Compound	2-Phenoxyethanol	*Data collection sheet*
N°CAS 122-99-6 1 ppm (in air, 23°C) = 5.68 mg/m^3	**CLP:** Acute Tox. 4, Eye Irrit. 2	

Organisation name	**DFG**	**Reach registrants**	**Reach registrants**
Risk value name	MAK	DNEL consumer	DNEL worker
Risk value (mg/m³)	110	2.41	8.07
Risk value (ppm)	20	0.43 (calculated)	1.42 (calculated)
Reference period	chronic (worker)	chronic (general population)	chronic (worker)
Year	1998	2016 (last modification)	2016 (last modification)
Key study	Relevant data on effects in man caused by 2-Phenoxyethanol were not available. Therefore, data from the structural analogue 2-butoxyethanol (CAS 111-76-2) were used and the MAK value of 110 mg/m^3 was provisionally adopted for 2-phenoxyethanol.	DNEL was derived by industry, no further information available	DNEL was derived by industry, no further information available
Study type	health surveillance		
Species	human		
Duration of exposure in key study	8-hour inhalative exposure of volunteers		
Critical effect	irritation	systemic toxicity	systemic toxicity
Critical dose value		NAEC 12.05 mg/m^3	NAEC 24.22 mg/m^3
Adjusted critical dose	chronic	chronic	chronic
Single assessment factors (see table R.8.6)	not indicated	overall assessment factor of 5 applied (AF for intraspecies differences of 5)	overall assessment factor of 3 applied (AF for intraspecies differences of 3)
Other effects			

Compound	**2-Phenoxyethanol**		***Factsheet***
Parameter	**Note**	**Comments**	**Value / descriptor**
EU-LCI value and status			
EU-LCI value	1	Mass/volume [µg/m^3]	60
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	603-098-00-9
EC No	5	EINECS – ELINCS - NLP	204-589-7
CAS No	6	Chemical Abstracts Service number	122-99-6
Harmonised CLP classification	7	Human health risk-related classification	Acute Tox. 4 Eye Irrit. 2
Molar mass and conversion factor	8	[g/mol] and [ppm – mg/m^3]	138.16 1 ppm = 5.68 mg/m^3
Key data / database			
Key study, author(s), year	9	Critical study with lowest relevant effect level	BASF AG (2007)
Read-across compound	10	Where applicable	
Species	11	Rat etc. / human	Rodent Male and female Wistar rats
Route/type of study	12	Inhalation, oral feed, etc.	Inhalation
Study length	13	Days, subchronic, chronic	Subacute 2 weeks
Exposure duration	14	Hours/day, days/week	6 h/day, 5 days/week
Critical endpoint	15	Effect(s), site of	Irritation, inflammation and degeneration on the respiratory epithelium in the nasal cavity
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]	48.2 mg/m^3
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 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)	840
POD/TAF	28	Calculated value (µg/m³ and ppb)	…. 57.38 µg/m³ ….10.1 ppb
Molar adjustment factor	29	Used in read-across	
Rounded value	30	[µg/m³]	60
Additional comments	31		
Rationale section	32		

Data compilation and evaluation for 2-phenoxyethanol is based on a project funded by the German Environment Agency (Wibbertmann et al., 2017).

2-Phenoxyethanol is a colourless liquid with a low solubility in water. The substance has bactericidal properties and is used in cooling lubricants, as a preservative or solvent. In indoor measurements, concentrations of 2-phenoxyethanol were reported to be ≤ 3 µg/m^3 (median), with maximum concentrations of 908 µg/m^3.

In both oral studies with volunteers and studies with experimental animals, 2-phenoxyethanol was found to be rapidly absorbed, metabolised and excreted mainly via urine. The main metabolite is phenoxyacetic acid. In several studies either with volunteers or with experimental animals, 2-phenoxyethanol was non-skin-irritating to slightly skin-irritating, eye-irritating and non-skin-sensitising to slightly skin-sensitising.

