Compound	Ethylene glycol	*Data collection sheet*
N°CAS 107-21-1	**CLP:** Acute Tox. 4 (H302: Harmful if swallowed.) Self classification: Acute Tox. 4 (H302), STOT Rep. Exp. 2, (kidney, oral)	

Organisation name	**SCOEL**	**DFG MAK**	**TLV**	**REACH registrants (worker/consumer)**	**OEHHA**
Risk value name	SCOEL	MAK	TLV ceiling	DNEL	REL
Risk value (µg/m³)	52000	25700	100000	35000 (worker) / 7000 (consumer)	400
Risk value (ppb)	20000	10000	39000	13000	200
Reference period					
Year	1995	1991	2001	2014	2000
Key study	Wills et al. 1974	Wills et al. 1974	Wills et al. 1974	Wills et al. 1974	Wills et al. 1974
Study type	clinical study	clinical study	clinical study	clinical study	clinical study
Species	human	human	human	human	human
Duration of exposure in key study	20-22h/day, for 30 days	20-22h/day, for 30 days	20-22h/day, for 30 days	20-22h/day, for 30 days	20-22h/day, for 30 days
Critical effect	respiratory tract irritation	respiratory tract irritation	respiratory tract irritation	respiratory tract irritation	respiratory tract irritation
Critical dose value	LOAEC	LOAEC	LOAEC	NOAEC	NOAEC
	50 ppm (140 mg/m³)	50 ppm (140 mg/m³)	50 ppm (140 mg/m³)	67 mg/m³	20 ppm
Adjusted critical dose	NOAEC	NOAEC	NOAEC		
	25 ppm	10 ppm	not indicated	35 mg/m³ (worker) 7 mg/m³ (consumer)	
Single assessment factors (see table R.8.6)	LOAEC→NOAEC 2	LOAEC→NOAEC 5	not indicated	"general factor" 2 (workers), 10 (consumer)	subchronic-chronic 10 intraspecies 10
Other effects					

Compound	**Ethylene glycol**		***Factsheet***
Parameter	**Note**	**Comments**	**Value / descriptor**
EU-LCI value and status			
EU-LCI value	1	Mass/volume [µg/m^3]	3400
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	603-027-00-1
EC No	5	EINECS – ELINCS - NLP	203-473-3
CAS No	6	Chemical Abstracts Service number	107-21-1
Harmonised CLP classification	7	Human health risk-related classification	Annex 6, CLP : Acute Tox. 4 (H302) Self-classification: Acute Tox. 4 (H302), STOT Rep. Exp. 2 (kidney, oral)
Molar mass and conversion factor	8	[g/mol] and [ppm – mg/m^3]	62.07 1 ppm = 2.6 mg/m^3
Key data / database			
Key study, author(s), year	9	Critical study with lowest relevant effect level	Wills et al. (1974)
Read-across compound	10	Where applicable	-
Species	11	Rat etc. / human	Human
Route/type of study	12	Inhalation, oral feed, etc.	Inhalation
Study length	13	Days, subchronic, chronic	30 days
Exposure duration	14	Hours/day, days/week	20-22h/day
Critical endpoint	15	Effect(s), site of	Irritation of upper respiratory tract
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]	67 mg/m^3
Assessment factors (AF)	**18**		
Adjustment for exposure duration	19	Study exposure hours/day, days/week	1
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)*	1
Interspecies differences	23 a	Allometric Metabolic rate *(R8-3)*	1
	23 b	Kinetic + dynamic	1
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)	20
POD/TAF	28	Calculated value (µg/m³ and ppb)	3350 µg/m³ = 1300 ppb
Molar adjustment factor	29	Used in read-across	-
Rounded value	30	[µg/m³]	3400
Additional comments	31		
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Toxicity profile
Ethylene glycol (EG) is not classifiable for skin or mucosal irritation based on guideline animal assays.
In a human clinical study, signs indicating an upper respiratory irritation were identified. In that study, 20 male participants were exposed in a closed room for 20-22 hours/day for 30 days. Ethylene glycol aerosol was respirable (particle size 1-5 µm). Concentrations were varied daily, resulting in weekly median concentrations of 17-49 mg/m³ in the first stage of the experiment. Short-term increases in exposure concentration to 188 mg/m³ for 15 min were well tolerated; increases to 244 and 305 mg/m³ for 1-2 min were not tolerated. Irritation to the throat was reported from exposure levels of 140 mg/m³ and above (NOAEC for local effects 67 mg/m³; Wills, 1974).

