Compound	Propylene glycol diacetate (PGDA)	*Data collection sheet (1/1)*
N°CAS 623-84-7 **1 ppm = 6.59 mg/m³**	**CLP:** No harmonised classification	

Organisation name	**AgBB**	**ANSES**	**Denmark**
Risk value name	NIK (=LCI)	CLI (=LCI)	OEL (8 hr)
Risk value	5300 µg/m³	6500 µg/m³	659 000 µg/m³
Risk value	800 ppb	990 ppb	100 ppm (provisional)
Reference period	Chronic	Chronic	Chronic
Year	2015	1994	
Key study	Value derived from propylene glycol value of 2500 µg/m³	No further information available	No further information available
Study type			
Species			
Duration of exposure in key study			
Critical effect			
Critical dose value			
Adjusted critical dose			
Single assessment factors			
Other effects/comments			

UF_H Intraspecies variability; UF_A Interspecies variability; UF_S Used subchronic study; UF_D Data deficiencies

Compound	**Propylene glycol diacetate**		***Factsheet***
Parameter	**Note**	**Comments**	**Value / descriptor**
EU-LCI value and status			
EU-LCI value	1	Mass/volume [µg/m^3]	1600
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	
EC-No.	5	EINECS – ELINCS - NLP	210-817-6
CAS-No.	6	Chemical Abstracts Service number	623-84-7
Harmonised CLP classification	7	Human health risk related classification	No harmonised classification
Molar mass and conversion factor	8	[g/mol] and [ppm – mg/m^3]	160.17 1 ppm = 6.59 mg/m^3
Key data / database			
Key study, author(s), year	9	Critical study with lowest relevant effect level	
Read across compound	10	Where applicable	Acetic acid CAS 64-19-7
Species	11	Rat, human, etc.	
Route/type of study	12	Inhalation, oral feed, etc.	
Study length	13	Days, subchronic, chronic	
Exposure duration	14	Hours/day, days/week	
Critical endpoint	15	Effect(s), site of	
Point of departure (POD)	16	LOAEC*L, NOAEC*L, NOEC*L, benchmark dose, etc.	POD/TAF in EU-LCI factsheet for acetic acid
POD value	17	[mg/m^3] or [ppm] or [mg/kg$_{BW}$×d]	1.235 mg/m^3
Assessment factors (AF)	**18**		
Adjustment for exposure duration	19	Study exposure hrs/day, days/week	-
Study length	20	sa→ sc→ c *(R8-5)*	-
Route-to-route extrapolation factor	21		-
Dose-response	22 a	Reliability of dose-response, LOAEL → NOAEL	-
	22 b	Severity of effect *(R 8-6d)*	-
Interspecies differences	23 a	Allometric Metabolic rate *(R8-3)*	-
	23 b	Kinetic + dynamic	-
Intraspecies differences	24	Kinetic + dynamic Worker - general population	-
AF (sensitive population)	25	Children or other sensitive groups	-
Other adjustment factors Quality of whole database	26	Completeness and consistency Reliability of alternative data *(R8-6 d,e)*	-

Result			
Summary of assessment factors	27	Total Assessment Factor (TAF)	
POD/TAF	28	Calculated value (µg/m³ and ppb)	1235 µg/m³ and 500 ppb
Molar adjustment factor	29	Used in read-across (160.17/(60.05 x 2))	1.33
Rounded value	30	[µg/m³]	1600
Additional comments	31		
Rationale section	32		

Data compilation and evaluation for propylene glycol diacetate is based on a project funded by the European Commission and prepared by Ramboll Environment & Health GmbH (formerly BiPRO GmbH).

Rationale for read-across

Propylene glycol diacetate (PGDA) is a data-poor compound. There is an existing REACH registration dossier for PGDA, which served as the primary source for data compilation for this substance (ECHA, 2017). Nevertheless, there is a paucity of toxicological data for PGDA for the derivation of an EU-LCI value using the *de novo* procedure. The EU-LCI derivation for PGDA was consequently conducted via read-across from the *de novo* EU-LCI value of acetic acid.

