

PROPANE SULTONE

CAS number: 1120-71-4

Synonyms: 3-Hydroxy-1-propanesulphonic acid sultone,
1,2-oxithiolane-2,2-dioxide, 1,3-propane sultone

Chemical formula: C₃H₆O₃S

Structural formula: —

Workplace exposure standard (new)

TWA: —

STEL: —

Peak limitation: —

Notations: Carc. 1B, Sk.

IDLH: —

Sampling and analysis: NA

Recommendation and basis for workplace exposure standard

Insufficient data are available to derive a risk-based occupational exposure level. Any exposure at the workplace is recommended to be strictly avoided to protect workers from cancer.

A priority in-depth assessment of additional data sources for propane sultone is recommended.

Discussion and conclusions

Propane sultone was used as a chemical intermediate to introduce sulfopropyl groups into molecules and to confer water solubility and anionic character. No specific Australian use, import or manufacturing information is identified.

The critical effect of exposure is cancer.

Propane sultone is carcinogenic in animals through multiple routes of exposure and it is assumed to have carcinogenic potential in humans by some sources. ACGIH (2018) classify its carcinogenicity as 'of unknown relevance to humans' and IARC (2017) has classified it as a possible human carcinogen. SCOEL (2013) conclude that it is a genotoxic carcinogen without a threshold. DFG (1992) and NICNAS (2013) cite the critical effects to humans as carcinogenicity and genotoxicity. Mutagenicity is demonstrated in both *in vitro* and *in vivo* studies. The mechanism of action for carcinogenicity may act *via* a mutagenic mode of action (DFG, 2013; IARC, 2017; SCOEL 2013). For the purposes of this assessment, propane sultone is assumed to be a non-threshold-based genotoxic carcinogen.

Insufficient data are available to derive a risk-based TWA. Noting there are inconsistent data and decisions about the carcinogenicity potential of propane sultone in humans, it is recommended that an investigation of additional data sources is undertaken as a priority.

Recommendation for notations

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

Not classified as a skin sensitiser or respiratory sensitiser according to the GHS.

A skin notation is recommended based on evidence in animals of dermal uptake and adverse systemic effects.

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APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	NA	NA
No report.		
ACGIH	2001	Not assigned
TLV-TWA not recommended due to insufficient data to derive a concentration. Summary of data: <ul style="list-style-type: none"> No human data presented. Animal data: <ul style="list-style-type: none"> Carcinogenic in rats and mice by several routes of administration A single subcutaneous dose of 100 mg/kg produced local sarcomas in all treated rats (n = 18) In rats treated with a single iv bolus of 150 mg/kg, 1/32 rat died with a brain tumour after 235 d and 9/32 died with malignant tumours of a variety of sites within 459 d Malignant neurogenic tumours in the offspring of pregnant rats given a single iv dose of 20 mg/kg of GD 15 Various types of malignant tumours including tumours of the brain in rats dosed chronically <i>via</i> oral intubation at 30 mg/kg/wk or 56 mg/kg twice weekly In mice, weekly subcutaneous injections of 0.3 mg in distilled water produced tumours at the injection site In rats, weekly or single IV administration of 20, 40 or 150 mg/kg, resulted in various types of tumours, mostly affecting the nervous system Skin painting in mice resulted in statistically significant increase in systemic neoplasia including cancers of lymphoreticular and lung origin; mammary gland and uterine tumours observed in female mice; no further information. Confirmed animal carcinogen. Insufficient data to recommend skin or sensitiser notations or TLV.		
DFG	1992	Not assigned
No MAK assigned due to carcinogenicity. Summary of additional data: <ul style="list-style-type: none"> Considered as unequivocally carcinogenic as evidenced in animals Tumour induction in humans not yet reported at time of review Tumours developed in rats and mice following single and repeated application (cited by ACGIH, 2018) 52 rats treated orally at 28 mg/kg, 2/wk for 60 wk: <ul style="list-style-type: none"> 27 gliomas 12 mixed tumours 8 mammary carcinomas 5 intestinal tumours 		

Source	Year set	Standard
		<ul style="list-style-type: none"> ○ 2 leukoses ○ 1 tumour of the auditory canal. • 12 rats dosed at 15 mg/kg by iv injection 1/wk, for 21 wk: <ul style="list-style-type: none"> ○ 7/12 local sarcomas at the injection site (4 myosarcomas, 3 fibrosarcomas) ○ 1 neurosarcoma ○ 1 carcinoma in the large intestine. • Produces both local tumours (skin, mucosa of the small intestine) and systemic tumours in rats and mice; systemic tumours practically independent of the application route • Induces systemic tumours after skin application in mice; skin notation warranted. <p>Genotoxicity</p> <ul style="list-style-type: none"> • Ames plate-incorporation assay in <i>S. typhimurium</i> TA98, TA100, TA1535, TA1536, TA1537, TA1538: <ul style="list-style-type: none"> ○ positive without S9 mix in TA100 and TA1535; negative in TA98, TA1536, TA1537, TA1538. • 6 tests in combination: Ames test in <i>S. typhimurium</i> (4 strains); mammalian cell transformation test (BHK21/cl13 + Syrian hamster kidney cells); degranulation of rat liver rough endoplasmic reticulum; tetrazolium reduction test; mouse skin sebaceous gland suppression test; subcutaneous implantation test; all tests returned positive results apart from mouse skin sebaceous gland suppression test • Positive in <i>E. coli</i> Ames • Mutagenicity demonstrated in a large number of tests.



