Compound	2,2,4-Trimethylpentanediol diisobutyrate	*Data collection sheet*
N°CAS 6846-50-0 **1 ppm (in air, 23°C) = 11.78 mg/m³**	**EU- Classification:** - **CLP:** -	

Organisation name	**REACH Registrants**	**MPI Research**
Risk value name	DNEL	-
Risk value (mg/m³)	4.35	-
Risk value (ppm)	0.37	-
Reference period	Chronic (consumer)	Subchronic
Year	2019 (last modification)	2005
Key study	DNEL was derived by industry, no further information available	A Thirteen-Week Dietary Toxicity Study of TXIB Plasticizer in Rats. Study No.: 777-005
Study type		Oral via diet
Species		Male and female Sprague-Dawley rats
Duration of exposure in key study		Continuously via diet
Critical effect	Developmental toxicity / teratogenicity	α2u-globulin nephropathy, increased liver weights
Critical dose value	NOAEL = 300 mg/kg bw/day	NOAEL = 150 mg/kg bw/day
Adjusted critical dose	NOAEC = 130.43 mg/m^3	
Single assessment factors	UFH 5, UFA 3, overall assessment factor of 30	
Other effects		

UFL Used LOAEL; UFH Intraspecies variability; UFA interspecies variability; UFS Used subchronic study; UFD data deficiencies

Compound	**2,2,4-Trimethylpentanediol diisobutyrate**		***Factsheet***
Parameter	**Note**	**Comments**	**Value / descriptor**
EU-LCI value and status			
EU-LCI value	1	Mass/volume [µg/m^3]	1300
EU-LCI status	2	Draft/final	Final
EU-LCI year of issue	3	Year when the EU-LCI value has been issued	2016
General information			
CLP-INDEX-No.	4	INDEX	Not listed
EC-No.	5	EINECS – ELINCS - NLP	229-934-9
CAS-No.	6	Chemical Abstracts Service number	6846-50-0
Harmonised CLP classification	7	Human health risk related classification	
Molar mass and conversion factor	8	[g/mol] and [ppm – mg/m^3]	286.41 1 ppm = 11.78 mg/m^3
Key data / database			
Key study, author(s), year	9	Critical study with lowest relevant effect level	MPI Research, 2005
Read across compound	10	Where applicable	
Species	11	Rat, human, etc.	Male and female Sprague-Dawley rats
Route/type of study	12	Inhalation, oral feed, etc.	Oral via diet
Study length	13	Days, subchronic, chronic	Subchronic 13 weeks
Exposure duration	14	Hrs/day, days/week	Continuously via diet
Critical endpoint	15	Effect(s), site of	increased liver weights
Point of departure (POD)	16	LOAEC*L, NOAEC*L, NOEC*L, benchmark dose, etc.	NOAEL
POD value	17	[mg/m^3] or [ppm] or [mg/kg$_{BW}$×d]	150 mg/kg bw/day, corr. POD: 130.43 mg/m^3
Assessment factors (AF)	18		
Adjustment for exposure duration	19	Study exposure hrs/day, days/week	1
Study length	20	sa→ sc→ c *(R8-5)*	2
Route-to-route extrapolation factor	21	Oral → Inhalation	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 Quality of whole database	26	Completeness and consistency Reliability of alternative data *(R8-6 d,e)*	2

Result			
Summary of assessment factors	27	Total assessment factor (TAF)	100
POD/TAF	28	Calculated value (µg/m³ and ppb)	1304.30 µg/m³ and 104 ppb
Molar adjustment factor	29	Used in read-across	
Rounded value	30	[µg/m³]	1300
Additional comments	31		
Rationale section	32		

Data compilation and evaluation for 2,2,4-trimethyl-1,3-pentanediol diisobutyrate is based on a project funded by the German Environment Agency (Wibbertmann et al., 2017).

2,2,4-Trimethyl-1,3-pentanediol diisobutyrate (TMPD-DIB) is a colourless liquid with a faint odour, which is mainly used as a plasticizer in the production of plastic, vinyl products and as binders in latex paints. During indoor measurements, concentrations of TMPD-DIB were reported with < 4 µg/m³ (median) and with maximum concentrations of up to 15 µg/m³.

Toxicokinetic data are only available after oral administration to rats. TMPD-DIB was well absorbed and the majority of the administered dose (up to about 70%) was excreted within 10 days via urine, mostly within 72 hours. An accumulation in the body is not to be expected and apart from unchanged TMPD-DIB, 2,2,4-trimethyl-1,3-pentanediol and its monohydrate 2,2,4-trimethyl-3-hydroxy-pentanoic acid as well as the corresponding glucuronide and sulphate conjugates were identified as metabolites.

In animal studies, TMPD-DIB was not skin irritating and only slightly eye irritating. In studies with human volunteers and experimental animals, TMPD-DIB did not show skin sensitising properties.

Studies on inhalation exposure with TMPD-DIB are not available. In two oral studies male and female Sprague-Dawley rats were dosed with 0, 30, 150 or 750 mg/kg bw/day via their diet for 13 weeks (MPI Research, 2005) or via gavage over 40 – 53 days (Hagita et al., 1993). The liver and kidneys were the target organs. The treatment caused no clinical signs of intoxication, but did lead to increased liver and/or kidney weights in high-dosed rats. The histopathological examination of male rats showed α2u-globulin nephropathy; this specific finding in male rats is not relevant for human risk assessment. The increased liver weights are an adaptive high-dose effect (enzyme induction), as the corresponding liver enzymes were in a physiological range. In studies concerning reproductive and developmental toxicity, adverse effects were noted at dose levels of 160 mg/kg bw/day (Yamano et al., 2005). For the endpoint carcinogenicity, no data are available. Concerning mutagenic or genotoxic effects, TMPD-DIB was tested negative in the Ames test and in several *in vitro* studies with mammalian cell lines (CHO and CHL cells).

The 13-week oral study from MPI Research, 2005 was chosen as the key study.

POD

The EU-LCI derivation is based on an oral NOAEL value of 150 mg/kg bw/day (MPI Research, 2005). Differences in respiratory volumes were considered: the respiratory volume of the rat in 24 hours corresponds to 1.15 m³/kg bw, correction factor 1 ÷ 1.15 = 0.87. The corrected POD is 130.43 mg/m³.

Assessment factors

To calculate the EU-LCI value, the default assessment factors were used, i.e. 2 for study length, 2.5 for interspecies differences, 10 for intraspecies differences. An assessment factor of 2 for the quality of the whole database (lack of inhalation studies and data for the carcinogenicity endpoint) was applied.

The total assessment factor is 2 x 2.5 x 10 x 2 = 100. This leads to a rounded EU-LCI value of 1300 µg/m³.

References

Hagita K et al. (1993) Combined repeat dose and reproductive/developmental toxicity screening test of 2,2,4-trimethyl-1,3-pentanediol diisobutyrate by oral administration in rats. Biosafety Research Center, Foods, Drugs, Pesticides. Shizuoka, Japan. Cited in: Eastman (2007) Toxicity Summary for Eastman(R) TXIB Formulation Additive.

MPI Research (2005) A Thirteen-Week Dietary Toxicity Study of TXIB Plasticizer in Rats. Study No.: 777-005. Cited in: Eastman (2007) Toxicity Summary for Eastman(R) TXIB Formulation Additive.

Yamano T, Shimizu M and Noda T, (2005): Teratological Study of 2,2,4-Trimethyl-1,3-Pentanediol Diisobutyrate in Rats. Seikatsu Eisei, 49, 30 - 34.

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 (last retrieved on 3.12.2019).