In a two-week inhalation study of rats (nose/head only; test with mixtures of vapour and liquid aerosol), exposure to 0-1 000 mg/m^3 for 6 hours/day on 5 days/week caused primarily local effects at a concentration of 200 mg/m^3, i.e. irritation and degenerative changes in the upper respiratory tract (BASF AG, 2007; ECHA, 2016). From a 13-week study of rats, with oral administration of 0-20 000 ppm via drinking water, a NOAEL of 5 000 ppm was derived (MHLW, 2003b). In the high-dose animals, haematological and histopathological changes such as anaemia and hyperplasia in the renal pelvis and bladder were noted. In contrast, in another 13-week study of rats, oral doses of 0-10 000 ppm via the diet were tolerated without causing adverse effects (Bayer AG, 2002).

2-Phenoxyethanol was not carcinogenic in two long-term studies with rats and mice at doses of 0-10 000 ppm (rats) or 0-20 000 ppm (mice) via drinking water over 104 weeks (MHLW, 2007b). High-dose rats of both sexes showed altered haematological and biochemical parameters and, in males, kidney changes (hyperplasia, papillary necrosis and mineralisation). Altered haematological and biochemical parameters were also described for mice; however, these effects could not be clearly attributed to this treatment. In reproductive toxicity studies, effects on the offspring were noted only at maternal-toxic doses and in none of these studies were abnormalities found in testes or sperm quality.

Concerning mutagenic or genotoxic effects, 2-phenoxyethanol tested negative in a variety of in vitro and in vivo test systems (Ames test, chromosomal aberration with V79 CHL and CHO cells, micronucleus test with mice and rats, and UDS test with rats).

Relevant data on the health effects of 2-phenoxyethanol in humans are lacking. Therefore, a 14-day inhalation study according to OECD Guideline 412, with rats exposed to analytical concentrations of 0, 48.2, 246 or 1 070 mg/m^3, was selected as the key study for the derivation of the LCI value (BASF AG, 2007; ECHA, 2016). Due to the low vapour pressure of the test substance, mixtures of vapour and liquid aerosol were tested with all groups (the theoretical vapour concentration was given as up to 40 mg/m^3). The highest concentration, 1070 mg/m^3, caused decreased feed intake followed by slightly reduced body weight gain. At the middle dose, local effects (degenerative changes in the upper respiratory tract) were seen. Other systemic effects were not found. From this study, a NOAEC of 48.2 mg/m^3 (local effects) or 1070 mg/m^3 (systemic effects) can be derived.

Point of departure (POD)

Wibbertmann et al. proposed a NOAEC of 1070 mg/m^3 for systemic effects as the POD. However, the EU-LCI Working Group considered the local effects as being the most sensitive endpoint. Thus the NOAEC of 48.2 mg/m^3 for degenerative changes in the exposed upper respiratory epithelium (combined exposure of liquid droplets and the vapour phase) was chosen as the POD for deriving the EU-LCI value. Taking the NOAEC of 48.2 mg/m^3 as the POD can be regarded as conservative, because the observed degenerative effects above 246 mg/m^3 may have been caused by the osmotic activity of liquid droplets and not by the volatile phase.

Assessment factors

To calculate the LCI, the default assessment factors were used, i.e. 5.6 for an adjustment for exposure duration, 6 for study length, 2.5 for interspecies differences and 10 for intraspecies differences. The TAF is 5.6x6x2.5x10=840.

The calculated LCI value is 48.2/840 = 57.38 µg/m^3. After rounding, a final EU-LCI value of 60 µg/m^3 was set.

References

BASF AG (2007) Phenoxyethanol – Subacute 14-day inhalation study in Wistar rats – liquid aerosol exposure. Unpublished Report No. 3610498/01187. BASF AG, Ludwigshafen, Germany. Cited in: SCCS (2016) Scientific Committee on Consumer Safety - Opinion on Phenoxyethanol (SCCS/1575/16). European Commission, Luxembourg. http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_195.pdf

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