Compound	2-Methyl-1-propanol	*Data collection sheet*
N°CAS 78-83-1 1 ppm (in air, 23°C) = 3.05 mg/m^3	**CLP:** STOT SE 3, Skin Irrit. 2, Eye Dam. 1	

Organisation name	**DFG**	**Reach registrants**
Risk value name	MAK	DNEL
Risk value (mg/m^3)	305	55
Risk value (ppm)	100	18.03
Reference period	chronic (worker)	chronic (general population)
Year	1999	2016 (last modification)
Key study	Relevant data on effects in man caused by isobutyl alcohol were not available and it was assumed that the local irritation and central nervous depression is similar to that caused by exposure to n-butyl alcohol, a structurally closely related compound. Therefore, the MAK value for isobutyl alcohol (100 ppm) was provisionally adopted. (Sterner JH, Crouch HC, Brockmyre HF et al. (1949): A ten-year study of butyl alcohol exposure. Am Ind Hyg Assoc J 10: 53-59).	DNEL was derived by industry: Presumably, as basis the German MAK value of 100 ppm was used. An overall assessment factor of 5.6 was applied to POD according to ECHA.
Study type	health surveillance	
Species	human	
Duration of exposure in key study	observation at workplaces for about 10 years	
Critical effect	skin and eye irritation	skin and eye irritation
Critical dose value	NOAEC > 100 ppm	long-term inhalation DNEL for general population (local effects) derived by industry
Adjusted critical dose	chronic	chronic
Single assessment factors (see table R.8.6)	not indicated	not indicated, an overall assessment factor of 5.6 was applied
Other effects		

Most occupational limit values (8 hrs average) as compiled by GESTIS are 50 ppm (Austria, Belgium, Canada, Denmark, France, Ireland, Japan, New Zealand, Singapore, South Korea, Spain, Sweden, Switzerland, USA (NIOSH), UK); 100 ppm (Germany (AGS, DFG) and USA (OSHA)).

Lowest (absolute) odour threshold is from Nagata (2003) (Isobutanol 0.001 ppm, 34 µg/m^3 (23°C)), most other published absolute odour thresholds are in the range of 2600–5000 µg/m^3. Above the odour recognition threshold, the substance has an odour described as sweet, wine-like, penetrating, musty, disagreeable, and suffocating.

Compound	**2-methyl-1-propanol (isobutanol)**		***Fact Sheet***
Parameter	**Note**	**Comments**	**Value / descriptor**
EU-LCI value and status			
EU-LCI value	1	Mass/volume [µg/m^3]	11 000
EU-LCI status	2	Draft/final	Final
EU-LCI year of issue	3	Year when the EU-LCI value was issued	2016
General information			
CLP Index No	4	INDEX	603-108-00-1
EC No	5	EINECS – ELINCS - NLP	201-148-0
CAS No	6	Chemical Abstracts Service number	78-83-1
Harmonised CLP classification	7	Human health risk-related classification	STOT SE 3, Skin Irrit. 2, Eye Dam. 1
Molar mass and conversion factor	8	[g/mol] and [ppm – mg/m^3]	74.12 1 ppm = 3.05 mg/m^3
Key Data / database			
Key study, author(s), year	9	Critical study with lowest relevant effect level	Branch et al. (1996)
Read-across compound	10	Where applicable	
Species	11	Rat etc. / human	Rodent Male and female Sprague-Dawley rats
Route/type of study	12	Inhalation, oral feed, etc.	Inhalation
Study length	13	Days, subchronic, chronic	Subchronic 13 weeks
Exposure duration	14	Hours/day, days/week	6 h/day, 5 days/week
Critical endpoint	15	Effect(s), site of	Slight (but statistically significant) increase in red blood cell counts, haematocrit, and haemoglobin parameters in female rats
Point of departure (POD)	16	LOAEC*L, NOAEC*L, NOEC*L, benchmark dose, etc.	NOAEC
POD value	17	[mg/m^3] or [ppm] or [mg/kg$_{BW}$×d]	1 000 ppm
Assessment factors (AF)	**18**		
Adjustment for exposure duration	19	Study exposure hours/day, days/week	5.6
Study Length	20	sa→ sc→ c *(R8-5)*	2
Route-to-route extrapolation factor	21		1
Dose-response	22 a	Reliability of dose-response, LOAEL → NOAEL	1
	22 b	Severity of effect *(R 8-6d)*	1
Interspecies differences	23 a	Allometric Metabolic rate *(R8-3)*	1
	23 b	Kinetic + dynamic	2.5
Intraspecies differences	24	Kinetic + dynamic Worker - general population	10
AF (sensitive population)	25	Children or other sensitive groups	1
Other adjustment factors	26	Completeness and consistency	1

Quality of whole database		Reliability of alternative data *(R8-6 d,e)*	
Result			
Summary of assessment factors	27	Total Assessment Factor (TAF)	280
POD/TAF	28	Calculated value (µg/m³ and ppb)	…. 10,893 µg/m³ …. 3,570 ppb
Molar adjustment factor	29	Used in read-across	
Rounded value	30	[µg/m³]	11 000
Additional comments	31		
Rationale section	32		

Data compilation and evaluation for 2-methyl-1-propanol is based on a project funded by the German Environment Agency (Wibbertmann et al., 2017).

