Compound	2-Butenal		Factsheet
Parameter	**Note**	**Comments**	**Value / descriptor**
EU-LCI value and status			
EU-LCI value	1	Mass/volume [µg/m^3]	5
EU-LCI status	2	Draft/final	Final
EU-LCI year of issue	3	Year when the EU-LCI value was issued	2015
General Information			
CLP Index No	4	INDEX	605-009-00-
EC No	5	EINECS — ELINCS — NLP	224-030-0 204-647-1
CAS No	6	Chemical Abstracts Service number	4170-30-3 123-73-9 15798-64-8
Harmonised CLP classification	7	Human health risk-related classification	Acute Tox. 3, Acute Tox. 3, Skin Irrit. 2, Eye Dam.1, Acute Tox. 2, STOT SE 3, Muta.2, STOT RE 2
Molar mass and conversion factor	8	[g/mol] and [ppm — mg/m^3]	70.08 1 ppm = 2.88 mg/m^3
Key data / database			
Key study, author(s), year	9	Critical study with lowest relevant effect level	Fannick, 1982
Read-across compound	10	Where applicable	
Species	11	Rat etc. / human	Human (workers)
Route/type of study	12	Inhalation, oral feed, etc.	Inhalation
Study length	13	Days, subchronic, chronic	Chronic
Exposure duration	14	Hours/day, days/week	8 hours
Critical endpoint	15	Effect(s), site of	Irritation
Point of departure (POD)	16	LOAEC*L, NOAEC*L, NOEC*L, benchmark dose, etc.	LOAEL
POD value	17	[mg/m^3] or [ppm] or [mg/kg$_{BW}$×d]	0.35 ppm
Assessment factors (AF)	**18**		
Adjustment for exposure duration	19	Study exposure hours/day, days/week	4.2 (8h/day & 5 days/week)
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	3
	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	5

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)*	3
Result			
Summary of assessment factors	27	Total Assessment Factor (TAF)	189
POD/TAF	28	Calculated value (µg/m^3 and ppb)	5.31 µg/m^3 (1.85 ppb)
Molar adjustment factor	29	Used in read-across	
Rounded value	30	[µg/m^3]	5
Additional comments	31		
Rationale section	32		

Data compilation sheet

Crotonaldehyde (2-butenal) exists as the cis and the trans isomer; commercial crotonaldehyde is a mixture of the two isomers consisting of >95 % trans isomer.

A data compilation sheet was created for 2-butenal. However, there was a scarcity of data: no reference values for inhalation non-cancer have been derived by ATSDR, US EPA, WHO or OEHHA. The SCOEL evaluation of 2-butenal (2013) mentioned several human and animal inhalation studies. SCOEL concluded that no health based OEL could be established based on the available data. In addition, IPCS (2008) concluded that it is not possible to adequately evaluate the toxicity of 2-butenal in humans or to derive a tolerable concentration due to lack of reliable data.

The National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances has established AEGL-1 values for 2-butenal. The AEGL-1 is the airborne concentration (expressed as ppm or mg/m^3) of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic nonsensory effects. However, the effects are not disabling and are transient and reversible upon cessation of exposure. The AEGL-1 value for 2-butenal of 0.19 ppm (550 µg/m^3) for 10 minutes — 8 hours is based on the workers study of Fannick (1982). At a U.S. chemical plant some workers who were exposed to approximately 0.56 ppm of crotonaldehyde reported occasional minor eye irritation (Fannick 1982).

POD and assessment factors

Some acute inhalation studies have been carried out on volunteers and workers. Most of these studies were carried out over a very short period of time (Table 1).

Table 1. Human data on odorous and irritative properties of 2-butenal (adapted from AEGL 2007; and SCOEL 2013).

Exposure level (ppm)	Exposure duration	Effects	References
0.035-0.2 0.037-1.05 0.12	Undefined (few seconds)	Odour threshold. Secondary sources, descriptions of most original studies unavailable.	Verschueren 1996, Ruth 1986, Amoore and Hautala 1983
0.038	Undefined (few seconds)	Subjects exposed multiple times. Roughly half of them detected odour at this level.	Tepikina *et al* 1997
0.17	1 min	Odour detection and/or irritation, exposure via mask, undefined analytical method.	Trofimov 1962

