

Compound	Diethylene glycol n-hexyl ether (2-(2-hexyloxyethoxy)-ethanol, DEGHE)	Data collection sheet
N° CAS 112-59-4	EU-Classification: - CLP: harmonised classification, Acute Tox. 4 * (H312), Eye Dam. 1 (H318) *minimum classification	
1 ppm = 6.732 mg/m ³		
Organisation name	AgBB	REACH registrants
Risk value name	NIK ('Lowest Concentration of Interest')	DNEL
Risk value (mg/m ³)	0.74 (read-across from DEGBE)	4.1 (read-across from EGHE)
Reference period	Chronic (general population)	Chronic (general population)
Risk value (mg/m ³) Short term (15 min)	-	-
Year	2008	2018
Key study	Study report from BASF (1992) mentioned by SCOEL (2002)	Study report from 1985 reported as „key“ study for repeated dose inhalation
Study type	Inhalation study (0, 13, 40 or 94 mg/m ³ , whole body) with DEGBE (read-across, CAS: 112-34-5)	Inhalation study, similar OECD 413 (mean concentrations: 0, 20, 41, or 71 ppm, whole body) with EGHE (read-across, CAS: 112-25-4)
Species	Rat	Fischer 344 rats (n=20/sex/group)
Duration of exposure in key study	6 h/d, for 90 d	6 h/d, 5 d/w for 14 weeks
Critical effect	No critical effect	Increased liver weight
Critical dose value	NOEL (DEGBE): 94 mg/m ³ (14 ppm)	NOAEC (EGHE): 245 mg/m ³ (41 ppm) Converted NOAEC (DEGHE): 325 mg/m ³
Adjusted critical dose	Value derived using "preferred value approach" ^s is 67.5 mg/m ³ (10 ppm) for DEGBE	325 mg/m ³ x 6/24 = 81.25 mg/m ³
Single assessment factors	EU OEL (adopted from SCOEL) /100 = 67500 µg/m ³ /100 = 675 µg/m ³	UF _H 10 x UF _A 1 x UF _S 2 = 20
Other effects		
Remarks	Read-across from DEGBE was applied. The derived NIK value for DEGBE was transformed into a NIK value for DEGHE by considering a molar adjustment.	Read-across from EGHE was applied. The NOAEC for EGHE was transformed into a NOAEC for DEGHE by considering a molar adjustment. No interspecies factor was applied by the registrant, because increase in liver weight was regarded as an unspecific effect not significantly differing between species (ECHA Dissemination, 2019)

AgBB = Ausschuss zur gesundheitlichen Bewertung von Bauprodukten

UF_H Intraspecies variability; UF_A interspecies variability; UF_S Used subchronic study

DEGBE = 2-(2-butoxyethoxy)ethanol (CAS: 112-34-5)

EGHE = ethylene glycol monohexyl ether (CAS: 112-25-4)

§ Preferred value approach means that OELs will be rounded up or down to decimals of the integers 1, 2 or 5 ppm. For example, SCOEL recommends to use 0.05, 0.1, 0.2, 0.5, 1, 2, 5, 10 or 50 ppm and to refrain from discriminating any further, except if scientific data or reasons suggest a more specific value (SCOEL, 2013).

Compound	Diethylene glycol n-hexyl ether (2-(2-hexyloxyethoxy)-ethanol, DEGHE) C10H22O3		Factsheet
Parameter	Note	Comments	Value / descriptor
EU-LCI value and status			
EU-LCI value	1	[µg/m ³]	400
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	603-175-00-7
EC-No.	5	EINECS	203-988-3
CAS-No.	6	Chemical Abstract Service number	112-59-4
Harmonised CLP classification	7	Human health risk related classification	Acute Tox. 4 (H312), Eye Dam. 1 (H318)
Molar mass and conversion factor	8	[g/mol] and [ppm – mg/m ³]	190.28 1 ppm = 7.83 mg/m ³
Key data / database			
Key study, authors, year	9	Critical study with lowest relevant effect level	
Read across compound	10	Where applicable	2-(2-butoxyethoxy)ethanol (DEGBE)
Species	11	Rat	
Route / type of study	12	Inhalation, oral feed, etc.	
Study length	13	Days, subchronic, chronic, etc.	
Exposure duration	14	h/d, d/w	
Critical endpoint	15	Effect (s), site of	
Point of departure (POD)	16	LOAEC, NOAEC, BMD, etc.	
POD value	17	[mg/m ³] or ppm or [mg/kg _{BW} ×d]	POD/TAF from the DEGBE fact sheet: 0.335 mg/m ³
Assessment factors (AF)			
Adjustment for exposure duration	19	Study exposure h/d, d/w	-
Study length	20	sa→sc→c	-
Route-to-route extrapolation factor	21	-	-
Dose-response	22a	Reliability of dose-response, LOAEL to NOAEL	-
	22b	Severity of effect (R8 6d)	-
<u>Interspecies</u> differences	23a	Allometric Metabolic rate (R8-3)	-
	23b	Kinetic + dynamic	-
<u>Intraspecies</u> differences	24	Kinetic + dynamic general population	-
AF (sensitive population)	25		-
Other adjustment factors Quality of database	26		-

