Australian Government
Department of Health and Aged Care
Australian Industrial Chemicals Introduction Scheme

1-Propanesulfonic acid, 2-hydroxy-3-(2-propenyloxy)-, monosodium salt

Evaluation statement

14 December 2023

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AICIS evaluation statement

Subject of the evaluation

1-Propanesulfonic acid, 2-hydroxy-3-(2-propenyloxy)-, monosodium salt

Chemical in this evaluation

Name	CAS registry number
1-Propanesulfonic acid, 2-hydroxy-3-(2-propenyloxy)-, monosodium salt	52556-42-0

Reason for the evaluation

Evaluation Selection Analysis indicated a potential human health risk.

Parameters of evaluation

The chemical is listed on the Australian Inventory of industrial Chemicals (the Inventory). The evaluation is a human health risk assessment for all identified industrial uses of the chemical.

Summary of evaluation

Summary of introduction, use and end use

There is currently no specific information about the introduction, use or end use of the chemical in Australia. Based on international information, the chemical is mainly used in commercial production of:

- resin products
- water treatment products
- paints and coatings
- adhesives
- sealants.

The chemical is also used as an intermediate, as a fuel additive, in polymerisation and formulations and in latex particle stabilisation. No consumer uses were identified.

Human health

Summary of health hazards

The identified health hazards are based on available data for the chemical. Based on the physicochemical properties the chemical is expected to be poorly absorbed following oral, dermal and inhalation exposure.

Based on the available data, the chemical:

- has low acute and dermal toxicity
- is not considered to be a skin sensitiser
- is not expected to cause serious systemic health effects following repeated oral or dermal exposure
- is not considered to have genotoxic potential.

Based on the results from available in vitro studies the chemical (in powder form) is a slight skin irritant. However, in aqueous solution the chemical may cause corrosive effects due to formation of basic solutions. The chemical is considered to be corrosive to the eye, based on the results from an available in vitro study (OECD TG 437).

Based on the available data, the chemical is potentially toxic to reproduction (loss/lack of pregnancy) following repeated exposure at doses of 62.5 mg/kg bw/day and higher. The effects on fertility observed were: a dose dependent decrease in female mating index, a dose-dependent reduction in corpora lutea, and adverse effects on litter size and pup survival. Although some marginal effects on development were observed in reproductive/developmental toxicity screening study (OECD TG421), a dose response could not be established due to complete lack of pregnancies at higher dose levels. These effects were not observed in two developmental toxicity studies (OECD TG 414).

No inhalation toxicity data were available. For further details of the health hazard information see **Supporting information**.

Hazard classifications relevant for worker health and safety

The chemical satisfies the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (UNECE 2017) for hazard classes relevant for work health and safety as follows. This does not consider classification of physical hazards and environmental hazards.

Health hazards	Hazard category	Hazard statement
Serious eye damage/eye irritation	Eye Damage 1	H318: Causes serious eye damage
Reproductive toxicity	Repr.1B	H360F: May damage fertility

Summary of health risk

Public

Based on the available use information it is unlikely that the public will be significantly exposed to the chemical. Although the public could come into contact with articles and/or coated surfaces, it is expected that the chemical will be bound within articles and coated surfaces.

Overall, there are no identified risks to the public that require management.

Workers

During product formulation and packaging, oral, dermal, ocular and inhalation exposure might occur, particularly where manual or open processes are used. These may include transfer and blending activities, quality control analysis, cleaning and maintaining equipment. Worker exposure to the chemicals at lower concentration could also occur while using formulated products, such as paints and coatings, containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical local and systemic long-term effects, the chemical could pose a risk to workers. The risks of the chemical may vary depending on the physical form of the chemical i.e. neat powder or aqueous solution. Control measures to minimise dermal, ocular and inhalation exposure are needed to manage the risk to workers (see **Proposed means for managing risks** section).

Proposed means for managing risk

Workers

Recommendation to Safe Work Australia

It is recommended that Safe Work Australia (SWA) update the Hazardous Chemical Information System (HCIS) to include classifications relevant to work health and safety.

Information relating to safe introduction and use

The information in this statement including recommended hazard classifications, should be used by a person conducting a business or undertaking at a workplace (such as an employer) to determine the appropriate controls under the relevant jurisdiction Work Health and Safety laws.

Control measures that could be implemented to manage the risk arising from exposure to the chemical include, but are not limited to:

- using closed systems or isolating operations
- minimising manual processes and work tasks through automating processes
- adopting work procedures that minimise splashes and spills
- cleaning equipment and work areas regularly
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

Measures required to eliminate or manage risk arising from storing, handling and using this hazardous chemical depend on the physical form and how this chemical is used.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk.

