Compounds	Ethylene glycol monomethyl ether (EGME)	*Data collection sheet (1/3)*
N°CAS 109-86-4 **1 ppm ~ 3.13 mg/m³**	**CLP: Acute tox. 4, Repr. 1B**	

Organisation name	**ACGIH**	**AFS**	**AgBB**	**ANSES**	**DFG**
Risk value name	TLV-TWA	OEL-TWA	NIK (=LCI)	CLI (=LCI)	MAK
Risk value	0.3 mg/m³	0.31 mg/m³	3 µg/m³	60 µg/m³	3.1 mg/m³
Risk value	0.1 ppm	0.1 ppm	0.001 ppm	0.02 ppm	1 ppm
Reference period	Chronic (worker)	Chronic (worker)	Chronic	Chronic	Chronic (worker)
Year	2006	2014	2015	2015	2008
Key study	Shih et al., 2003	No information available	NIK derivation based on the review performed by the Scientific Committee on Occupational Exposure Limits (SCOEL)	Miller et al., 1983	Shih et al., 2000 Shih et al., 2003 (follow-up)
Study type	Analysis of blood and sperm			Subchronic vapour inhalation study	Analysis of blood and sperm
Species	Human (29 workers of a copper clad laminate manufacturing plant)			Rats (Sprague-Dawley; 6-8 weeks old) Rabbits (New Zealand White; 6-7 months old)	Human (29-53 workers of a copper clad laminate manufacturing plant)
Duration of exposure in key study	Average duration of employment of 2.9 years			6 h/d, 5 d/w, 13 weeks	Average duration of employment of 2.6-2.9 years
Critical effect	Haematological effects (decreased haemoglobin, packed cell volume and red blood cell count)			Decreased testes weight & degenerative changes in the testicular germinal epithelium	Haematological effects (decreased haemoglobin, packed cell volume and red blood cell count)
Critical dose value	NOAEC: 0.55 ppm	"As a guide value, 0.1 ppm for exposure via inhalation as a time weighted average during	3.11 mg/m³	NOAEC 93 mg/m³ (30 ppm)	Average NOAEC: 7.4 mg/m³ (2.3 ppm = GM of air EGME)

		a working day should not be exceeded."			
Adjusted critical dose	Chronic			Chronic	Chronic
	"Based upon the absence of anemia in humans at 0.55 ppm and reproductive consequence at 10 ppm in rodents, a TLV-TWA of 0.1 ppm for EGME is recommended."			17 mg/m^3 (5.4 ppm) = 93 mg/m^3 x 6h/24h x 5d/7d	In view of the haematological effects seen in workers at 4 ppm but no longer observed at 2.3 ppm, a health-based OEL of 1 ppm is recommended.
Single assessment factors	Not indicated		1000 (due to the classification as Repr. 1B)	UF_A 10 x UF_S 10 x UF_H 3 = 300	Not indicated
Other effects				Reduced body weight, haematological changes (pancytopenia), lymphoid tissue atrophy	
UF_H Intraspecies variability; UF_A Interspecies variability; UF_S Used subchronic study; UF_D Data deficiencies					

Compounds	Ethylene glycol monomethyl ether (EGME)	*Data collection sheet (2/3)*
CAS 109-86-4 **1 ppm ~ 3.13 mg/m³**	**CLP: Acute tox. 4, Repr. 1B**	

