Propanoic acid: Human health tier II assessment

01 July 2016

CAS Number: 79-09-4

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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.

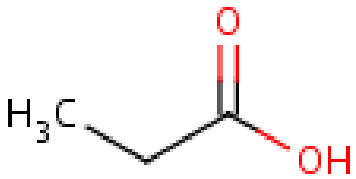
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	propionic acid carboxyethane ethanecarboxylic acid ethylformic acid metacetonic acid
Structural Formula	
Molecular Formula	C3H6O2
Molecular Weight (g/mol)	74.1
Appearance and Odour (where available)	Clear, colourless liquid with a slightly pungent disagreeable odour
SMILES	C(=O)(O)CC

Import, Manufacture and Use

Australian

The following Australian industrial uses were reported under previous mandatory and/or voluntary calls for information with a volume of less than 1000 tonnes per annum.

The chemical has reported cosmetic uses as a:

- softener; and
- solvent.

The chemical has reported domestic use as a solvent.

The chemical has reported site-limited use in manufacturing other chemicals.

International

The following international uses have been identified through: the European Union (EU) Registration, Evaluation and Authorisation and Restriction of Chemicals (REACH) dossiers; the Organisation for Economic Co-operation and Development Screening information: Initial Assessment Profile (OECD SIDS); Galleria Chemica; the Substances and Preparations in Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database; the United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary; the OECD High Production Volume chemical program (HPV); the US Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR); the US National Library of Medicine's Hazardous Substances Data Bank (HSDB); and the International Programme on Chemical Safety (IPCS).

The chemical has reported cosmetic use as a preservative.

The chemical has reported domestic uses including as:

- a surface active agent;
- an emulsifying agent;
- an ingredient in paints, lacquers and varnishes; and
- a lubricating agent.

The chemical has reported commercial use as a formulation agent.

The chemical has reported site-limited uses, including:

- as an intermediate in producing plastics, polymers, rubber and paints; and
- in manufacturing other substances.

The chemical has reported non-industrial uses, including:

- in animal nutrition and other agrochemical uses;
- as a food preservative;
- in manufacturing synthetic flavouring agents; and
- as a herbicide/pesticide.

Restrictions

Australian

This chemical is listed in the *Poisons standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) in Schedules 5 and 6 (SUSMP, 2015).

Schedule 6 with:

'PROPIONIC ACID (excluding its salts and derivatives) **except**:

(a) when included in Schedule 5;

(b) in preparations containing 30 per cent or less of propionic acid; or

(c) for therapeutic use'; and

Schedule 5 with:

'PROPIONIC ACID (excluding its salts and derivatives) in preparations containing 80 per cent or less of propionic acid, **except**:

(a) in preparations containing 30 per cent or less of propionic acid; or

(b) for therapeutic use.'

Schedule 6 chemicals are described as 'Substances with a moderate potential for causing harm, the extent of which can be reduced through the use of distinctive packaging with strong warnings and safety directions on the label'. Schedule 6 chemicals are labelled with 'Poison' (SUSMP, 2015).

Schedule 5 chemicals are described as 'Substances with a low potential for causing harm, the extent of which can be reduced through the use of appropriate packaging with simple warnings and safety directions on the label.' Schedule 5 chemicals are labelled with 'Caution' (SUSMP, 2015).

International

Using the chemical in cosmetics in the European Union is subject to the restrictions described in the EU Regulation Cosmetic Directive No. 1223/2009 Annex V/2. This chemical may be used in cosmetics and personal care products as a preservative at a maximum concentration of 2 % (CosIng).

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):

- C; R34 (corrosion)

Exposure Standards

Australian

The chemical has an exposure standard of 30 mg/m^3 (10 ppm) time weighted average (TWA).

International

The following exposure standards are identified (Galleria Chemica).

A TWA of 30–31 mg/m^3 (10 ppm) and a short-term exposure limit (STEL) of 46–62 mg/m^3 (15–20 ppm) in countries such as Austria, Belgium, Bulgaria, Columbia, Croatia, Denmark, Egypt, France, Germany, Iceland, New Zealand, Poland, the United Kingdom and the USA.