Model codes of practice, available from the Safe Work Australia website, provide information on how to manage risks of hazardous chemicals in the workplace, prepare an SDS and label containers of hazardous chemicals. Your Work Health and Safety regulator should be contacted for information on Work Health and Safety laws and relevant Codes of Practice in your jurisdiction.

Conclusions

The Executive Director is satisfied that the identified risks to human health from the introduction and use of the industrial chemical can be managed.

Note:

1. Obligations to report additional information about hazards under *Section 100* of the *Industrial Chemicals Act 2019* apply.
2. You should be aware of your obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

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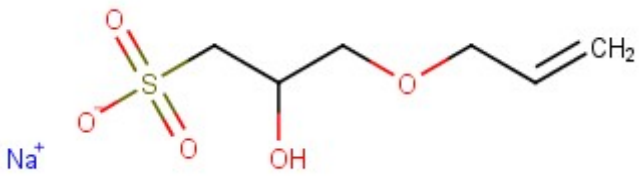
Supporting information

Chemical identity

Chemical name	1-Propanesulfonic acid, 2-hydroxy-3-(2-propenyloxy)-, monosodium salt
CAS No.	52556-42-0
Synonyms	sodium 2-hydroxy-3-(prop-2-en-1-yloxy) propane-1-sulfonate sodium 3- (allyloxy)-2-hydroxypropanesulphonate (HAPS) 3-prop-2-enyloxyprop-1-en-2-ol, sodium salt (IUPAC)
Molecular formula	C6H12O5S.Na
Molecular weight (g/mol)	219.21
SMILES	[Na].O=S(=O)(O)CC(O)COCC=C
Chemical description	-



Structural formula

Relevant physical and chemical properties

The following measured physical and chemical property data were identified (REACH n.d.)

Physical form	Pale yellow powder at 20°C and 1013 hPa, with slight odour
Melting point	No melting point determined because of decomposition of the test item beginning at approximately 177 ºC
Boiling point	N/A
Vapour pressure	0.0002Pa at 20 °C

Water solubility	781.1 g/L at 20 °C
pH	12 (aqueous solution)
pKa	11.0 at 20 °C
log Kow	-1.51 at 25 °C

Introduction and use

Australia

No specific information on the introduction, use and end use of the chemical in Australia has been identified.

International

The chemical has the following reported commercial uses as a component in (REACH n.d.; SPIN; US CDR 2016):

- resin products
- water treatment products and formulations
- paints and coatings
- adhesives and sealants
- fuel additives

The chemical also has various site-limited uses as an intermediate in:

- polymerisation and formulations
- latex particle stabilisation.

There were no products containing the chemical identified in the North American consumer product databases (DeLima Associates). Reported chemical uses in the United States of America were commercial (US CDR 2012; US CDR 2016). No cosmetic uses were reported (Personal care council).

The chemical is listed on the OECD List of HPV (High Production Volume) chemicals (OECD 2009) and US Environmental Protection Authority, 1990 High Production Volume (HPV) Challenge Program Chemical List (US EPA 2006).

Existing Australian regulatory controls

AICIS

No specific controls are currently available for the chemical.

Public

No specific controls are currently available for the chemical.

Workers

The chemical is not listed on the HCIS, and no specific exposure standards are available in Australia (Safe Work Australia).

International regulatory status

Exposure standards

No specific exposure standards were identified.

Health hazard information

Toxicokinetics

Information on the oral, dermal and inhalation adsorption of the chemical is not available.

Based on the physico-chemical properties, the chemical is expected to have low absorption via the dermal route (low log Kow and high ionisation- pKa 11.004) unless the stratum corneum is damaged.

No potential for bioaccumulation is expected due to its hydrophilic nature and low log Kow. Metabolism is expected to be via Phase I and Phase II metabolic reactions and renal and/or faecal excretion of the unchanged molecule is expected (REACH n.d.).

Acute toxicity

Oral

Based on the available data, the chemical has low acute oral toxicity with reported median lethal dose (LD50) of greater than 2000 mg/kg bw in animal studies.

In an acute oral toxicity study, conducted according to OECD Test Guideline (TG) 423, the LD50 was >2000 mg/kg bw in female Sprague Dawley (SD) rats (REACH n.d.).

Dermal

Based on the available data, the chemical is expected to have low acute dermal toxicity.

