Compound	**Tripropylene glycol mono-methylether**	***Data collection sheet***
N°CAS 25498-49-1[a] **N°CAS 20324-33-8[b]**	**EU-Classification:** **CLP: no harmonised classification**	

Organisation name	**CARB**	**REACH registrants**
Risk value name	8-hour REL	DNEL
Risk value (µg/m³)	0.1 (0.012 ppm)	19
Reference period	acute (8 h)	Chronic (DNEL $_{\text{Gen. Pop. long term}}$)
Risk value (mg/m³) / Short term (15 min)		19
Year	2010	2017
Key study	Miller R, Lomax LG, Calhoun L, Kociba R (1985) Tripropylene Glycol Monomethyl Ether: 2-Week aerosol inhalation toxicity study in rats and mice. Confidential report of the Dow Chemical Company, November 12, 1985. Unpublished report. Cited in OECD SIDS (2003) and ECHA (2017)	Not indicated, probably subacute inhalation study with rats and mice
Study type	Subacute exposure study, 2 weeks	Probably subacute exposure study, 2 weeks
Species	Mouse	Not indicated
Duration of exposure in key study	6 h/d, 5 d/Week, 9 d	Probably 6 h/d, 5 d/week, 9 exposures
Critical effect	Eosinophilia in the liver	Not indicated
Critical dose value	NOAEC 360 mg/m³	NOAEC 133 mg/m³
Adjusted critical dose	193 mg/m³ (360 X 6/8 X 5/7), RGDR*: 1 → Human Concentration Adjustment: 193 mg/m³	
Single assessment factors (see table R.8.6)	UF_L 1 x UF_H 10 x √10 x UF_A 2 x √10 x UF_S 10 x UF_D 1 = 2000	UF_H 5 x UF_A 1 x UF_S 1.4 = 7
Other effects		
Remarks	Derived for [2-(2-methoxy-methylethoxy)-methylethoxy]-propanol (CAS 25498-49-1)	DNEL derivation not presented in detail

UF_L Used LOAEL; UF_H Intraspecies variability; UF_A interspecies variability; UF_S Used subchronic study UF_D data deficiencies

*RGDR: Regional gas dose ratio for gases with systemic effects.
a: for [2-(2-methoxymethylethoxy)methylethoxy]propanol; b: for 1-[2-(2-methoxy-1-methylethoxy)-1-methylethoxy]propan-2-ol

Compound	**Tripropylene glycol mono-methyl ether (TPGME)**		**Factsheet**
Parameter	**Note**	**Comments**	**Value / descriptor**
EU-LCI value and status			
EU-LCI value	1	Mass/volume [µg/m^3]	1200
EU-LCI status	2	Draft/final	Final
EU-LCI year of issue	3	Year when the EU-LCI value was issued	2018
General information			
CLP Index No	4	INDEX	-
EC No	5	EINECS – ELINCS - NLP	247-045-4 and 243-734-9
CAS No	6	Chemical Abstracts Service number	25498-49-1 and 20324-33-8
Harmonised CLP classification	7	Human health risk-related classification	none
Molar mass and conversion factor	8	[g/mol] and [ppm – mg/m^3]	206.32 1 ppm = 8.5 mg/m^3
Key data / database			
Key study, author(s), year	9	Critical study with lowest relevant effect level	Miller et al., (1985)
Read-across compound	10	Where applicable	
Species	11	Rat, human, etc.	Rat, Sprague-Dawley, mouse, B6C3F1 (5 M + 5 F/group)
Route/type of study	12	Inhalation, oral feed, etc.	Inhalation
Study length	13	Days, subchronic, chronic	subacute
Exposure duration	14	Hours/day, days/week	6 h/d, 5 d/week, 2 weeks (9 exposures)
Critical endpoint	15	Effect(s), site of	No adverse effect up to highest test concentration
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]	1010 mg/m^3 (120 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)*	6
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)	840
POD/TAF	28	Calculated value (µg/m³ and ppb)	1200 µg/m³ and 141 ppb
Molar adjustment factor	29	Used in read-across	
Rounded value	30	[µg/m³]	1200
Additional comments	31		
Rationale section	32		

Data compilation and evaluation for tripropylene glycol mono-methyl ether (TPGME) is based on a project funded by the German Environment Agency (Voss, 2018).