Health Hazard Information

Toxicokinetics

Propionic acid occurs in foods as a naturally occurring short chain fatty acid. It is rapidly absorbed through the gastrointestinal tract in both rats and humans. It metabolises by interaction with co-enzyme A and is carboxylated to form methylmalonyl-coenzyme A. Finally, it is trans-carboxylated to succinyl-CoA, which then enters the Krebs cycle to be metabolised to carbon dioxide and water (OECD SIDS, 2007). Approximately 80 % of the propionate is oxidised to carbon dioxide after extensive metabolism and is excreted by exhalation (EFSA, 2014).

Acute Toxicity

Oral

The chemical has moderate to low acute toxicity based on results from animal tests following oral exposure. The median lethal dose (LD50) values are 351– 4290 mg/kg bw. The available data indicate that the chemical warrants a hazard classification.

Groups of non-fasted female Harlan-Wistar rats were administered increasing doses of undiluted n-propionic acid by a stomach tube. The number of animals tested per group and the dose levels are not reported. Signs of toxicity were observed after dosing and throughout the 14–day observation period. The LD50 was reported to be 351 mg/kg for female rats (OECD SIDS, 2007; EFSA, 2014).

In another study, propionic acid was administered to Sprague Dawley (SD) rats by a single gavage dose to five animals/sex/dose at 1980, 2475, 3168, 3960, 4950 or 6336 mg/kg bw. The animals were observed for mortality and for clinical signs of toxicity for 14 days. The test substance concentration and whether the animals were fasted before dosing were not reported. Observed sub-lethal effects included apathy, dyspnoea, cyanosis, intermittent breathing, a crouching position and agitation. The LD50 was reported to be 3455 mg/kg bw (REACH).

Propionic acid was administered to 12 Chinchilla Bastard rabbits by a single gavage dose to two animals/sex/dose at 49.5, 99, 198, 495, 990 or 1980 mg/kg bw. The animals were observed for clinical signs of toxicity for 14 days. Observed sub-lethal effects included coronary dilation, liver and lung congestion and lung oedema; and some animals showed eroded stomach mucosa. The LD50 was reported to be 693 mg/kg bw (OECD SIDS, 2007; REACH).

In another animal acute oral toxicity study, propionic acid was administered as a 10 % aqueous solution to groups of five male Carworth-Wistar rats at 0, 2, 4 or 8 mL/kg bw (0, 1987, 3979 or 7947 mg/kg bw) by oral gavage. Animals were observed for signs of toxicity after dosing, and throughout the 14-day observation period. All animals in the highest dose group (8.0 mL/kg bw) died and 2/5 died in the group that received the 4.0 mL/kg bw dose. All deaths occurred either on the day of dose administration or the following day. No mortality occurred in the animals that received the lowest dose of 2.0 mL/kg bw. Observed clinical signs included haemorrhaged and congested lungs and gastrointestinal tracts (GI tracts); and 'burned' surfaces on the kidneys, liver, spleen and adrenals where contact with the GI tract was made. The LD50 of propionic acid was reported to be 4290 mg/kg bw (OECD SIDS, 2007; REACH). The concentration-dependence of the LD50 values, with LD50

values of 351 mg/kg (undiluted) and 4290 mg/kg (10 % aqueous), is consistent with acute toxicity due to local effects on the gastrointestinal tract.

Dermal

Based on the available information, the chemical has moderate to low acute toxicity in animal tests following dermal exposure. While the effects are local, the available data warrant hazard classification (refer to **Recommendation** section).

In an animal study in groups of male New Zealand White rabbits (four animals/group), propionic acid was applied undiluted to the non-abraded skin at concentrations of 0.3125 or 0.625 mL/kg. During the 24-hour skin contact, the rabbits were immobilised and the test material was retained on the skin under an impervious sheet of vinylite. Signs of toxicity were observed after dosing and throughout the 14-day observation period. The dermal LD50 was 0.5 mL/kg or 490 mg/kg bw. In the group receiving 0.625 mL/kg, 3/4 animals died on the day of dosing. Skin necrosis was observed in the covered application area. At necropsy, the animals that died showed petechial haemorrhages, haemorrhages in the lungs, mottled livers, congested kidneys and haemorrhages in the intestines (OECD SIDS, 2007).