An LD50 of >2000 mg/kg bw in SD rats was reported in an acute dermal toxicity study conducted according to OECD TG 402 (REACH n.d.).

Inhalation

No data are available for the chemical.

Corrosion/Irritation

Skin irritation

Based on the weight of evidence from available data, the chemical (in powder form) may be slightly irritating to the skin. However, in aqueous solution the chemical may cause irritant or corrosive effects.

The chemical is considered to be not corrosive in an in vitro reconstructed human epidermis (RhE) (OECD TG 431) using the human skin model EpiDerm™. The mean tissue viability was 81.9% and 42.6% after 3 and 60 min exposures, respectively (REACH n.d.).

The chemical is considered to be not irritating to skin in an in vitro reconstructed human epidermis (RhE) test (OECD TG 439) using the human skin model EpiDerm™. The mean tissue viability was 96.9% after 60 min exposure REACH n.d.).

In an in vivo acute dermal toxicity study, where the chemical was tested as an aqueous solution, erythema was observed 24 hours post dose in all animals and was totally reversible on day 7. However, scabs were noted in all animals from 48 hours post exposure remaining on day 14. It is expected that the pH of the aqueous solution is basic because the chemical will dissociate upon dissolution in water. This may explain the formation of scabs in this study (ECHA 2022).

Eye irritation

Based on the available data, the chemical has the potential to cause serious eye damage, warranting hazard classification (see **Hazard classification relevant for worker health and safety** section).

In an ex vivo eye corrosive test conducted in accordance with the OECD TG 437 (Bovine Corneal Opacity and Permeability (BCOP)), an aqueous solution of the chemical produced in vitro irritancy score (IVIS) of 150.3. Based on the prediction model criteria (IVIS greater than 55), the chemical warrants classification for serious eye damage (category 1) according to the UN criteria (ECHA 2022; REACH n.d.).

Sensitisation

Skin sensitisation

Based on the available information, the chemical is not expected to have skin sensitisation potential.

In a local lymph node assay (LLNA) conducted in accordance with OECD TG 429, female CBA/J mice (5/dose) were treated on the ear with the chemical dissolved in ethanol: water (3:7 v/v) at 0, 5, 10 and 25% for 3 consecutive days. Vehicle and positive controls were conducted in parallel with the test chemical. No irritation or clinical toxicity were observed. Non-dose dependent stimulation indices (SI) of 0, 0.69, 0.87 and 0.56 were reported for the tested concentrations, respectively. The chemical was not considered to be a skin sensitiser (REACH n.d.).

The lack of skin sensitisation potential is supported by negative results for skin sensitisation using the mechanistic profiling functionality of the Organisation for Economic Co-operation and Development (OECD) QSAR Application Toolbox (OECD QSAR Toolbox v 4.2- 2018).

Repeat dose toxicity

Oral

Based on the available data, the chemical is not expected to cause serious systemic health effects following repeated oral exposure.

A 28 day gavage study, similar to OECD TG 407, was conducted in Crj:CD (SD) rats (5/sex/dose) with the chemical in water at 0, 25, 150 or 1000 mg/kg bw/day. Loose faeces, diarrhoea and salivation were reported in all animals in the high dose group and 3/10 animals in the mid dose group. Decreased motility and hyperplasia of the squamous epithelium in the anterior stomach in 2/5 males and 3/5 females were also observed in the high dose group. Other observations in this group included significantly decreased basophils in females and high albumin/globulin and low creatinine levels in males. A no observed adverse effect level (NOAEL) of 25 mg/kg bw/day was reported (REACH n.d.).

In a GLP-complaint 90 day gavage study (OECD TG 408; 4-week recovery); Wistar rats 10/sex/dose) were administered the chemical as a neutralised aqueous solution at 0, 100, 300 or 1000 mg/kg bw/day. The NOAEL was reported to be 1000 mg/kg bw/day based on no mortality, no adverse effects on body weight, food consumption and no test item related changes on the gross pathology or histopathology of the treated animals (REACH n.d.).

Dermal

No data are available for the chemical.

Inhalation

No data are available for the chemical.

Genotoxicity

Negative results were reported for the chemical in in vitro mutagenicity tests. In vivo data are not available.

