2-Propenoic acid: Human health tier II assessment

04 July 2014

CAS Number: 79-10-7

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

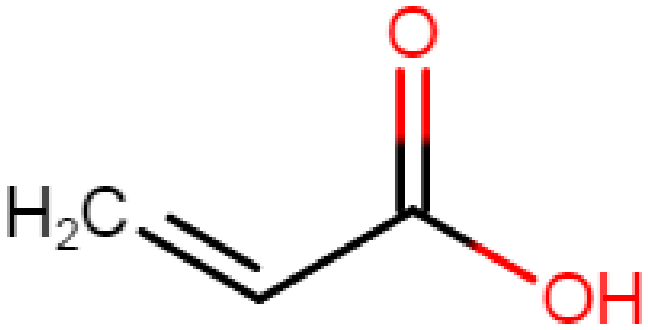
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:www.nicnas.gov.au

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	acrylic acid acroleic acid glacial acrylic acid ethylenecarboxylic acid propene acid
Structural Formula	
Molecular Formula	C3H4O2
Molecular Weight (g/mol)	72.06
Appearance and Odour (where available)	Colourless liquid with a distinctive acrid odour
SMILES	C(=O)(O)C=C

Import, Manufacture and Use

Australian

The following Australian industrial uses were reported under previous mandatory and/or voluntary calls for information:

The chemical has reported domestic use including in adhesives and binding agents.

The chemical has reported commercial use including as a viscosity adjuster.

The chemical is listed on the 2006 High Volume Industrial Chemical List (HVICL) with a total reported volume between 1000 and 9999 tonnes.

The National Pollutant Inventory (NPI) holds data for all sources of the chemical in Australia.

International

The following international uses have been identified through European Union Registration, Evaluation, Authorisation and Restriction of Chemicals (EU REACH) dossiers; Galleria Chemica; Substances and Preparations in the Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database; and eChemPortal: OECD High Production Volume chemical program (OECD HPV), and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB). Some of the reported uses might relate to polymers manufactured from this monomer.

The chemical has reported cosmetic uses:

- as an artificial nail builder; and
- in tonics, dressings and other hair grooming aids.

The chemical has reported domestic uses including in:

- adhesives and binding agents;
- bleaching agents;
- cleaning and washing;
- colouring agents;
- corrosion inhibitors;
- fillers;
- insulating materials;
- paints, lacquers and varnishes; and
- surface treatment and surface-active agents.

The chemical is reported to be present in a range of domestic products including home maintenance products such as lubricants and adhesives up to a concentration of 3 %, auto products up to a concentration of 5 %, and personal care products up to a concentration of 1 % (Household Products Database, US Department of Health and Human Services; HSDB).

The chemical has reported commercial uses including:

- as an anti-set off and anti-adhesive agent;
- in construction materials;
- in friction agents;
- in impregnation materials;
- in lubricants and additives;
- as a process regulator;
- in reprographic agents;
- in softeners;
- in solvents; and
- in viscosity adjustors.

The chemical has reported site-limited use including as a monomer in producing polymers used in complexing and flocculating agents.

The following non-industrial use has been identified internationally in non–agricultural pesticides and preservatives.

Restrictions

Australian

No known restrictions have been identified.

International

The chemical may be used with a specific migration limit (SML) of 6 mg/kg in food packaging, under Annex I of the European Commission Regulation (EU) No 10/2011 of 14 January 2011 on plastics materials and articles intended to come in contact with food (Galleria Chemica).

Existing Work Health and Safety Controls

Hazard Classification

The chemical is classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

- Xn; R20/21/22 (acute toxicity); and
- C; R35 (corrosive).

Exposure Standards

Australian

The chemical has an exposure standard of 5.9 mg/m³ (2 ppm) time weighted average (TWA).

International

The following exposure standard is identified (Galleria Chemica).

An exposure limit (TWA) of 6–30 mg/m³ (2–10 ppm) and STEL of 30–60 mg/m³ (10–20 ppm) in different countries such as Canada, Denmark, France, Germany, Greece and the USA.

Health Hazard Information

Toxicokinetics

The chemical can be readily absorbed through oral, inhalation or dermal exposure (OECD, 2002). Rats that were treated orally with the chemical (150 mg/kg bw) rapidly absorbed and metabolised the chemical, with 80 % of the dose exhaled as CO_2 within 24 hours. Excretion in urine and faeces accounted for 3 % and 1 % of the dose, respectively. Elimination of the chemical from the kidney, liver and plasma was rapid; although, elimination was much slower from fat tissue. After cutaneous application to mice, 12 % of the dose was absorbed resulting in a similar distribution and excretion profile to that observed in orally dosed rats.