2-Methylpropan-1-ol (isobutanol) is a colourless and flammable liquid with high solubility in water. It is mainly used as a solvent, as a starting material for the synthesis of plasticisers and esters and as an additive in detergents. During indoor measurements, concentrations of 2-methylpropan-1-ol were reported with <2 µg/m³ (median) and with maximum concentrations of up to 120 µg/m³.

Relevant data for 2-Methylpropan-1-ol concerning health effects in humans are missing.

Isobutanol was tested in a 13-week inhalation study with male and female Sprague-Dawley rats (Branch et al., 1996), where the animals were exposed on 6 hours/day and 5 days/week to concentrations of 0, 250, 1 000 or 2 500 ppm. Besides standard parameters for subchronic studies, expanded neurotoxicity endpoints were included in this study. The highest exposure concentration of 2 500 ppm caused no adverse effects on the central or peripheral nervous system, although a slight reduction in responsiveness to external stimuli occurred in all treated groups during exposure. There was no difference from the control animals with regard to responsiveness during non-exposure periods, therefore the slight decrease in responsiveness was attributed to transient effects from acute exposure to isobutanol. In female rats exposed to 2 500 ppm, an increase (9 %) in red blood cell parameters (count, haematocrit and haemoglobin) was noted; however, due to the slight nature of these findings their biological significance is questionable. There were no changes in any other parameters. From this study a NOAEC of 1 000 ppm is derived for systemic toxicity.

In another subchronic study with rats, Li et al. (1999) found no effects at any concentration tested (neurotoxicity, histopathology, blood chemistry). In this study, Sprague-Dawley rats were exposed to isobutanol vapour concentrations of 0, 250, 1 000, and 2 500 ppm for 6 hours/day, 5 days/week, for 3 months.

Isobutanol was also tested in studies with oral application. From a 90-day study (Tompkins, 1987) with male and female CD rats dosed once daily with 0, 100, 316 or 1 000 mg/kg bw via gavage, a NOAEL of 316 mg/kg bw/day was derived. In another 90-day-study with male and female Wistar rats (Schilling et al., 1997) dosed continuously with 0, 1 000, 4 000 or 16 000 ppm via drinking water (calculated daily intake: ca. 0, 80, 340 or 1 450 mg/kg bw), no adverse effects caused by the treatment were reported, i.e. the NOAEL was about 1 450 mg/kg bw/day. Route-to-route extrapolation to inhalation according to ECHA guidance for these two studies leads NOAELs of 5.53 mg/m³ and 25.36 mg/m³, respectively.

Point of departure

The LCI derivation is based on the 13-week inhalation study with male and female Sprague-Dawley rats (Branch et al., 1996).

Assessment factors

For the calculation of the LCI the default assessment factors were used, i.e. 5.6 for an adjustment for exposure duration, 2 for study length, 2.5 for interspecies differences and 10 for intraspecies differences. The TAF is 5.6×2×2.5×10=280.

The EU-LCI is POD/TAF=1 000ppm/280=3.5714ppm=10 893 µg/m³ (at 23 °C). After rounding, the EU-LCI is 11 000 µg/m³ (3 600 ppb). The EU-LCI value is above the reported absolute odour threshold of 11 ppb (Nagata, 2003).

References

Branch et al. (1996) Three Month Neurotoxicity Study of Isobutanol administered by Whole-Body Inhalation to CDC Rats. Lab. Proj. No. EHL 94075, MSL 14525. Monsanto Company for the Oxo-Process Panel, Chemical Manufacturers Association. Cited in: OECD (2005) OECD SIDS Isobutanol (CAS 78-83-1) http://www.inchem.org/documents/sids/sids/78831.pdf

Li et al. (1999) Neurotoxicity evaluation of rats after subchronic inhalation exposure to isobutanol. Neurotoxicology, 20, 889-900

Nagata Y. (2003): Measurement of odour threshold by triangle odour bag method. Odour Measurement Rev 118–127.

Schilling et al. (1997) Subchronic toxicity studies of 3-methyl-1-butanol and 2-methyl-1-propanol in rats. Hum Exp Toxicol, 16, 722-726

Tompkins (1987) Rat oral subchronic toxicity study. Final report. Compound: Isobutyl alcohol: TRL Study #032-002. Prepared for Research Triangle Institute under EPA Contract No. 68-01-7075. Muskegon, MI: Toxicity Research Laboratories, Ltd. Access possible via: https://ntrl.ntis.gov/NTRL/dashboard/searchResults.xhtml#

Wibbertmann A., Wahnschaffe U. and Wiedemeier P. (2017): Toxikologische Basisdaten und Textentwürfe für die Ableitung eines EU-LCI Wertes für 2,2,4-Trimethyl-1,3-pentandiol monoisobutyrat, 2,2,4-Trimethylpentandiol diisobutyrat, 2-Methyl-1-propanol, 2-Phenoxyethanol, Isopropylbenzol, UBA Texte 32/2017, https://www.umweltbundesamt.de/publikationen/toxikologische-basisdaten-textentwuerfe-fuer-die