

ISOBUTYL ALCOHOL

CAS number: 78-83-1

Synonyms: Isobutanol, isopropyl carbinol, 2-methyl-1-propanol

Chemical formula: C₄H₁₀O

Structural formula: —

Workplace exposure standard (retained)

TWA: 50 ppm (152 mg/m³)

STEL: —

Peak limitation: —

Notations: —

IDLH: 1,600 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 50 ppm (152 mg/m³) is recommended to protect for local irritant effects and potential adverse central nervous system (CNS) effects in exposed workers.

Discussion and conclusions

Isobutyl alcohol is used as a solvent and flavouring agent.

Critical effects from exposure are local irritation and central nervous system depression at higher concentrations (ACGIH, 2018; DFG, 2003).

Human exposure data for the substance and the structurally related n-butyl alcohol isomer indicate the threshold for eye irritation is above 100 ppm (ACGIH, 2018; DFG, 2003). No eye irritation was caused by repeated eight-hour exposure at 100 ppm (ACGIH, 2018). The compound has low systemic toxicity with a NOAEC of 1,000 and 2,500 ppm reported for haematological changes and neurotoxicity, respectively, in a thirteen-week inhalation study of rats (DFG, 2003; OECD, 2004). ACGIH (2018) assign a TLV-TWA of 50 ppm to minimise eye and skin irritation based on human data. DFG (2003) derived the recommended MAK value based on analogy to 1-butyl alcohol.

Insufficient evidence for carcinogenicity based on two carcinogenicity studies in rats exposed by gavage and subcutaneous injections in rats (ACGIH, 2018; DFG, 2003).

Based on the weight of available evidence, the current TWA of 50 ppm is retained and expected to be protective of local irritant effects and potential CNS depression observed in rats at higher concentrations (ACGIH, 2018; DFG, 2003).

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.

There are insufficient data to recommend a skin notation.

DRAFT

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	1991	TWA: 50 ppm (152 mg/m³)
ACGIH	2001	TLV-TWA: 50 ppm (152 mg/m³)
<p>TLV-TWA intended to minimise potential for irritation of eyes and skin. Evidence for tumorigenicity in rats receiving repeat gavage or subcutaneous injections; administration routes not considered relevant to workplace conditions and carcinogenicity notation therefore currently withheld. Insufficient data to recommend a STEL or notations for skin absorption or sensitisation.</p> <p>Summary of data:</p> <p>No reports of dizziness, auditory impairment, or other vestibular disorders exist. TLV-TWA is expected to be sufficiently protective of potential eye and skin irritation that may occur above 100 ppm or on skin contact, respectively (no further explanation on derivation of TLV-TWA).</p> <p>Human data:</p> <ul style="list-style-type: none"> Slight erythema and hyperaemia when applied to skin (no further details provided) 100 ppm over 8 h in repeat exposure study did not cause eye irritation (no further details provided). <p>Animal data:</p> <ul style="list-style-type: none"> Lethal at 8,000 ppm (rats, 4 h); slightly more toxic than 1-butyl alcohol, which is not lethal at this concentration LD₅₀: 3,750 mg/kg (rabbits) Moderate to severe eye irritation when applied directly, no permanent corneal damage reported (rabbits) Single oral dose (not specified) was lethal after several days (not specified) in rats; liver degeneration observed No significant effects at 2,125 ppm in 2 separate repeat inhalation studies (mice, 9.25 h/exposure, total 223 h); no mortality when repeatedly narcotised at 6,400 ppm over 136 h total exposure Higher incidence of malignant tumours e.g. forestomach, liver carcinomas and leukaemia at 150 mg/kg (gavage) or 0.05 mL/kg (subcutaneous injection) in lifetime carcinogenicity studies (rats, n=19-24, 2 times/wk, lifetime) Positive mutagenicity <i>in vitro</i> in bacteria without metabolic activation No ADME data presented. 		
DFG	1969	MAK: 100 ppm (310 mg/m³)
<p>Summary of additional data:</p> <p>Original MAK based on ACGIH (1969) recommendation and provisionally retained to protect for local irritation and potential CNS depression. MAK is supported by analogy to 1-butyl alcohol, which is expected to act similarly and is more extensively reviewed. Transient CNS depression above 250 ppm in a repeat inhalation study with rats is only considered in the assignment of the peak limitation category. Skin notation not warranted due to low effective dose delivery from skin absorption. Very small number of positive sensitisation results in humans do not warrant a sensitiser notation. Insufficient data to recommend a carcinogenicity notation.</p> <p>Human data:</p>		