Rationale for critical effects

No relevant human data are available for the derivation of an EU-LCI for TPGME.
No adverse effects were observed in a subacute inhalation study with TPGME in rats and mice (5 M + 5 F/concentration, exposed to 0, 150, 360 or 1010 mg/m³ (at least partially as aerosol) for 6 hours/day, 5 days/week for a total of 9 days) after exposure of up to 1010 mg/m³ (Miller et al., 1985). Slight alterations in the liver of male mice were considered to be an adaptive response and not adverse.

There is no evidence for genotoxic effects of TPGME from limited *in vitro* data or from read-across with other propylene glycol ethers. Propylene glycol methyl ether (1-Methoxypropan-2-ol) was not carcinogenic in an inhalation study with rats and mice. Depending on the structure of the isomer, propylene glycol ethers may cause developmental toxicity and teratogenicity, mediated by the metabolic formation of 2-methoxypropionic acid.

In a prenatal developmental toxicity study (equivalent or similar to OECD Test Guideline 414) with inhalation exposure of pregnant Sprague-Dawley rats on GD 6-15 to an aerosol of TPGME (CAS No 25498-49-1 or 20324-33-8), no evidence of developmental toxicity or systemic toxicity to dams was observed up to the highest concentration of 1000 mg/m³. However, a high incidence (15/25) of muzzle staining in dams at the highest concentration indicated a local irritation effect (Breckenridge et al., 1985).

No developmental toxicity study is available with TPGME with a second species, especially with rabbits, which are known to be more sensitive than rats to developmental and teratogenic effects of teratogenic isomers of glycol ethers. However, a prenatal developmental toxicity study with dipropylene glycol methyl ether (DPGME, CAS No 34590-94-8) with rabbits revealed no such effects up to the highest tested concentration of 1850 mg/m³ (300 ppm), which is even higher than the highest tested concentration of TPGME in rats (ECHA dissemination, 2018).

Rationale for starting point

The NOAEC of 1010 mg/m³ (120 ppm) from a subacute inhalation toxicity study with rats and mice (Miller et al., 1985) served as a POD for the derivation of an EU-LCI value. The only effects observed in this study were considered adaptive and not adverse. The study has not been published, but was described in sufficient detail in OECD SIDS (2003) and in the REACH registration dossier (ECHA dissemination, 2018).

Rationale for assessment factors

- Factor for adjustment for exposure duration: 5.6
- Adjusted study length factor: 6 (subacute exposure)
- Interspecies differences: 2.5 (interspecies factor for systemic effects)
- Intraspecies differences: 10 (default value).

The total assessment factor is 840, leading to a value of 1010000 µg/m³: 840 = 1200 µg/m³.

A very similar value of 1250 µg/m³ may be derived from the NOAEC of 300 mg/m³ (75 mg/m³ for continuous exposure) for slight local irritation in pregnant rats observed in a prenatal developmental toxicity study, taking into account an extrapolation of 6 for study length (subacute to chronic), 1 for interspecies differences (local irritating effect) and 10 for intraspecies extrapolation. This study has not been published, but was described in sufficient detail in the OECD SIDS (2003) and in the REACH registration dossier (ECHA dissemination, 2018).

The following EU-LCI value is proposed for TPGME: 1200 µg/m³.
No odour thresholds are available for TPGME. However, TPGME is described as nearly odourless.

References

Breckenridge C, Collins C, Robinson K, et al. (1985) A teratological study of inhaled Dowanol TPM in the albino rat. Bio-Research Laboratories Ltd. Confidential report of the Dow Chemical Company, August 2, 1985. Cited in OECD-SIDS (2003) and ECHA dissemination (2018).

ECHA dissemination (2018) [2-(2-methoxymethylethoxy)methylethoxy]propanol (Tripropylene glycol monomethyl ether, TPGME). In: European Chemicals Agency (ECHA), Annankatu 18, P.O. Box 400, FI-00121 Helsinki, Finland. https://echa.europa.eu/registration-dossier/-/registered-dossier/13199 (last retrieved on 4.12.2019).

Miller R, Lomax LG, Calhoun L, Kociba R (1985) Tripropylene Glycol Monomethyl Ether: 2-Week aerosol inhalation toxicity study in rats and mice. Confidential report of the Dow Chemical Company, November 12, 1985. Unpublished report. Cited in OECD SIDS (2003) and ECHA dissemination (2018).

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Voss, J.-U. (2018) Toxicological basic data for the derivation of EU-LCI values for 5 substances from building products. UBA Texte 91/2018. https://www.umweltbundesamt.de/publikationen/toxicological-basic-data-for-the-derivation-of-eu-0 (last retrieved on 4.12.2019).