Organisation name	**ECHA (Annex XV dossier)**	**German IAGV**	**NIOSH**	**OEHHA**
Risk value name	DNEL(general population, long-term, inhalation)	IAGV (RW I/RW II)	REL-TWA (skin)	REL
Risk value	0.04 mg/m³	20/200 µg/m³	0.3 mg/m³	60 µg/m³
Risk value	0.013 ppm	0.006/0.06 ppm	0.1 ppm	0.02 ppm
Reference period	Chronic	Chronic	Chronic (worker)	Chronic
Year	2010	2013	1991	2000
Key study	Hanley et al., 1984b	Miller et al., 1983	Hanley et al., 1984a	Miller et al., 1983
Study type	Effects on reproduction after inhalation exposure	Subchronic vapour inhalation study	Effects on reproduction after inhalation exposure	Subchronic vapour inhalation study
Species	Pregnant rabbits, rats and mice	Rats (Sprague-Dawley; 6-8 weeks old) Rabbits (New Zealand White; 6-7 months old)	Pregnant rabbits, rats and mice	Rats (Sprague-Dawley; 6-8 weeks old) Rabbits (New Zealand White; 6-7 months old)
Duration of exposure in key study	6 h/d from GD 6-18 (rabbits) or GD 6-15 (rats/mice)	6 h/d, 5 d/w for 13 weeks	6 h/d from GD 6-18 (rabbits) or GD 6-15 (rats/mice)	6 h/d, 5 d/w for 13 weeks
Critical effect	Foetuses with delayed ossifications	Decreased testes weight & degenerative changes in the testicular germinal epithelium	Foetuses with delayed ossifications	Decreased testes weight & degenerative changes in the testicular germinal epithelium
Critical dose value	NOAEC: 9.3 mg/m³ (3 ppm)		NOAEC: 31 mg/m³ (10 ppm)	NOAEC: 93 mg/m³ (30 ppm)
		LOAEC: 310 mg/m³ (100 ppm)		LOAEC: 310 mg/m³ (100 ppm)
Adjusted critical dose	Chronic	Chronic	Chronic	Chronic
	2.3 mg/m³ (0.74 ppm) = 9.3 mg/m³ x 6h/24h	55 mg/m³ (20 ppm) = 310 mg/m³ x 6h/24h x 5d/7d	Human equivalent level: 25 mg/m³ = (NOAEC x [animal inhalation rate/animal bw] x 6	17 mg/m³ (5.4 ppm) = 93 mg/m³ x 6h/24h x 5d/7d

			h/24 h x 70-kg human bw ÷ 10 m^3/day human inhalation rate)	
Single assessment factors	UF_H 10 x UF_A 6 = 60	UF_L 10 x UF_S 2 x UF_A 2.5 x UF_H 10 x UF_{sen} 2 = 1000	UF_H 10 x UF_A 10 = 100	UF_S 10 x UF_A 3 x UF_H 10 = 300
Other effects		Reduced body weight, haematological changes (pancytopenia), lymphoid tissue atrophy		Reduced body weight, haematological changes (pancytopenia), lymphoid tissue atrophy
UF_H Intraspecies variability; UF_A Interspecies variability; UF_S Used subchronic study; UF_D Data deficiencies; UF_L Used LOAEL				

Compounds	Ethylene glycol monomethyl ether (EGME)	*Data collection sheet (3/3)*
CAS 109-86-4 **1 ppm ~ 3.13 mg/m³**	**CLP: Acute tox. 4, Repr. 1B**	

Organisation name	**OSHA**	**RIVM**	**SCOEL**	**U.S. EPA**
Risk value name	PEL-TWA (skin)	Limit value (8 h)	OEL-TWA	RfC
Risk value	80 mg/m³	0.5 mg/m³	3.1 mg/m³	20 µg/m³
Risk value	25 ppm	0.16 ppm	1 ppm	0.006 ppm
Reference period	Chronic (worker)	Chronic	Chronic (worker)	Chronic
Year	1989	2011	2008	1991
Key study	No information available	Hanley et al., 1984b	Shih et al., 2000 Shih et al., 2003 (follow-up)	Miller et al., 1983
Study type		Effects on reproduction after inhalation exposure	Analysis of blood and sperm	Subchronic vapour inhalation study
Species		Pregnant rabbits, rats and mice	Human (29-53 workers of a copper clad laminate manufacturing plant)	Rats (Sprague-Dawley; 6-8 weeks old) Rabbits (New Zealand White; 6-7 months old)
Duration of exposure in key study		6 h/d from GD 6-18 (rabbits) or GD 6-15 (rats/mice)	Average duration of employment of 2.6-2.9 years	6 h/d, 5 d/w, 13 weeks
Critical effect	No information available	Foetuses with delayed ossifications	Haematological effects (decreased haemoglobin, packed cell volume and red blood cell count)	Decreased testes weight & degenerative changes in the testicular germinal epithelium
Critical dose value		NOAEC: 9.5 mg/m³ (3 ppm)	Average NOAEC: 7.4 mg/m³ (2.3 ppm = GM of air EGME)	NOAEC: 93 mg/m³ (30 ppm)
		$BMDL_{10}$: 4.1 mg/m³ (1.3 ppm)		LOAEC: 310 mg/m³ (100 ppm)
Adjusted critical dose			Chronic	Chronic
			"In view of the haematological effects seen in workers at 4 ppm	17 mg/m³ (5.4 ppm) = 93 mg/m³ x 6h/24h x 5d/7d