0.56	< 8 hours	Occasional eye irritation, concentration up to 1.1 ppm, co-exposure to other chemicals.	Fannick 1982
4.1	15 min (10 min)	Marked respiratory irritation, lacrimation after 30 sec, co-exposure to cigarette smoke.	Sim and Pattle 1957
3.5-14	Undefined	Irritation sufficient to wake a sleeping person.	Fieldner *et al* 1954
3.8	10 sec	'Irritating within 10 sec'; no further details.	
7.3	Undefined (seconds?)	Very sharp odour and strong irritation to the eye and nose; no experimental details.	Dalla *et al* 1939
8 14 (nose) 19 (eyes)	Undefined (few seconds)	Irritation threshold; methods used to determine or define 'irritation' not given.	Ruth 1986, Amoore and Hautala 1983
15	<30 sec	Lab workers 'sniffed' 2-butenal. Odour strong but not intolerable; no eye discomfort.	Rinehart 1967
45-50		Odour strong, pungent, and dis-agreeable. Burning eye sensation but no lacrimation.	

The Fannick study (1982) is considered as the most relevant one for using as POD for deriving an EU-LCI value since the duration of the exposure in that study is up to 8 hours and the critical endpoint is eye irritation.

In the Fannick study (1982), NIOSH conducted a health hazard evaluation in a chemical plant (Sandoz Colors and Chemicals) in East Hanover, New Jersey, at the request of workers at the plant, some of whom complained of occasional minor eye irritation (Fannick 1982). NIOSH measured crotonaldehyde air concentrations using midget impingers; analysis was performed using gas chromatography with flame ionisation detection. Eight air samplers were placed near the vats of chemicals and two were worn by the NIOSH industrial hygienist, who was near the vats most of the time. These measurements likely overestimated the actual exposure concentrations because workers were allowed to move about and were not near the vats during an entire 8 hour work shift. NIOSH determined that the average crotonaldehyde concentration of general air samples was 1.6 mg/m^3 (0.56 ppm; range, <0.35 to 1.1 ppm).

These workers were also simultaneously exposed to acetic acid and small amounts of acetaldehyde (which occasionally caused a perceptible sweet odour), 3-hydroxybutyraldehyde, and dimethoxane. Crotonaldehyde was probably the most potent irritant among these chemicals, based on its greater quantity and its much lower RD50 (reference dose—the concentration that decreases the respiration rate of mice by 50 % due to respiratory irritation [Schaper, 1993; Fannick 1982]).

Since no personal monitoring data and related health complaints database was available from the Fannick study (1982), it is difficult to assess from which exposure onwards health complaints occurred, and hence deriving a NOAEL or LOAEL. As a conservative approach, it was assumed that health complaints could not be excluded at the lowest of the reported exposure concentrations in the study (0.35 ppm). The lowest value of exposure range of the workers (0.35 ppm) is therefore considered as a LOAEL and used as POD for deriving the EU-LCI value.

An adjustment factor of 4.2 was applied for adjustment of duration exposure, from 8 hour/day and 5 day/week. This could be regarded as a conservative factor since the exposure-relationship is probably concentration and not dose driven since the endpoint is irritation (which is in general concentration driven).

An adjustment factor of 3 was applied for dose-response relationship to convert a LOAEL into a NOAEL.

Additionally, the default intraspecies factor of 5 was applied, for cases where an occupational study is used as POD.

A factor of 3 was used for 'Quality of whole database'. This factor was applied given the scarcity of database. The poor present state of knowledge was used as argument by other agencies (IPCS, SCOEL) for the inability to derive tolerable concentrations safe for human exposure via inhalation.

The POD (0.35 ppm) divided by TAF of 189 results in an EU-LCI value of 1.85 ppb or 5.31 µg/m^3, which was rounded to 5 µg/m^3.

The derived EU-LCI value is below the odour threshold for 2-butenal (0.035 – 0.2 ppm: see table 1).

Literature:

SCOEL, 2013. Recommendation from the Scientific Committee on Occupational Exposure Limits for 2-butenal. SCOEL/SUM/180.

AEGL (2007). Committee on Acute Exposure Guideline Levels, Committee on Toxicology, National Research Council. Acute exposure guideline levels for selected airborne chemicals: Volume 6. Crotonaldehyde trans and cis +trans. ISBN: 0-309-11214-1, 318 pages. http://www.nap.edu/catalog/12018.html.

IPCS, International Programme on Chemical Safety (2008). Concise International Chemical Assessment Document 74. 2-Butenal. ISBN 978 92 4 153074 3. http://www.inchem.org/documents/cicads/cicads/cicad74.pdf.

Fannick N (1982). Health hazard evaluation report, No. HETA-81-102-1244, Sandoz Colors and Chemicals, East Hanover, New Jersey, United States National Institute for Occupational Safety and Health, Hazard Evaluations and Technical Assistance Branch, Cincinnati, OH, cited in AEGL 2007.