BETA-PROPIOLACTONE

CAS number:	57-57-8
Synonyms:	BPL, hydracrylic acid, β-lactone, 2-oxetanone, 3-propanolide, 3-propiolactone
Chemical formula:	$C_3H_4O_2$
Structural formula:	—

Workplace exposure standard (retained)

TWA:	**0.5 ppm (1.5 mg/m^3)**
STEL:	**—**
Peak limitation:	**—**
Notations:	**Carc. 1B, Sk., DSEN**
IDLH:	**—**

Sampling and analysis: The recommended value is quantifiable through available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 0.5 ppm (1.5 mg/m^3) is recommended to protect for respiratory irritation in exposed workers.

Given the limited data available from the primary sources about relevance of carcinogenic effects, it is recommended that a review of additional sources be conducted at the next scheduled review.

Discussion and conclusions

β-Propiolactone (BPL) is used as a vapour sterilant for plasma, vaccines, tissue grafts and surgical instruments and as a vapour-phase disinfectant in enclosed spaces.

The critical effect of exposure is respiratory irritation. Although respiratory irritation is not demonstrated, it is based on skin irritation observed in animals. There is also the potential for skin cancer as evidenced in animals.

There are no toxicological data in humans and limited data in animals. BPL is reported to be an irritant and to induce papillomas and carcinomas after topical application to mouse skin. Concentration-related increases in the number of papillomas and carcinomas is reported in studies following lifetime skin-painting of liquid in studies conducted in mice (ACGIH, 2018; IARC, 1999). Evidence suggests that carcinogenicity may act through a mutagenic mechanism and DFG (2005) note it is a proven genotoxic carcinogen. However, the cancers reported in animals manifest *via* dermal exposure to liquids and there is a lack of data available to confirm this effect in humans through the inhalational route. Therefore, it is unclear if a non-threshold mechanism for cancer is a critical effect in recommending a TWA.

The TWA of 0.5 ppm (1.5 mg/m^3) published by SWA and ACGIH is recommended to protect for irritation.

A review of additional data sources is recommended at the next scheduled review to confirm the relevance of carcinogenic effects.

Recommendation for notations

Classified as a category 1B carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Classified as a skin sensitiser and not a respiratory sensitiser according to the GHS.

A skin notation is recommended based on evidence in animals of carcinogenic effects following dermal exposure.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1991***	***TWA: 0.5 ppm (1.5 mg/m^3)***
ACGIH	***2001***	***TLV-TWA: 0.5 ppm (1.5 mg/m^3)***
TLV-TWA recommended to minimise the potential for respiratory irritation; also recommended to avoid all contact with liquid BPL to protect for skin carcinogenicity reported in animals following lifetime skin painting. Summary of data: No specific derivation of TLV provided; refers to ethylenimine. Human data: • Reports US EPA calculated a human skin permeability coefficient of 0.00033 cm/h. Animal data: • 30 min LC_{50} of ≈250 ppm; 6 h LC_{50} of 25 ppm (rats) • An irritant and induced papillomas and carcinomas after topical application to mouse skin; no further information • Concentration-related increase in the numbers of papillomas and carcinomas following lifetime skin-painting studies conducted in mice; application 3 times/wk at solution doses of 0.25%–5% BPL • Positive genotoxicity in *S. typhimurium*. Insufficient data to recommend a skin or sensitiser notation of TLV-STEL.		
DFG	***2004***	***Not assigned***
No MAK assigned due to carcinogenicity in rodents; cited 1976 review as justification. Summary of additional data: • 'H' skin absorption notation assigned based on calculated dermal flux of 0.480 mg/m^2/h.		
SCOEL	***NA***	***NA***
No report.		
OARS/AIHA	***NA***	***NA***
No report.		
HCOTN	***NA***	***NA***
No report.		

Secondary source reports relied upon

Source		Year	Additional information
NICNAS	✓	2015	• Rapidly metabolised and excreted in mammals as lactic acid (no further information) • LD_{50}: ≈50–100 mg/kg (rats, oral) • Strong skin sensitiser based on the positive results in a single LLNA.
IARC	✓	1999	• Direct-acting alkylating agent; forms DNA adducts; mutagenic in a wide variety of *in-vitro* and *in-vivo* systems, both in somatic and germ cells • Sufficient evidence in experimental animals for the carcinogenicity • Possibly carcinogenic to humans.
US EPA	✓	1991	• No further information.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic?	Yes
Is the chemical carcinogenic with a mutagenic mechanism of action?	Insufficient data

Insufficient data are available to determine if the chemical is a non-threshold based genotoxic carcinogen.

Notations

Source	Notations
SWA	Carc. 1B
HCIS	Carcinogenicity – category 1B, Skin sensitisation – category 1
NICNAS	Carc. Cat 2, Skin sensitisation
EU Annex	Carcinogenicity – category 1B
ECHA	Carc. 1B
ACGIH	Carcinogenicity – A3
DFG	Carcinogenicity – 2, H (skin)
SCOEL	NA
HCOTN	NA
IARC	Carcinogenicity – Group 2B
US NIOSH	NA

NA = not applicable (a recommendation has not been made by this Agency); — = the Agency has assessed available data for this chemical but has not recommended any notations

Skin notation assessment

Calculation		
Adverse effects in human case study:		
Dermal LD_{50} ≤1000 mg/kg:		
Dermal repeat-dose NOAEL ≤200 mg/kg:		
Dermal LD_{50}/Inhalation LD_{50} <10:		
In vivo dermal absorption rate >10%:		
Estimated dermal exposure at WES >10%:	yes	
		insufficient data to assign a skin notation

IDLH

Is there a suitable IDLH value available?	No

Additional information

Molecular weight:	72.06
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 2.94 mg/m^3; 1 mg/m^3 = 0.340 ppm
This chemical is used as a pesticide:	☐
This chemical is a biological product:	☐
This chemical is a by-product of a process:	☐
A biological exposure index has been recommended by these agencies:	☐ ACGIH ☐ DFG ☐ SCOEL

Workplace exposure standard history

Year	Standard
Click here to enter year	

References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7th Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the *TLVs® and BEIs® Guidelines section* on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (2004) b-Propiolacton – MAK value documentation.

European Chemicals Agency (ECHA) (2019) ,3-propiolactone – REACH assessment.

International Agency for Research on Cancer (IARC) (1999) beta-Propiolactone. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2015) 2-Oxetanone: Human health tier II assessment – IMAP report.

Tenth Adaptation to Technical Progress Commission Regulation (EU) No 2017/776 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures (the CLP Regulation).

US Environmental Protection Authority (US EPA) (1991) Integrated Risk Information System (IRIS) Chemical Assessment Summary – Beta-Propiolactone.