In a study similar to OECD Test Guideline (TG) 402, propionic acid was applied under occluded conditions to female Wistar rats (six animals/dose) at doses of 1000, 2500, 3150, 4000 or 5000 mg/kg bw for a 24-hour exposure. All six animals in the highest dose group (5000 mg/kg bw) died; pale spotted liver and a bloody small intestine were observed. The surviving animals did not show any abnormalities. The LD50 was reported to be 3235 mg/kg bw (REACH).

Inhalation

Based on the available information, the chemical has low acute inhalation toxicity.

In an inhalation study conducted similar to OECD TG 403, SD rats (six animals/dose) were exposed by a nose-head inhalation system to propionic acid at concentrations of 2.69 or 19.7 mg/L for one hour. One animal treated at a concentration of 19.7 mg/L died during the 14-day observation period. During exposure, all animals in the 2.69 mg/L dose group showed slightly constricted closed eyes, wet fur (from urine) and slight tearing of eyes, whereas animals in the 19.7 mg/L dose group showed slight to increased intermittent respiration, tightly closed eyes, slight to heavy salivation, slight to heavy nasal secretion, and slight corneal opacity. Males in the 19.7 mg/L dose group showed irreversible corneal opacity and females showed a slightly reduced respiration rate during the observation period. Corneal opacity in females lasted for 24 hours after the exposure. The median lethal concentration (LC50) was determined to be >19.7 mg/L chemical (OECD SIDS, 2007; REACH).

In another inhalation study conducted similarly to OECD TG 403, six albino rats were exposed to a nominal concentration of propionic acid at 12.2 mg/L for eight hours in an exposure chamber. All animals were observed for 14 days following administration. No mortalities or clinical signs were reported. The LC50 of >20 mg/L for a four-hour exposure interval was reported (REACH).

Corrosion / Irritation

Corrosivity

The chemical is classified with risk phrase 'Causes burns' (R34) in HSIS (Safe Work Australia). The available data support this classification.

Skin effects

In a skin irritation/corrosion study, undiluted propionic acid was applied to the intact skin of six Vienna white rabbits under occlusive conditions. The exposure period was one, five or 15 minutes. The chemical produced severe erythema (mean score = 4) and oedema (mean score = 4); the effects were fully reversed within a maximum of 53 days. All animals had swollen and brown coloured skin, with necrosis and crusty skin at the application site up to the last day of observation. While the test was done under occlusive conditions, the effects observed were clearly corrosive (REACH).

In another animal study, undiluted propionic acid at 0.01 mL, or approximately 10 mg/animal, was applied to the clipped skin of male New Zealand White rabbits. The test substance was allowed to remain on the skin for 24 hours under non-occlusive conditions. Observations after 24 hours showed necrosis. Moderate to marked erythema was seen after a follow-up application of a 10 % aqueous solution of the chemical for 24 hours under non-occlusive conditions (OECD SIDS, 2007).

In a skin irritation study, 0.5 mL of propionic acid was administered on the skin of five guinea pigs. Two hours after administration, slight to moderate oedema, moderate to severe erythema and necrosis were observed. The site was necrotic with erythema around the periphery after 24 hours. Eschar covered most of the treatment site on all animals at 48 hours. Petechial haemorrhages, erythema and scattered areas of necrosis were also observed. During the 14-day observation, all animals lost weight (OECD SIDS, 2007; REACH).

Eye effects

In an eye irritation and corrosion study in New Zealand White rabbits, 0.005 mL of undiluted propionic acid was instilled in the eyes of six rabbits. The chemical was found to be highly corrosive within one minute of application. The animals had a cornea score of 4 with no reversibility. Immediately after instillation, all animals showed severe signs of discomfort with pawing, squealing, and thrashing about the enclosure. Marked ulceration was observed after the 14-day observation period (OECD SIDS, 2007; REACH).