Source	Year set	Standard
SCOEL	2013	Not assigned
Categorised as a genotoxic carcinogen without a threshold and therefore a health-based OEL cannot be derived.		
Summary of additional data:		
<ul style="list-style-type: none"> Alkylating chemical, which is highly reactive towards DNA and proteins In Germany, a group of 55 male workers who previously handled the compound at 1 company were later subject to medical surveillance: <ul style="list-style-type: none"> production and use of propane sultone was discontinued after recognition of its carcinogenicity in experimental animals a first review revealed several malignancies at sites similar to those observed in animal experiments a follow-up revealed 20/55 workers were diseased with tumours at sites consistent with those identified experimentally in rodents (except mammary); <ul style="list-style-type: none"> noted were 1 case of a duodenal carcinoma and 1 malignant schwannoma, normally being a very rare human malignancy data interpreted to provide a clear indication of carcinogenicity in humans 12 cases legally compensated as having contract occupational cancer no dose-response data available. Causes DNA damage and mutation in bacteria and induces mitotic recombination in yeast DNA strand breaks are induced in brain cells from rats injected with propane sultone; directly mutagenic and carcinogenic Recommends that any contact of humans with propane sultone is avoided. 		
OARS/AIHA	NA	NA
No report.		
HCOTN	NA	NA
No report.		

Secondary source reports relied upon

Source	Year	Additional information
NICNAS	✓ 2016	<ul style="list-style-type: none"> No specific Australian use, import or manufacturing information has been identified LD₅₀: 660 mg/kg (rabbits, dermal) Bacterial reverse mutation assay (≡OECD TG 471) without metabolic activation showed positive results in <i>S. typhimurium</i> strains TA 1535, TA 1537, TA 98, TA 100, TA 102 and TA 97 On the case report of 55 male workers in Germany (as cited by SCOEL, 2013); confounding factors do not allow a clear conclusion as to carcinogenicity of the chemical in humans.



Source	Year	Additional information
IARC	✓ 2017	<ul style="list-style-type: none"> On the case report of 55 male workers in Germany (as cited by SCOEL, 2013); without comparative data on the number of cancers expected, it is difficult to interpret the findings of this study, which is essentially a case series among an exposed population DNA reactivity is evident in a variety of assays for genotoxicity, including in experimental animals and with human cells <i>in vitro</i>; considered to have strong direct genotoxic properties Inadequate evidence in humans for the carcinogenicity Sufficient evidence in experimental animals for carcinogenicity Probably carcinogenic to humans (Group 2A).

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? Yes

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

The chemical is a non-threshold based genotoxic carcinogen.

Is a cancer slope factor or inhalation unit risk value available? No

Notations

Source	Notations
SWA	NA
HCIS	Carcinogenicity – category 1B
NICNAS	Carc. Cat 2, Skin
EU Annex	Carcinogenicity – category 1B
ECHA	Carc. 1B
ACGIH	Carcinogenicity – A3
DFG	Carcinogenicity – 1, H (skin)
SCOEL	Carcinogenicity – A, Skin
HCOTN	NA
IARC	Carcinogenicity – Group 2A
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:	no
Dermal LD ₅₀ ≤ 1000 mg/kg:	yes
Dermal repeat-dose NOAEL ≤ 200 mg/kg:	
Dermal LD ₅₀ /Inhalation LD ₅₀ < 10:	
<i>In vivo</i> dermal absorption rate > 10%:	
Estimated dermal exposure at WES > 10%:	
consider assigning a skin notation	

IDLH

Is there a suitable IDLH value available? No

Additional information

Molecular weight:	122.15
Conversion factors at 25°C and 101.3 kPa:	1 ppm = Number mg/m ³ ; 1 mg/m ³ = Number ppm
This chemical is used as a pesticide:	<input type="checkbox"/>
This chemical is a biological product:	<input type="checkbox"/>
This chemical is a by-product of a process:	<input type="checkbox"/>
A biological exposure index has been recommended by these agencies:	<input type="checkbox"/> ACGIH <input type="checkbox"/> DFG <input type="checkbox"/> 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) (1992) Propane sultone – MAK value documentation.

European Chemicals Agency (ECHA) (2019) Propane sultone – REACH assessment.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2013) Recommendation from the Scientific Committee on Occupational Exposure Limits for Propane sultone. SCOEL/SUM/189.

International Agency for Research on Cancer (IARC) (2017) Propane sultone. IARC Monographs on the evaluation of the carcinogenic risk to humans.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2015) 1,2-Oxathiolane, 2,2-dioxide: 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).

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