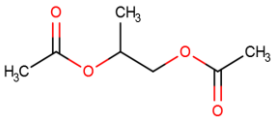
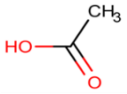
The key assumption underlying the use of read-across with the EU-LCI value for acetic acid is based on the quick hydrolysis of PGDA to acetic acid and propylene glycol (PG) by carboxylesterase.

Information on *in vivo* metabolism, i.e. the enzyme-catalysed hydrolytic cleavage of PGDA, is available from the REACH registration dossier of PGDA. Metabolism of PGDA occurs quickly in rats, the result being that the ester bond of PGDA is quickly hydrolysed and cleaved by carboxylesterases to form acetic acid and PG (calculated metabolic half-life = 0.2 h). One toxicokinetic study assessed the recovered radioactivity from urine, faeces and CO_2 after exposure to PGDA and PG and observed similar recovery patterns between PGDA and PG. In particular, the majority of the radioactivity (~50%) was identified as CO_2 (a breakdown product from the metabolism of PGDA and PG), and most of the radioactivity was recovered within the first 12 hours post-dosing for both PGDA and PG, supporting the hypothesis that 1 mole of PGDA is quickly hydrolysed to 1 mole of PG and 2 moles of acetic acid (ECHA, 2017). This hypothesis is further supported by several *in vivo* studies of glycol ether acetate metabolism, which showed that the ester group in glycol ether acetates is rapidly hydrolysed by carboxylesterases (Domoradzki et al., 2003; Gallaher & Loomis, 1975; Gargas et al., 2000; Stott & McKenna, 1985).

Carboxylesterases are widely distributed in nature and are abundant in various organs and tissues (e.g. nasal mucosa, blood, liver, skin, heart, muscle, adipose tissue and kidney) of many mammalian species, including humans. They are often involved in phase I metabolism of xenobiotics, and the resulting carboxylates are then further processed to increase their solubility and eventually be excreted from the body. Studies on the metabolism of glycol ether acetates have also shown that carboxylesterases have high affinity for their substrates. Altogether, it is assumed that exposure to PGDA will result in its rapid turnover in the body and exposure to breakdown products (i.e. PG and acetic acid) instead of the parent substance itself (Lewis et al., 1994; Ross & Crow, 2007; Satoh & Hosokawa, 1998; Stott & McKenna, 1985).

There are existing *de novo* EU-LCI values for both PG (unrounded value of 2133 µg/m³) and acetic acid (unrounded value of 1235 µg/m³). For PG, a subchronic 90-day inhalation study in rats (Suber et al., 1989) was selected as the key study with the toxicological critical endpoint of local ocular discharge and respiratory tract irritation appearing at 160 mg/m³, which was determined as the lowest-observed-adverse-effect-concentration (LOAEC) and taken as the point of departure (POD) for the EU-LCI derivation. On the other hand, for acetic acid, two studies involving healthy human volunteers (Ernstgård et al., 2006; van Thriel et al., 2008) were considered for the EU-LCI derivation with the reported effect of mild sensory irritation (e.g. nasal irritation) appearing at 10 ppm (24.7 mg/m³), which was determined as the LOAEC and taken as the POD for EU-LCI derivation.

The EU-LCI value for acetic acid was selected for the read-across for PGDA because irritative effects in humans upon exposure to acetic acid were reported at a much lower concentration (24.7 mg/m³) than irritative effects experienced by animals after exposure to PG (160 mg/m³). Furthermore, the EU-LCI value for acetic acid is lower than that of PG, so the read-across using acetic acid allows a more conservative and protective EU-LCI value for PGDA.

Compound	Structure	MW (g/mol)	EU-LCI value
Propylene glycol diacetate		160.17	Read-across to be used *1600 µg/m³*
Acetic acid		60.05	1200 µg/m³ (*de novo* protocol) Unrounded value: 1235 µg/m³ or 500 ppb

Unrounded EU-LCI value of acetic acid: 1235 µg/m³ ➔ to be used for read-across for the EU-LCI of PGDA.

Applying the molar adjustment factor: EU-LCI PGDA = 1235 µg/m³ x 1.33 = 1642 µg/m³ ➔ rounded to 1600 µg/m³. The final EU-LCI value for PGDA is 1600 µg/m³.

References

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