Compound	**2-Butoxyethyl acetate (EGBEA)**		***Factsheet***
Parameter	**Note**	**Comments**	**Value / descriptor**
EU-LCI value and status			
EU-LCI value	1	Mass/volume [µg/m^3]	2200
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	607-038-00-2
EC No	5	EINECS – ELINCS - NLP	203-933-3
CAS No	6	Chemical Abstracts Service number	112-07-2
Harmonised CLP classification	7	Human health risk-related classification	Acute tox 4
Molar mass and conversion factor	8	[g/mol] and [ppm – mg/m^3]	160.21 1 ppm = 6.65 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	2-Butoxyethanol (EGBE)
Species	11	Rat etc. / human	
Route/type of study	12	Inhalation, oral feed,…	
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 EGBE
POD value	17	[mg/m^3] or [ppm] or [mg/kg$_{BW}$×d]	1600 mg/m^3
Assessment factors (AF)	**18**		
Adjustment for exposure duration	19	Study exposure hours/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)	1600 µg/m³ and 242 ppb
Molar adjustment factor	29	Used in read-across	1.35 (160.21/118.18)
Rounded value	30	[µg/m³]	2200
Additional comments	31		
Rationale section	32		

In animals, 2-butoxyethyl acetate (EGBEA) is rapidly hydrolysed into 2-butoxyethanol (EGBE) and acetic acid. The metabolism of EGBEA was investigated in vitro in rat plasma. The plasma half-life is 0.96 minutes. For this reason, the systemic toxicity of EGBEA can be considered substantially similar to that of EGBE.

There is no data available on the absorption of 2-butoxyethyl acetate orally or by inhalation. The absorption of EGBE is 100 % by ingestion and 60 % by inhalation. Penetration via the skin is also relevant to the absorption of glycol ethers. Due to its very rapid hydrolysis, the distribution, transformation and elimination of EGBEA are the same as for EGBE; the major metabolite is butoxyacetic acid.

2-Butoxyethanol is a clear colourless liquid that smells like ether, with an odour threshold between 0.1 and 0.48 ppm (https://hazmap.nlm.nih.gov/category-details?table=copytblagents&id=130).

Toxicity in humans

No evidence exists to assess the toxicity of EGBEA. Because of its rapid metabolism into EGBE, it is assumed that the human effects of the two substances are similar.

Acute poisoning can cause neurological and metabolic disorders, especially acidosis and haemolysis. Workers exposed through inhalation and dermal routes to cleaning solvents, one of which was EGBEA, complained of headache, nausea, somnolence, sinus problems (unspecified) and chest burning.

There is no other specific data concerning the chronic toxicity of this substance and possible carcinogenic, mutagenic or reproductive toxicity.

Toxicity in animals

The data on repeated exposure to EGBEA are limited; the major effect is haematotoxicity. Orally (186 mg/kg/day, 5 days/week for 5 weeks), signs of haematological toxicity have been observed in two species (rabbit: slight decrease in haematocrit at the end of exposure; cat: decrease in the red blood cell count (RBC) and haemoglobin (30-50 %), reversible within 2 to 3 weeks) [BASF, 1964].

Two inhalation studies have been conducted on several species [BASF 1965; Dutertre-Catella 1978; Truhaut 1979]. Haematotoxicity was clear in rats and rabbits (340 ppm, 6 hours/day, 5 days/week for 4 weeks). It was related to lethality, apathy, hyperventilation and kidney damage. Females were more susceptible than males. Exposure to 100 ppm, 4 hours/day, 5 days/week for 10 months had no effect on haematological parameters. There were no significant renal or testicular effects. The renal histological lesions were slight: some tubular necrosis areas with inflammatory fibrosis.

In cats, the effects were less (salivation and nausea, hyperventilation, decreased haemoglobin reversible after 9 days, no haemoglobinuria). No effect was observed in mice and guinea pigs.

Two carcinogenicity studies indicated an increase of haemangiosarcoma in male mice and pre-stomach tumours in female mice. No effect was observed in rats.

Reproductive toxicity

Fertility

After inhalation of EGBEA, either acute (400 ppm or 2700 mg/m³) or repeated (100 ppm, 10 months), no lesions were observed in the testes or ovaries of rats or rabbits. The result was the same for oral exposure in rats (188

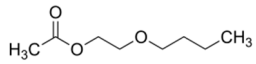
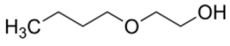
mg/kg/day for 1 month) and skin exposure in rabbits (≤ 10 000 mg/kg for 24 h) [Brondeau 2007]. However 2-Butoxyethanol was found to have testicular effects at low and high doses in combination with significant systemic toxicity [Nagano, 1979 and 1984].

Development
EGBEA's effects on development have not been tested. EGBE is embryo- and/or foetotoxic at doses toxic to the mothers. It is not teratogenic.

Due to the rapid hydrolysis of EGBEA into EGBE and acetic acid, health data on EGBE may be used as the basis for assessing the health effects of its acetate and for the derivation of the EU-LCI.

Rationale for read-across

- Data-poor compound: no adequate toxicological data for EGBEA; *de novo* derivation of EU-LCI is not possible.
- Read-across candidate compounds for starting value: within its chemical class, EGBE is the closest homologue with an EU-LCI value.
- Toxicological critical endpoints for homologue compound:
    - EGBE: haemosiderin deposition in the liver
- The key assumption underlying the read-across of the EU-LCI value from EGBE to EGBEA is that the two compounds have a similar toxicity profile.
- The chemical structure and molecular weight of EGBE and EGBEA are listed in the table below:

Compounds	Structure	MW [g/mol]	EU-LCI value
EGBEA		160.21	
EGBE		118.18	1600 µg/m^3 (*de novo* protocol) Unrounded value: 1600 µg/m^3 or 242 ppb

- No cut-off rule in place: the difference in change length between the two homologue compounds is smaller than two CH2 groups per aliphatic chain.
- Thus, after molar weight conversion at 23 °C and 1 atm: EU-LCI for EGBEA = 1600 µg/m^3 x 1.35 = 2160 µg/m^3 → to be rounded to 2200 µg/m^3.

References

BASF AG (1964). Abteilung Toxikologie, unveroeffentlichte Untersuchung Toxicology Division (XIII/99 und XIII/183).

BASF AG (1965). Abteilung Toxikologie, unveroeffentlichte Untersuchung Toxicology Division (XIII/99)

Brondeau M.T., Bonnard N., Jargot D., Falcy M., Schneider O. (2007). Acétate de 2-butoxyéthyle. Paris: Institut National de Recherche et de Sécurité (INRS). Fiche Toxicologique n°26.
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Dutertre-Catella H, Nguyen PL, Dang Quoc Q, and Truhaut R. 1978. Metabolic transformations of the 3,5,5-2-cyclohexene-1-one trimethyl (isophorone). Toxicol. Eur. Res. 1(4):209-216.

Nagano K., Nakayama E., Koyano M., Oobayashi H., Ad achi H., Yamada T. (1979). Testicular atrophy of mice induced by ethylene glycol mono alkyl ethers (author's transl). Sangyo Igaku; 21(1):29-35.

Nagano K., Nakayama E., Oobayashi H., Nishizawa T., Okuda H., Yamazaki K. (1984). Experimental studies on toxicity of ethylene glycol alkyl ethers in Japan. Environ Health Perspect. 57:75-84.

Truhaut R., Dutertre-Catella H., Phu-Lich N., Huyen V.N. (1979). Comparative toxicological study of ethylglycol acetate and butylglycol acetate. Toxicol Appl Pharmacol. 51(1):117-127.