Compound	Propylene glycol mono methyl ether acetate (PGMEA)	Data collection sheet		
N° CAS 108-65-6 1 ppm = 5.4 mg/m ³ (23 °C)	EU-Classification: - CLP, harmonised classification: none with respect to toxicity			
• • • •				
Organisation name	AgBB	Reach Registrants		
Risk value name	NIK ('Lowest Concentration of Interest')	DNEL		
Risk value (mg/m ³)	2.7 mg/m^3	33 mg/m^3		
Reference period	Chronic (general population)	Chronic (general population)		
Year	2015	2019		
Key study		Study report from 1981 reported as key study for repeated dose inhalation		
Study type		Inhalation study with 0, 300, 1000, 2000 ppm PGMEA, "whole body"		
Species		B6C3F1 mice (n=5 M + 5 F/concentration)		
Duration of exposure in key study		6 h/d, 4-5 d/week, 2 weeks (9 exposures)		
Critical effect		Irritation		
Critical dose value		LOAEC: 300 ppm		
Adjusted critical dose		6/24 x 5/7		
Single assessment factors		Overall factor: see below		
Other effects				
Remarks	The EU-LCI value of 2700 μg/m ³ for PGMEA was adopted. The EU- LCI value for DPGME is an "ascribed EU-LCI-value".	The dose descriptor used was the worker-DNEL-long term for the inhalation route (50 ppm, 275 mg/m ³) derived by SCOEL. This was corrected for the differences in duration of exposure between worker and consumer (24 h/d, 7 d/week vs. 8 h/d, 5 d/week) and the intraspecies differences (worker/general population: 2). This DNEL based on local effects is also considered to be sufficiently protective for systemic effects.		
AgBB = Ausschuss zur gesundheitlichen Bewertung von Bauprodukten UFL Used LOAEL; UFH Intraspecies variability; UFA interspecies variability; UFs Used subchronic study				

UF_D data deficiencies.

Compound	Propylene glycol mono methyl ether acetate (PGMEA, 2-methoxy-1- methylethyl acetate) C6H12O3		Factsheet
Parameter	Note	Comments	Value / descriptor
EU-LCI value and status			
EU-LCI value	1	[µg/m ³]	650
EU-LCI status	2	Draft/Final	Final
EU-LCI year of issue	3	Year when EU-LCI value has been issued	2019
General information			
CLP-Index No.	4	INDEX	203-603-9
EC-No.	5	EINECS	607-195-00-7
CAS-No.	6	Chemical Abstract Service number	108-65-6
Harmonised CLP classification	7	Human health risk related classification	-
Molar mass and conversion factor	8	[g/mol] and [ppm – mg/m ³]	132.16 1 ppm = 5.4 mg/m ³
Key data / database			
Key study, authors, year	9	Critical study with lowest relevant effect level	Miller et al., 1984
Read across compound	10	Where applicable	
Species	11	Rat, human, etc.	B6C3F1 mice
Route / type of study	12	Inhalation, oral feed, etc.	Inhalation
Study length	13	Days, subchronic, chronic, etc.	2 weeks
Exposure duration	14	h/d, d/w	6 h/d, 5 d/week, 2 weeks (11 exposures)
Critical endpoint	15	Effect (s), site of	Lesions of nasal olfactory epithelium
Point of departure (POD)	16	LOAEC, NOAEC, BMD, etc.	LOAEC
POD value	17	[mg/m ³] or ppm or [mg/kg _{BW} ×d]	1632 mg/m ³ (300 ppm)
Assessment factors (AF)	18		
Adjustment for exposure duration	19	Study exposure h/d, d/w	5.6
Study length	20	sa→sc→c	6
Route-to-route extrapolation factor	21	-	1
Dose-response	22a	Reliability of dose-response, LOAEL to NOAEL	3
	22b	Severity of effect (R8 6d)	1
Interspecies differences	23a	Allometric Metabolic rate (R8-3)	1
	23b	Kinetic + dynamic	2.5
Intraspecies differences	24	Kinetic + dynamic General population	10
AF (sensitive population)	25		1
Other adjustment factors Quality of database	26		1
Result			
Summary of assessment factors	27	Total Assessment Factor	2520

POD/TAF	28	Calculated value [µg/m ³ and ppb]	643 $\mu g/m^3$ and 119 ppb
Molar adjustment factor	29		
Rounded value	30	[µg/m ³]	650
Additional comments	31		
Rationale section	32		

The derivation of an EU-LCI value for 2-methoxy-1-methylethyl acetate (PGMEA) is based on a project funded by the German Environment Agency (Voss, 2020).

Rationale for critical effects

In a short-term repeated inhalation toxicity study (comparable to OECD guideline 412), F344 rats and B6C3F1 mice (5 M + 5 F/group) were exposed 'whole body' to analytically confirmed vapour concentrations of 0, 300, 1000, or 3000 ppm PGMEA for 6 hours/day, 5 days/week for 2 weeks (a total of 9 exposures). The highest concentration approached the saturated vapour concentration (4950 ppm PGMEA) (Miller et al., 1984, ECHA Dissemination, 2019).