Acute Toxicity

Oral

The chemical is classified as hazardous with the risk phrase ‘Harmful if swallowed’ (Xn; R22) in the HSIS (Safe Work Australia). The reported median lethal dose (LD50) values in rats support this classification.

In an acute oral toxicity study, rats were administered the chemical via oral gavage doses of 20, 79, 316, 1260, 2040, 3160 or 5010 mg/kg bw. An LD50 of 1500 mg/kg bw was determined in rats. In a similar study, Wistar rats were treated with a 10 % aqueous solution of the chemical (99 % purity, pH 2.5) via oral gavage doses of 700, 900, 1100 or 1350 mg/kg bw. An LD50 of 1350 mg/kg bw was established for the chemical. Histopathological examination revealed necrosis in the 'gastric epithels' and irritation infiltrating the gastric mucosa in approximately half of the animals assessed (EU RAR, 2002).

Oral LD50 values of 140–1400 mg/kg bw in rats, mice and rabbits were observed with various concentrations of the chemical (no details). The only sublethal effect observed was a short reflex period of motor excitation followed by lethargy (EU RAR, 2002).

Dermal

The chemical is classified as hazardous with the risk phrase ‘Harmful in contact with skin’ (Xn; R21) in the HSIS (Safe Work Australia). The available data support this classification.

In an acute dermal toxicity study, doses of 400 and 640 mg/kg bw of an undiluted sample of the chemical were applied occlusively to the skin of Vienna White rabbits (n = 5/sex/dose). At 400 mg/kg bw, one male and one female rabbit died seven days after exposure, while 2/5 males and 3/5 females died within 24 hours of receiving the 640 mg/kg bw dose. The LD50 was 640 mg/kg bw in rabbits. Reported signs of toxicity included severe local necrosis, apathy, laboured respiration and a poor general state (EU RAR, 2002).

Inhalation

The chemical is classified as hazardous with the risk phrase ‘Harmful by inhalation’ (Xn; R20) in the HSIS (Safe Work Australia). The available data support this classification.

In an acute inhalation toxicity study, male Wistar rats were exposed to vapours of the chemical (99 % purity) at 2.97 or 3.60 mg/L over four hours. Mortalities occurred (numbers not provided) within 48 hours of exposure at 3.60 mg/L, while there were no mortalities at the low dose.

A similar study that exposed rats (n = 6/sex/dose) to vapours of the chemical at 1300, 1600 or 2100 ppm (3.89, 4.78 or 6.28 mg/L) for four hours found no mortalities at 3.89 mg/L. However, all test animals died at 4.78 mg/L. The median lethal concentration (LC50) was reported to be 3.6 mg/L (EU RAR, 2002, REACH). Reported sublethal signs of toxicity included lacrimation, salivation, eyelid closure, dyspnoea (shortness of breath), unresponsiveness, rhinorrhoea (running nose) and bradypnoea (slow breathing rate) (EU RAR, 2002).

In reports of other acute inhalation studies, toxicity is stated to be low, supposedly because acrylic acid interacts with air humidity before reaching the respiratory tract, causing respiratory irritation instead of acute inhalation toxicity (EU RAR, 2002).

Corrosion / Irritation

Corrosivity

The chemical is classified as hazardous with the risk phrase 'Causes severe burns' (C; R35) in the HSIS (Safe Work Australia). The available data support this classification.

Studies were performed in accordance with OECD TG 404. Of the test rabbits (n = 5), two were discontinued because of severe irritation. Moderate to severe erythema and slight oedema were observed beyond the area of exposure in the remaining rabbits. Full thickness destruction of the skin tissue resulted from a three-minute exposure; this was not reversible after 72 hours (EU RAR, 2005; REACH).

Human data are available indicating severe local corrosive effects when exposed to the chemical (EU RAR, 2002).

Sensitisation

Skin Sensitisation

The chemical is not considered to be a skin sensitiser.

In a modified Freund's Complete Adjuvant (FCA) test, female Hartley guinea pigs received three intradermal injections of the chemical (at 1.2 %) during the induction phase on days zero, five and nine. A non-irritant concentration of the chemical (at 7.2 %) was used for the challenge at day 21. The distilled chemical showed negative results for skin sensitisation. However, commercial acrylic acid was a strong skin sensitiser, with positive skin reactions lasting up to day 49, due to the presence of varying quantities (up to 7%) of a,β–diacryloxypropionic acid (DAPA) (EU RAR, 2002). The more recent investigations have shown that DAPA is not present at the detection limit of 20 ppm in current commercial samples of the chemical (EU RAR, 2002).

Negative results have been observed in several other skin sensitisation animal studies (guinea pig maximisation tests), although these have used dilutions of the chemical (EU RAR, 2002).