Source	Year set	Standard
<ul style="list-style-type: none"> Penetration rate through human skin calculated as $1.78 \text{ mg/cm}^2 \approx 0.2 \text{ mg/cm}^2/\text{h}$ for saturated aqueous solution Plasma half-life: 1.45 h when co-administered with ethyl alcohol in volunteer study (n=6) Poorly documented studies indicate critical effects are like those of 1-butyl alcohol, e.g. adverse corneal effects (concentration and duration not specified) Potential cross-reactions in sensitisation studies with individuals allergic to ethyl alcohol <ul style="list-style-type: none"> limited positive skin sensitisation results do not warrant sensitiser notation <p>Animal data:</p> <ul style="list-style-type: none"> Absorbed substance is distributed evenly in body and likely oxidised metabolically to the corresponding carboxylic acid <ul style="list-style-type: none"> irritational effects caused by receptor interactions at sensory nerve endings; CNS effects caused by neuronal membrane disruptions LC₅₀: 5,100–8,660 ppm (rats, mice, rabbits, guinea pigs, duration not specified) <ul style="list-style-type: none"> respiratory tract irritation at 5,000 ppm (rats, guinea pigs, 4 h) central nervous effects, reduced lymphocytes in bone marrow, and hepatocyte changes observed 3 d after exposure to 5,000–8,000 ppm reduced bone marrow lymphocytes observed at 430 ppm changed respiration rate at 32 ppm Median respiratory depression (RD₅₀): 1,818 ppm (mice, 5 min) LD₅₀: 2,500–4,200 mg/kg (rabbit, dermal) No effects on offspring at 3,300 ppm (rats, rabbits, 6 h/d, last 9–12 d of gestation) Reversible CNS impairment in sub-chronic inhalation studies with exposure groups 250–3,000 ppm (rats, 6 h/d, 5 d/wk, 2 wk or 90 d); <ul style="list-style-type: none"> reduced sensitivity to external stimuli at 750 ppm; laboured breathing at higher concentrations; no changes in behavioural assessment post-exposure similar findings in 90-d exposure study; only observed effect was higher erythrocyte count in females exposed to 2,500 ppm, not considered toxicologically relevant agency concludes that, except for reversible non-specific CNS depression >250 ppm, no exposure-related effects were observed in either study NOAEL of 1,450 mg/kg in repeat feeding study (rats, drinking water, 90 d) Non-mutagenic <i>in vitro</i> in presence or absence of metabolic activation in bacteria; positive <i>in vitro</i> result cited in ACGIH (2018) occurred only at cytotoxic concentrations (0.7%) Carcinogenicity studies presented in ACGIH (2018) not considered for evaluation due to exposure near maximally tolerated dose, and insufficient documentation and analysis. 		
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
HSE	✓ 2002	8 h TWA: 50 ppm (154mg/m ³); 15 min STEL: 75 ppm (231 mg/m ³)
NICNAS	✓ 2013	<ul style="list-style-type: none"> • Critical health effects are local irritation effects and intoxication at higher concentrations • Not expected to be genotoxic.
US EPA	✓ 1987	<ul style="list-style-type: none"> • Carcinogenicity assessment incomplete • Animal toxicity studies indicate butyl alcohol may produce liver/ kidney effects and decreased red blood cell numbers • Ataxia and hypoactivity observed in repeat oral dose study at 1,000 mg/kg/d (rats, 13 wk); <ul style="list-style-type: none"> ○ NOAEL: 316 mg/kg/d.
ECHA	✓ 2019	<ul style="list-style-type: none"> • No carcinogenicity data available • Not considered systemically toxic below local irritation threshold of 100 ppm <ul style="list-style-type: none"> ○ Derived no-effect-level (DNEL) of 100 ppm adopted from DFG MAK values for isobutyl alcohol (DFG, 2003) and by analogy to 1-butyl alcohol (DFG, 2000).
OECD	✓ 2004	<ul style="list-style-type: none"> • Not considered genotoxic <i>in vitro</i> or <i>in vivo</i> • 90 d inhalation study, also presented in DFG (2003), reported NOAEL: 1,000 ppm for haematological changes, and NOAEL: 2,500 ppm for neurotoxicity • No parental systemic, reproductive effects, or neonatal toxicity at 2,500 ppm in 2-generation reproductive toxicity study (mice).
US NIOSH	✓ 1994	<ul style="list-style-type: none"> • IDLH based on acute inhalation toxicity data in animals.

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	—
DFG	—
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 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? Yes

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 checked="" 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
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[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) (2003) Isobutyl alcohol – MAK value documentation.

Deutsche Forschungsgemeinschaft (DFG) (2000) n-Butyl alcohol – MAK value documentation.

European Chemicals Agency (ECHA) (2019) 2-methylpropan-1-ol – REACH assessment.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2013) 1-Propanol, 2-methyl: Human health tier II assessment – IMAP report.

Organisation for Economic Cooperation and Development (OECD) (2004) SIDS initial assessment profile – Isobutanol.

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).

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

US Environmental Protection Authority (US EPA) (1987) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Isobutyl alcohol.

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