No lethality was observed in rats, and all animals appeared normal. The body weights and weight gain of exposed animals were similar to those of controls. The relative liver weight of high-dose females was significantly increased (by about 5 %) without any gross or histopathological changes. Slight kidney changes (slightly reticulated, pale appearance) were observed in all high-dose males and females, in 11/5 mid-dose males and in 2/5 high-dose females. The mean urinary specific gravity of high-dose males and females tended to be slightly lower than those for controls (Miller et al., 1984, ECHA Dissemination, 2019).

Regarding local effects, an exposure-related slight to moderate degeneration of the olfactory epithelium was observed in the nasal cavities of 3/5 males and 1/5 high-dose females. The changes were characterised by loss of cells in the neuron layer and flattening of the sustentacular cell layer, resulting in decreased thickness of the neuroepithelium. As such observations are not common in young rats, the changes noted were attributed to the exposure with vapours of PGMEA. The ciliated respiratory epithelium remained unaffected (Miller et al., 1984, ECHA Dissemination, 2019).

In mice, the only histopathologic changes attributable to exposure occurred in the nasal cavities. Degeneration (metaplasia) of the olfactory epithelium, similar to that described for rats, was present to some degree in all male and female mice in all PGMEA exposed groups. This acute degenerative change occurred in a dose-related manner and was generally more severe and more extensive in animals exposed to 3000 ppm. However, even at 300 ppm, slight changes were generally present in the dorsomedial aspects of the ethmoid recess in addition to those in the more anterior portions of the olfactory epithelium in the nasal cavity proper. Most animals at the two higher concentrations and 1/5 of female mice in the 300 ppm group had slight focal areas of 'respiratory metaplasia', a condition in which the compromised olfactory epithelium is replaced by ciliated respiratory epithelium similar to that normally present throughout the rest of the respiratory tree. An acute inflammatory exudate was present in the lumen of the nasal cavities in some of the animals that received the two higher doses (Miller et al., 1984, ECHA Dissemination, 2019).

A LOAEC of 300 ppm PGMEA can be derived from these data.

Rationale for the point of departure (POD)

The LOAEC for effects on the nasal epithelium of mice at 300 ppm PGMEA served as the POD for the derivation of the EU-LCI.

Assessment factors

The following assessment factors were applied:

- Factor for adjustment for exposure duration: 5.6
- Adjusted study length factor: 6 (subacute exposure)
- LOAEC \rightarrow NAEC extrapolation: 3
- Interspecies differences:
- allometry 1 (inhalation exposure, local effect)

remaining differences 2.5 (According to the ECA report No. 29, no correction has to be made for differences in systemic metabolism when the POD is related to local effects. For remaining uncertainties, a value of 1 is used for remaining specific differences for effects on skin, eye and GI tract if the mode of action implies only a simple destruction of membranes, and a default value of 2.5 is used for effects on the skin, eye and GI tract if local metabolism or receptor binding reactions are involved. Since acetate esters are metabolically hydrolysed in the nasal epithelium, the factor of 2.5 is retained.)

• Intraspecies differences: 10.

The total assessment factor is 2520, leading to a value of 300 ppm : 2520 = 0.119 ppm for PGMEA. Applying the conversion factor (1 ppm PGMEA = 5.4 mg/m³), an EU-LCI value for PGMEA of 643 µg/m³ was calculated.

After rounding, an EU LCI value for PGMEA of 650 μ g/m³ is proposed.

References

ECHA Dissemination (2019) 2-methoxy-1-methylethyl acetate (Propylene glycol monomethyl ether acetate). In: European Chemicals Agency (ECHA), Annankatu 18, P.O. Box 400, FI-00121 Helsinki, Finland. https://echa.europa.eu/registration-dossier/-/registered-dossier/14773 (last accessed on 10.02.2021)

ECA 29 (2013) (European Collaborative Action - Urban Air, Indoor Environment and Human Exposure): Harmonisation framework for health based evaluation of indoor emissions from construction products in the European Union using the EU-LCI concept. Report No. 29 EUR 26168 EN, European Commission, Joint Research Center, Institute for Health & Consumer Protection.

http://publications.jrc.ec.europa.eu/repository/handle/JRC83683 (last accessed on 10.02.2021)

Miller RR, Hermann EA, Young JT, Calhoun LL, Kastl PE (1984) Propylene glycol monomethyl ether acetate (PGMEA) metabolism, disposition, and short-term vapor inhalation toxicity studies. Toxicol Appl Pharmacol 75:521-530

OECD SIDS (2003) SIDS Initial Assessment Report for SIAM 17: Propylene Glycol Ethers. UNEP Publications. <u>https://hpvchemicals.oecd.org/ui/handler.axd?id=fdbb6972-3dd4-4046-ba21-eeb6e28c05fb</u> (last accessed on 10.02.2021)

Voss, J.-U. (2020) Toxicological basic data for the derivation of EU-LCI values for five substances from building products. UBA Texte 16/2020. <u>https://www.umweltbundesamt.de/publikationen/toxicological-basic-data-for-the-derivation-of-eu-1</u> (last accessed on 10.02.2021)