			but no longer observed at 2.3 ppm, a health-based OEL of 1 ppm is recommended.“	
Single assessment factors		UF_A 3 x UF_H 3 = 9	Not indicated	UF_S 10 x $UF_{A/D}$ 10 x UF_H 10 = 1000
Other effects				Reduced body weight, haematological changes (pancytopenia), lymphoid tissue atrophy
UF_H Intraspecies variability; UF_A Interspecies variability; UF_S Used subchronic study; UF_D Data deficiencies				

Compound	**Ethylene glycol monomethyl ether (EGME)**		***Factsheet***
Parameter	**Note**	**Comments**	**Value / descriptor**
EU-LCI value and status			
EU-LCI value	1	Mass/volume [µg/m^3]	100
EU-LCI status	2	Draft/final	Final
EU-LCI year of issue	3	Year when the EU-LCI value has been issued	2018
General information			
CLP-INDEX-No.	4	INDEX	603-011-00-4
EC-No.	5	EINECS – ELINCS - NLP	203-713-7
CAS-No.	6	Chemical Abstracts Service number	109-86-4
Harmonised CLP classification	7	Human Health Risk related classification	Acute tox. 4, Repr. 1B
Molar mass and conversion factor	8	[g/mol] and [ppm – mg/m^3]	76.09 1 ppm = 3.13 mg/m^3
Key data / database			
Key study, author(s), year	9	Critical study with lowest relevant effect level	Hanley et al., 1984a
Read across compound	10	Where applicable	
Species	11	Rat, human, etc.	Rabbits, rats and mice
Route/type of study	12	Inhalation, oral feed, etc.	Inhalation
Study length	13	Days, subchronic, chronic	During organogenesis
Exposure duration	14	Hrs/day, days/week	6 h/d from GD 6-18 (rabbits) or GD 6-15 (rats/mice)
Critical endpoint	15	Effect(s), site of	Developmental toxicity (foetal malformations in rabbits)
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]	10 ppm
Assessment factors (AF)	**18**		
Adjustment for exposure duration	19	Study exposure hrs/day, days/week	4
Study length	20	sa→ sc→ c *(R8-5)*	1
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)*	3
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)*	1
Result			
Summary of assessment factors	27	Total Assessment Factor (TAF)	300
POD/TAF	28	Calculated value (µg/m³ and ppb)	104 µg/m³ and 33 ppb
Molar adjustment factor	29	Used in read-across	
Rounded value	30	[µg/m³]	100
Additional comments	31		
Rationale section	32		

Data compilation and evaluation for ethylene glycol monomethyl ether (EGME) is based on a project funded by the European Commission and prepared by Ramboll Environment & Health GmbH (formerly s BiPRO GmbH).

Several organisations or national agencies have published comprehensive assessments or evaluations of EGME (and ethylene glycol monomethyl ether acetate (EGMEA)), which were considered for the EU-LCI derivation (ACGIH, 2006a, 2006b; Canadian EPA, 1999; ECETOC, 2005; Health Council of the Netherlands, 2011; Johanson, 1999; MAK Commission, 2016; OEHHA, 1999; SCOEL, 2006).