Nephrosis is the most sensitive systemic health effect following repeated oral uptake. Metabolites are the plausible explanation (oxalic acid). The most relevant study is a 12-month feeding study with rats, in which a NOAEL of 150 mg/kg bw/day was identified (Corley, 2008).

Teratogenicity (reduced pup weights) was observed, with high doses of EG in rodents. The NOAEL was identified to be 150 mg/kg bw/day in mice (BRRC, 1989) and 500 mg/kg bw/day in rats (BRRC, 1990). No teratogenicity was observed in rabbits (Tyl, 1993) or in a nose-only inhalation developmental toxicity study with mice exposed to up to 2500 mg/m³ (Tyl, 1985). Accumulation of metabolites is considered to be relevant for developmental effects (oxalic acid, glycolic acid), with kinetic differences in metabolism being responsible for species differences. Current information indicates that metabolism in humans can be compared with that of rabbits.

Rationale
In agreement with the German MAK (maximum workplace concentration) and SCOEL, irritation to the respiratory tract observed in a human volunteer study is identified as the most relevant effect for inhalation exposure.

Protecting from respiratory irritation is protecting from systemic toxicity, both acute (nephrotoxicity, CNS depression) and chronic (nephrotoxicity, teratogenicity). Furthermore, a more recent investigation shows that under conditions of the MAK value (25 mg/m³) the excretion of oxalic acid and glycolic acid is within the natural background range (Upadhyay et al., 2008).

Choice of assessment factors (AF)
No AFs are applied for study length or exposure duration, since irritation of upper respiratory tract is the critical endpoint. Furthermore no AFs were necessary for route-to-route or interspecies extrapolations, since the effect is local in the airways and the POD is based on inhalation exposure of humans. The critical effect is of low severity, allowing an AF of 1. An AF of 10 is used to account for variability in the general population (the intraspecies factor). This factor is thought to be sufficient for sensitive populations. Due to high variations in daily tested concentrations levels, an AF of 2 is applied for other adjustment factors.

References

Wills et al. (1974): Inhalation of aerosolised ethylene glycol by man. Clin Toxicol 7: 463-476, cited in MAK documentation 1991.

Corley et al. (2008): Dosimetry considerations in the enhanced sensitivity of male Wistar rats to chronic ethylene glycol-induced nephrotoxicity. Toxicol Appl Pharmacol 228: 165-178.

Tyl et al. (1993): Developmental toxicity evaluation of ethylene glycol by gavage in New Zealand white rabbits. Fundamental and Applied Toxicology 20: 402-412.

Tyl et al. (1985): Evaluation of the teratogenic potential of ethylene glycol aerosol in the CD rat and CD-1 mouse. BRRC Report No 48-100.

Bushy Run Research Center (1989), Report No 51-591. Published in Neeper-Bradley (1995): Determination of a no-observed-effect level for developmental toxicity of ethylene glycol administered by gavage to CD rats and CD1 mice. Fundamental and Applied Toxicology 27: 121-130.

Bushy Run Research Center (1990), Report No 52-656. Published in Neeper-Bradley (1995): Determination of a no-observed-effect level for developmental toxicity of ethylene glycol administered by gavage to CD rats and CD1 mice. Fundamental and Applied Toxicology 27: 121-130.

Upadhyay et al. (2008): Inhalation and epidermal exposure of volunteers to ethylene glycol: Kinetics of absorption, urinary excretion, and metabolism to glycolate and oxalate. Toxicol. Lett. 178, 132 -140.