Observation in humans

Since 1989, more than 450 workers in a production plant using the chemical have been regularly tested and no cases of sensitisation have been observed (EU RAR, 2002).

Repeated Dose Toxicity

Oral

Based on the treatment-related effects reported in various repeated dose toxicity studies, the chemical is not considered to cause serious damage to health from repeated oral exposure.

In a 90-day oral gavage study in rats, a lowest observed adverse effect level (LOAEL) of 150 mg/kg bw/d was reported based on reduced body weight. Effects observed at 375 mg/kg bw/d included mortality, irritation and ulceration of the stomach, and renal tubular necrosis in rats (EU RAR, 2002).

A chronic toxicity study (OECD TG 452) was conducted on Wistar rats, which received the chemical in drinking water at 0, 120, 800, 2000 or 5000 ppm (approx. 0, 6, 40, 100 or 200 mg/kg bw/d in males, and 0, 10, 66, 150 or 375 mg/kg bw/d in females) for three months (n = 10/sex/dose) or 12 months (n = 20/sex/dose). Based on the reduced body weight gain in males (and with low water consumption in both sexes), the no observed adverse effect level (NOAEL) was established as 800 ppm (40 mg/kg bw/d). In females, the NOAEL was considered to be 5000 ppm (375 mg/kg bw/d) (EU RAR, 2002; REACH).

No systemic toxic effects were noted in several subacute (seven days) repeated dose toxicity studies (EU RAR, 2002).

Dermal

Only limited data are available due to the corrosivity of the chemical.

Mice treated dermally with the chemical at 4 % in acetone for 13 weeks (three days/week), showed severe incidence of skin irritation, compared with those treated with the 1 % concentration (EU RAR, 2002; REACH). No other systemic effects were reported at these concentrations.

Inhalation

Based on the available data, the chemical is not considered to cause serious systemic effects from repeated inhalation exposure. However, local corrosive/irritant effects are expected.

In a 90-day repeated dose inhalation toxicity study (OECD TG 413), Fischer 344 rats (n = 15/sex/dose) were exposed to the chemical vapour at 0, 5, 25 or 75 ppm (0.015, 0.074 or 0.221 mg/L) for six hours a day, five days a week. There were no treatment-related systemic effects on body weight, haematology, urinalysis, organ weights, gross pathology or histopathology. The treatment induced slight focal degeneration of the nasal olfactory epithelium in 7/10 male and 10/10 female rats at 75 ppm. A no observed adverse effect concentration (NOAEC) of 25 ppm was determined for local effects (EU RAR, 2002).

A similar study in B6C3F1 mice (n = 15/sex/dose) found the chemical to induce degenerative lesions in the olfactory mucosa at all doses (5, 25 and 75 ppm). Mice seemed to be more sensitive to local effects than rats and a NOAEC of 5 ppm (0.015 mg/L) was derived for systemic effects, based on lower body weight gain in females (EU RAR, 2002).

Genotoxicity

Based on the results of available in vitro and in vivo genotoxicity studies, the chemical is not considered to be genotoxic.

The chemical gave negative results for genotoxicity in several in vitro bacterial reverse mutation assays (Ames test, OECD TG 471) with *Salmonella typhimurium* strains (TA 98, 100, 1535, 1537 and 1538) (EU RAR, 2002).

The chemical showed positive results for genotoxicity in several in vitro tests for gene mutations and chromosomal aberrations in:

- mammalian gene mutation tests (OECD TG 476) using mouse lymphoma cells (L5178Y), with and without metabolic activation (EU RAR, 2002); and
- mammalian chromosomal aberration assays (OECD TG 473) using Chinese hamster ovary cells, with and without metabolic activation (REACH).

The chemical gave negative results for genotoxicity in the following in vivo assays (EU RAR, 2002):

- in a mammalian bone marrow chromosome aberration assays (OECD TG 475) using Sprague Dawley (SD) rats at 100, 333 and 1000 mg/kg bw; and
- in a chromosome aberration assay using CD1 mice at 32, 108 and 324 mg/kg bw.

Carcinogenicity

Based on the available data, the chemical is not expected to be carcinogenic. There was no evidence of carcinogenicity when the chemical was administered orally to rats.

In a 28-month carcinogenicity study (OECD TG 451), rats (n = 50/sex/dose) were orally administered (via drinking water) the chemical at doses of 0, 120, 400 or 1200 ppm (0, 8, 27 or 78 mg/kg bw/d). The water consumption was slightly reduced in the high-dose animals. No treatment-related clinical, haematological or histopathological changes were observed in any dose group. The incidence (and distribution) of tumours was comparable between the treatment and control groups (EU RAR, 2002).