The chemical was reported to have negative results in a:

- GLP-compliant mammalian cell gene mutation assay (OECD TG 476) using thymidine kinase locus (TK1) on mouse lymphoma L5178Y cells, with or without metabolic activation at up to 2180 µg/ml (REACH n.d.)
- GLP-compliant non-guideline bacterial reverse mutation assay in *Salmonella typhimurium* TA1535, TA1537, TA 98, TA 100, and *Escherichia coli* WP2 uvr A, with or without metabolic activation at up to 5000 µg/plate (REACH n. d.)
- GLP-complaint non-guideline mammalian chromosome aberration test in CHL/IU cells, with or without metabolic activation at up to 2.182 mg/mL (REACH n. d.)

No structural alerts for mutagenicity or clastogenicity were observed for the chemical or its metabolites using the OECD QSAR Toolbox v 4.2 (2018).

Carcinogenicity

No data are available for the chemical.

Reproductive and development toxicity

Based on the available information, the chemical is considered potentially toxic to reproduction (effects on fertility) due to reduction or lack of pregnancies, which warrants hazard classification (see **Hazard classification relevant for worker health and safety** section). Although some marginal effects on development were observed in reproductive/developmental toxicity screening study, a dose response could not be established due to complete lack of pregnancies at higher dose levels. These effects were not observed in two developmental toxicity studies.

In a reproductive/developmental toxicity screening study, conducted according to OECD TG 421, the chemical (35.2 % neutralised aqueous solution) was administered by oral gavage to Wistar Han rats (12 /sex/dose) at 0, 62.5, 250 or 1000 mg/kg bw/day. Both males and females were treated with the chemical for two weeks prior to mating. For males, the duration of treatment was 57 days, including during mating and a 42 day post mating period. For females, the duration of treatment was between 40 to 49 days, depending on the date of mating. This included treatment during the mating period, through gestation and up to lactation day 14. Due to high mortality in the high dose group, a satellite was introduced with treatment duration of 42 days in males and 47 days in females. The study results indicated:

- a statistically significant increase in the mean ovaries and uterus weights in all treatment groups.
- no pregnancies were achieved in the mid and high dose groups, and satellite high dose group.
- low dose females achieved 5/12 pregnancy.
- morphological changes were noted in the ovaries of infertile females in the high dose group.

- minimal to slight ovarian hypertrophy/hyperplasia characterised by presence of several tertiary follicles and increased number of interstitial cells
- mean number of corpora lutea was dose dependently decreased in low (7.6), mid (3.3) and high (1.5) dose group, suggesting an effect on fertility
- pregnant dams (4/5) in the low dose group gave birth to 27/29 (mean 5.4) live pups and 2/29 pups were stillborn.
- post-implantation loss in the low dose females was slightly higher than those of control.
- no observed effect on spermatogenesis; however, the treatment duration may not have covered a complete spermatogenesis cycle.
- no significant changes were observed in the body weight and food consumption during the treatment.
- a lowest observed adverse effect level (LOAEL) of 62.5 mg/kg bw/day based on effects on ovaries and uterus and lack of pregnancy (ECHA 2022; REACH n.d.).

In a GLP compliant prenatal development study, similar to OECD TG 414, pregnant Wistar rats (24/dose) were administered the chemical (38.2 % neutralised aqueous solution) by gavage at 0, 100, 300 or 1000 mg/kg bw/day on gestational days (GD) 6–19. No mortality or adverse effects on body weights of dams were noted. No changes in post-implantation or total intrauterine mortality, foetal weights, number of live offspring, litter size and weights, sex-ratio and visceral malformations were observed. Number of litters with skeletal malformations were 2/22 (9.1%), 0/23 (0%) and 3/22 (13.6 %) in the low, mid and high dose groups, respectively. Skeletal malformations included bent scapula, bent ulna, shorter femur, bipartite thoracic vertebra with dumb-bell shaped cartilage, short tail, multiple malformed vertebrae, and fused ribs. Malformations occurred in low incidences and without dose response. Statistically significant increase in incidences of markedly incomplete ossification of one or more skull bones in mid and high dose groups were observed along with statistically significant increase in incidences of wavy ribs in low and high groups. However, effects were within the historical control level. The maternal and foetal NOAELs were considered to be 1000 mg/kg bw/day in this study (ECHA 2022; REACH n.d.).

In OECD TG 414 range finding study, pregnant Wistar rats (5/dose) were treated with 0, 10, 37.5, 125 or 500 mg/kg bw/day by gavage on gestational days (GD) 5-19. Skeletal malformations - split and misaligned sternum and bent ulna were reported in two foetuses at 37.5 mg/kg bw/day dose group. These were not considered treatment related by the study author. No other treatment related adverse effects were reported (ECHA 2022; REACH n.d.).

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