Rationale for key study/POD

The derivation of the EU-LCI for EGME is based on the developmental inhalation study of EGME using mice, rats and rabbits (Hanley et al., 1984a). In this study, pregnant Fischer 344 rats and New Zealand White rabbits were exposed via inhalation to 0, 3, 10, or 50 ppm EGME for 6 hours/day from gestation day (GD) 6 to 15 and GD 6 to 18, respectively. Pregnant CF-1 mice were exposed via inhalation to 0, 10, or 50 ppm EGME for 6 hours/day from GD 6 to 15. For each species and vapour concentration, 24-32 animals were exposed. Exposure of pregnant rabbits to 50 ppm EGME produced significant increases in the incidence of foetal malformations and resorptions as well as a decrease in foetal body weight. Rats and mice exposed to 50 ppm showed a slight degree of evidence of foetotoxicity (e.g. delayed ossification and increased malformation of the lumbar spurs in rats as well as unilateral hypoplastic testicle and extra lumbar ribs in mice). The NOAEC for this study was set at 10 ppm, which showed no treatment-related teratologic effects in all tested species.

Aside from the key study of Hanley et al. (1984a), two other inhalation studies (Miller et al., 1983; Shih et al., 2000, 2003) were selected as the key study by a number of regulatory agencies and organisations for the derivation of health-based inhalation limit values of EGME and EGMEA.

The study of Miller et al. (1983a) investigated health effects on Sprague-Dawley rats (10 per sex and concentration) and New Zealand White rabbits (5 per sex and concentration) exposed to 0, 30, 100 and 300 ppm EGME in a subchronic inhalation setting (6 hours/day, 5 days/week for 13 weeks). A moderate to severe degeneration of the germinal epithelium and seminiferous tubules of the testes was found in male rats exposed to 300 ppm and male rabbits exposed to ≥ 100 ppm. Both species exposed to 300 ppm also exhibited pancytopenia, lymphoid tissue atrophy and decreased body weights (Miller et al., 1983a). As slight microscopic changes in the testes were observed in a small percentage of rabbits exposed to 30 ppm, the NOAEC for this study was set at 30 ppm.

In the study of Shih et al. (2000), haematological effects were examined in 53 impregnation workers from two copper clad laminate factories mainly exposed to EGME, compared with a control group of 121 lamination workers with minimal and indirect exposure to EGME. The average EGME concentrations in the two copper factories were in the range of 4.0-4.3 ppm, whereas the EGME concentration in the control lamination area ranged from non-detectable to 0.28 ppm. The average duration of employment of these workers was about 2.6 years. It was reported that haemoglobin, packed cell volume, and red blood cell count in male workers were significantly negatively associated with urinary concentrations of methoxyacetic acid. This study concluded that there is clear evidence of haematological effects in males at

an average exposure of about 4 ppm EGME (Shih et al., 2000). In the follow-up study, 29 exposed and 90 non-exposed workers were recruited. It was shown that when the airborne concentration of EGME dropped to 2.3 ppm, the haematological effects were no longer observed and remained normal in the second follow-up. Therefore, the EGME-induced haematological effects appear to be reversible upon reduction in exposure (Shih et al., 2003). The limitations of the Shih et al. studies include the small sample population of lamination workers (29-53 EGME-exposed workers and 90-121 workers serving as control) and the exposure of workers to other solvents such as acetone.

Overall, considering the severity of effects and the exposed concentrations among these studies, the critical effect of foetal malformations in rabbits observed in Hanley et al. (1984a) is considered as the most severe when compared to the effects reported in Miller et al. (1983a) (testicular effects in male animals at ≥ 100 ppm) and in Shih et al. (2000 and 2003) (reversible haematological effects in occupational workers mainly exposed to ~4 ppm EGME). The point of departure (POD) is then set at 10 ppm, which is the NOAEC of the study by Hanley et al., (1984a).

Assessment factors (AF)

Given that the EGME exposure in the Hanley et al. (1984a) study occurred during organogenesis (e.g. 6 hours/day from GD 6-18 in rabbits), a critical window during development, and the critical effects were foetotoxicity, no assessment factor was applied to adjust for study length. Standard default assessment factors to adjust for exposure duration, interspecies and intraspecies differences were applied. In addition, because of the critical effect of foetal malformations, an assessment factor of 3 was applied to account for the severity of effects (as recommended by ECETOC, 2010). The assessment factors applied are shown below:

- Exposure duration: 4
- Severity of effects: 3
- Interspecies differences: 2.5
- Intraspecies differences: 10

The total assessment factor is 300.

This results in a calculated value of 104 µg/m^3 and a derived EU-LCI for EGME of 100 µg/m^3.

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