenicity and sensitisation. A skin notation is recommended by analogy to 2-butoxyethanol, for which adverse systemic effects are reported following dermal application in rabbits.		
DFG	2018	MAK: 10 ppm (43 mg/m³)
Irritation of the respiratory tract is assumed based on positive eye irritation in rabbits. Haemolytic critical effect in rats considered less relevant to human exposures. MAK based on a NOAEL of 30 ppm and corresponding LOAEL of 100 ppm for slight haemolytic effects from a sub chronic inhalation study of rats. The NOAEL is halved to account for translation from experimental conditions to the workplace and rounded down to arrive at the recommended value of 10 ppm. The value is expected to be protective of potential irritant effects based on the structurally related 2-butoxyethanol (MAK of 10 ppm based on a LOAEL of 31 ppm for nasal irritation in a 2 yr inhalation study in rats). A skin notation is recommended based on <i>in vitro</i> skin penetration calculations that indicate dermal exposure contributes significantly to total exposure if the MAK is observed. Human data: <i>In vitro</i> dermal flux through human skin (undiluted): 240 µg/cm²/h. Animal data:		

Source	Year set	Standard
- LD₅₀: 1,445 mg/kg (rabbits, dermal) - Nose irritation observed in 3 wk inhalation study (rats) (also cited in ACGIH, 2018) - Reversible iritis and corneal damage when applied undiluted to eye (rabbit); 7 d recovery - Non-sensitising in poorly documented maximisation test; no positive reactions (n=20) to challenge of 1% solution (no further details provided) - Haemopoietic changes and haemolytic anaemia at 142 ppm in subchronic inhalation study (rats, 6 h/d, 5 d/wk, 28 d); no NOAEL determined: - follow-up study with lower concentration range 10–100 ppm determined NOAEL: 30 ppm and LOAEL: 100 ppm for slight haemolytic effects - Pulmonary congestion at 300 ppm in repeat inhalation study (rats, 6 h/d, 5 d/wk, 3 wk, as cited by ACGIH, 2018); nasal irritation noted at 1,000 ppm - NOAEL: 600 ppm (highest tested dose) for foetal toxicity (rats, 6 h/d, GD 6–15) - NOAEL: 125 mg/kg/d for fertility in standardised reproductive gavage study (rats, duration not specified) - Non-mutagenic <i>in vitro</i>, no <i>in vivo</i> studies available. Insufficient data to recommend notations for carcinogenicity or sensitisation.		
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
NICNAS	✓ 2013	- Grouped with isopropoxyethyl acetate due to limited data for corresponding alcohol; acetate is expected to be rapidly metabolised to alcohol and justifies grouping rationale - Moderate acute toxicity from dermal exposure 2 carcinogenicity 2 yr inhalation studies (rats, mice) with 2-butoxyethanol reported significant increase in the incidence of liver sarcomas in male mice, forestomach tumours observed in female mice: - several international reviews of this data consider these results irrelevant to humans 2-butoxyethanol therefore not considered a human carcinogen - due to expected similar mode of action of isopropoxyethanol, 2-butoxyethanol is considered a suitable analogue for carcinogenicity endpoint - Substances in group are not considered genotoxic; supported by negative results for isopropoxyethanol <i>in vitro</i> in bacteria.



Source	Year	Additional information
ECHA	✓ 2019	• NOAEL: 100 ppm for reduced maternal bw and uterine weight, and haematological changes in 2 developmental studies with 2-butoxyethanol (rats, rabbits, GD 6–15 for rats or 6–18 for rabbits) • NOAELs of 100ppm for developmental toxicity used as starting point for long-term DNEL • Derivation accounts for haemolytic effects observed in rats, less pronounced in humans; overall factor of 6 applied to arrive at DNEL of 17 ppm • Short-term DNEL of 42 ppm calculated by extrapolation of long-term DNEL.
OECD	✓ 2009	• Major occupational exposure routes are inhalation and dermal • Non-mutagenic <i>in vitro</i> in bacteria and Chinese hamster ovarian cells without metabolic activation; these negative results <i>in vitro</i> preclude necessity for <i>in vivo</i> testing: ○ substance therefore considered non-genotoxic <i>in vitro</i>.

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	—
HCIS	—
NICNAS	—
EU Annex	—
ECHA	—
ACGIH	Skin
DFG	H (skin)
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:
Dermal LD₅₀ ≤ 1000 mg/kg: no
Dermal repeat-dose NOAEL ≤ 200 mg/kg:
Dermal LD₅₀/Inhalation LD₅₀ < 10:
In vivo dermal absorption rate > 10%:
Estimated dermal exposure at WES > 10%: yes

insufficient data to assign a skin notation

IDLH

Is there a suitable IDLH value available? No

Additional information

Molecular weight:	104.15
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 4.25 mg/m ³ ; 1 mg/m ³ = 0.235 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
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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) (2018) Isopropoxyethanol – MAK value documentation.

European Chemicals Agency (ECHA) (2019) Isopropoxyethanol – REACH assessment.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2013) 2-(1-methylethoxy) ethanol and its acetate: Human health tier II assessment – IMAP report.

Organisation for Economic Cooperation and Development (OECD) (2009) SIDS initial assessment profile – 2-(1-methylethoxy) ethanol.

Tenth Adaptation to Technical Progress Commission Regulation (EU Annex) No 2017/776 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008

of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the CLP Regulation).

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