Reproductive and Developmental Toxicity

The chemical is not considered to have reproductive or developmental toxicity.

In a one-generation reproductive toxicity study (OECD TG 415), F334/N rats (n = 10 males and 20 females per dose/group) received the chemical at 0, 500, 2500 or 5000 mg/L (equivalent to 0, 83, 250 or 750 mg/kg bw/d) in drinking water over a 13-week period. The rats were then mated and exposure continued throughout gestation and lactation. In the high dose group, the gestation index, number of pups born alive and percentage of pups weaned were reduced. These findings were not considered to be treatment-related as there was no statistical significance when compared with the control group. However, it was stated that the fertility index and litter size were low in the control group of this study (EU RAR, 2002).

In a two-generation study (OECD TG 416), the chemical was administered to Wistar rats at doses of 53, 250 or 460 mg/kg bw/d. In both sexes of the F0 and F1 generations, there were no abnormal clinical signs and no adverse effects on fertility or the reproductive organs. The mating index of males in both generations and all dose groups was 100 %. There was no difference in the rate of pregnancy in either generation or in the number of pups born alive. The NOAEL for reproductive function was reported to be 460 mg/kg bw/d (REACH). The NOAEL for developmental toxicity was stated as 53 mg/kg bw/d, based on reduced body weight gain observed in the F1 offspring at the high doses (EU RAR, 2002).

In two studies, the chemical was administered via inhalation to pregnant SD rats and New Zealand White rabbits (OECD TG 414). SD rats (n = 30/dose) were exposed (six hours/day, whole-body) to the chemical at 0, 40, 120 or 360 ppm (equivalent to 0, 120, 350 or 1060 mg/m³) during GD 6–15; and New Zealand White rabbits (n = 16/dose) were exposed (six hours/day, whole-body) to the chemical at 0, 25, 75 or 225 ppm (equivalent to 0, 0.075, 0.224 or 0.673 mg/L) during GD 6–18. Both studies concluded that there was no developmental toxicity observed from exposure to the chemical via inhalation in rats (NOAEL = 1060 mg/m³) and rabbits (NOAEL = 663 mg/m³) (EU RAR, 2002; REACH).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic acute effects (by oral, dermal and inhalation exposure) and local effects (corrosivity).

Public Risk Characterisation

Currently there are no regulatory controls for the chemical's use in cosmetics and domestic products in Australia. Although use in cosmetic products in Australia is not known, the chemical is reported to be used in cosmetic products overseas (concentrations not specified). Considering the range of cosmetic and personal care products that could contain the chemical, the main routes of public exposure is expected to be through the skin and via inhalation.

When used in nail building products, short-term small volume skin contact in the immediate vicinity of the fingernail can occur. Depending on the concentration used, the characterised critical health effects (corrosivity) has the potential to pose an unreasonable risk under the uses identified.

The chemical is used in domestic products in Australia and is reported to be used in domestic products overseas at concentrations up to 5 %. The general public could be exposed to the chemical through dermal and/or inhalation routes when using domestic products containing the chemical.

If used at high concentrations in cosmetics/domestic products, the risk of corrosive or irritation effects could be mitigated by implementing concentration limits for these products.

Occupational Risk Characterisation

During product formulation, dermal and inhalation exposure of workers to the chemical might occur, particularly where manual or open processes are used. Worker exposure to the chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical acute health effects (corrosivity), the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise dermal, ocular and inhalation exposure to the chemical are implemented. The chemical should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine appropriate controls.

Based on the available data, the hazard classification in HSIS is considered appropriate.

NICNAS Recommendation

Current risk management measures are considered adequate to protect public and workers' health and safety, provided that all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory. No further assessment is required.

If any information becomes available to indicate significant consumer exposure to the chemical in Australia (i.e. higher concentrations or quantities in cosmetics or domestic products), risks to public health and safety may have to be managed by changes to poisons scheduling.

Regulatory Control

Public Health

Products containing the chemical should be labelled in accordance with state and territory legislation (SUSMP).

Work Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical hazards and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22)* Harmful in contact with skin (Xn; R21)* Harmful by inhalation (Xn; R20)*	Harmful if swallowed - Cat. 4 (H302) Toxic in contact with skin - Cat. 3 (H311) Toxic if inhaled - Cat. 3 (H331)
Irritation / Corrosivity	Causes severe burns (C; R35)*	Causes severe skin burns and eye damage - Cat. 1A (H314)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for consumers

Products containing the chemical should be used according to label instructions.

Advice for industry

Control measures

Control measures to minimise the risk from oral, dermal and inhalation exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures which could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

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. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to assist with meeting obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((m)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (m)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals— Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of the chemical has not been undertaken as part of this assessment.

References

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