Result			
Summary of assessment factors	27	Total Assessment Factor	
POD/TAF	28	Calculated value [$\mu\text{g}/\text{m}^3$ and ppb]	335.71 $\mu\text{g}/\text{m}^3$ and 53.57 ppb
Molar adjustment factor	29		1.173 (= 190.28 / 162.23)
Rounded value	30	$[\mu\text{g}/\text{m}^3]$ (335.71 $\mu\text{g}/\text{m}^3 \times 1.173 =$ 393.7 $\mu\text{g}/\text{m}^3$)	400
Additional comments	31		

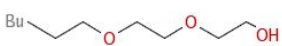
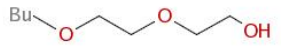
Rationale section

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Data compilation and evaluation for diethylene glycol n-hexyl ether (DEGHE) is based on a project funded by the German Environment Agency (Voss, 2020).

Rationale for read-across

- Data poor compound: no adequate toxicological data for DEGHE; *de novo* derivation of EU-LCI for DEGHE is not possible.
- Read-across from EU-LCI value of DEGBE: within the chemical class 'diethylene glycol ethers', DEGBE is the closest homologue compound with an EU-LCI value. Two additional CH_2 groups in the aliphatic chain of DEGHE are the only difference between the two substances.
- Toxicological critical endpoint for DEGBE: irritation of eyes and mucous membranes. As these local effects cannot be detected by route-to-route extrapolation, a read-across approach from an inhalation study is necessary.
- The key assumption underlying the read-across of the EU-LCI value from DEGBE to DEGHE is that both compounds have the same critical endpoint (irritation) and this is caused by the common functional group (and not by the additional CH_2 groups). Furthermore, DEGBE was also regarded as a suitable read-across substance for DEGHE in assessments performed by OECD (OECD SIDS, 2005) and AgBB (2012, 2018), thus supporting the applied read-across approach for the derivation of an EU-LCI value for DEGHE.

Compound	Structure	Molar mass [g/mol]	EU-LCI value
2-(2-hexyloxyethoxy)-ethanol (DEGHE)		190.28	(Read-across to DEGBE) Rounded value: 400 $\mu\text{g}/\text{m}^3$
2-(2-butoxyethoxy)ethanol (DEGBE)		162.23	Newly derived EU-LCI value in 2019 according to the derivation procedure in the ECA Report No. 29: 335.7 $\mu\text{g}/\text{m}^3$ 670 $\mu\text{g}/\text{m}^3$ (ascribed LCI value, adopted 2013)

- EU-LCI value for DEGBE derived by applying default assessment factors: 335.7 $\mu\text{g}/\text{m}^3$ to be used for read-across for calculating the EU-LCI of DEGHE.
- No cut-off rule in place: difference in chain length between the two homologue compounds is not larger than two CH_2 groups per aliphatic chain.

- When applying the EU-LCI value for DEGBE of 335.7 µg/m³ and performing MW conversion: EU-LCI of DEGBE = 335.7 µg/m³ x 1.173 = 393.7 µg/m³ is rounded to 400 µg/m³.

Comparison of proposed EU-LCI with a derived EU-LCI value from a subacute oral study

In the registration dossier of DEGHE a combined repeated dose and reproduction / developmental screening study is described (according to OECD 422 and GLP) as the key study for repeated oral exposure (ECHA, Dissemination 2019). Rats (n=12/sex/dose) were exposed to 0, 100, 300, or 1000 mg DEGHE/(kg bw x d) in their diet for a total of 33 days (males) or 39–52 days (females). Based on liver and body weight effects observed in the highest tested dose, a NOAEL of 300 mg/(kg bw x d) was derived. A route-to-route extrapolation from oral to inhalation route needs to be conducted to derive an EU-LCI value. In line with ECHA guidance (2012) and under the assumption of 50 % oral and 100 % inhalation absorption, the NOAEL was converted into a human equivalent inhalation dose of 300 mg/kg bw x d / 1.15 m³/kg bw x d x 50% / 100% = 130.4 mg/m³. Assessment factors of 2.5 (remaining interspecies differences in inhalation studies), 10 (intraspecies variance), and 6 (time extrapolation from subacute to chronic) were applied (total 150), resulting in a value of 0.87 mg/m³ (= 870 µg/m³).

The derived value of 870 µg/m³ for DEGHE from an oral study with subacute exposure (OECD 422) is higher than the proposed EU-LCI value of 400 µg/m³ based on a read-across approach with DEGBE and applying default assessment factors. The value derived in this way therefore protects against systemic effects of DEGHE when comparing the derived values, since route-to-route extrapolation results in a higher LCI. The proposed EU-LCI value for DEGHE is therefore 400 µg/m³.

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