In a study, all animals treated with 2.69 mg/L of propionic acid showed slightly constricted closed eyes, slight tearing of eyes, tightly closed eyes and slight corneal opacity. Males in the 19.7 mg/L dose group showed irreversible corneal opacity, and corneal opacity in females lasted for 24 hours after the exposure (refer **Acute toxicity inhalation** section).

Respiratory effects

Based on the available data on acute inhalation toxicity, all animals treated with 2.69 mg/L of propionic acid showed wet fur (from urine) and the animals in the group that received 19.7 mg/L showed reduced respiratory frequency, slight to increased intermittent respiration, slight to heavy salivation and slight to heavy nasal secretion. Males in the dose group that received 19.7 mg/L showed irreversible corneal opacity, and females showed a slightly reduced respiration rate during the observation period. Corneal opacity in females lasted for 24 hours after the exposure. The LC50 was determined to be >19.7 mg/L (refer **Acute toxicity inhalation** section).

Sensitisation

Skin Sensitisation

The available data suggest that the chemical is not a sensitiser.

In a guinea pig maximisation test conducted according to the OECD TG 406, six albino specific pathogen-free guinea pigs (SPF) were treated in two phases. All animals were treated intradermally with 2 % (0.05 mL/site) of the test chemical with Freund's Complete Adjuvant in the induction phase. One week following the intradermal injection, 20 % of the test chemical in vaseline was administered topically under occlusive conditions. Two weeks after the induction phase, 20 % of the chemical was applied as a challenge dose. No reaction to indicate sensitisation was reported (REACH).

Observation in humans

A range of case reports suggest that the chemical is not a skin sensitiser.

In a study with volunteers suffering from chronic urticaria, a 5 % aqueous solution of propionic acid was tested in a pin-prick test. Three of the 91 patients suffering from chronic urticaria had a positive pin prick response, while the 247 normal controls had no response to the chemical (OECD SIDS, 2007; REACH).

In another case, medical reports of workers with acute exposure to propionic acid showed mild to moderate skin irritation, mild eye redness and one case of mild cough and asthmatic response (ACGIH, 2005).

Repeated Dose Toxicity

Oral

Other than local irritant effects, the main systemic effect seen in repeated dose toxicity studies was reduced body weight. However, this effect is transient and is not considered a severe effect that meets the criteria for hazard classification.

In a repeated dose toxicity study similar to OECD TG 408, male and female SD rats (10 animals/sex/dose) were exposed to the chemical at concentrations of 0, 6200, 12500, 25000 or 50000 ppm in the diet for 91 days. The only treatment-related effect was significantly reduced body weight gain in males in the 50000 ppm group. No treatment-related abnormalities were noted after the recovery period. The no observed effect level (NOEL) for male and female rats was 25000 ppm in the diet (approx. 1600 mg/kg bw/day) (OECD SIDS, 2007; REACH).

In a dog feeding study, beagle dogs (eight/sex) were exposed to the chemical at a concentration of 0, 201, 669 or 2007 mg/kg bw/day for males and 0, 208, 695 or 2084 mg/kg bw/day for females in the diet for approximately 100 days. No clinical signs were observed during the six-week recovery period. Three animals in the high dose group showed diffuse epithelial hyperplasia of the oesophageal mucosa. No mortality was noted during the treatment period. The lowest observed adverse effect level (LOAEL) for local oesophageal effects was 669 mg/kg bw/day in male dogs and 695 mg/kg bw/day in female dogs. The no observed adverse effect level (NOAEL) was 201 mg/kg bw/day for male dogs and 208 mg/kg bw/day for female dogs (EFSA, 2014).

In a 12-week oral repeated dose toxicity study, six male Wistar rats were fed propionic acid in the diet at either 0 or 4 %. Pronounced hyperplasia and severe inflammatory lesions were observed in the forestomach of the animals fed 4 % propionic acid when checked at 12 weeks. No mortality was noted. No effects were observed in the control animals. The lesions were most pronounced in the area near the glandular stomach, whereas no changes were seen in the adjacent glandular stomach epithelium in the control animals (OECD SIDS, 2007; REACH).

In a lifetime study, groups of 30 male Wistar rats received 0, 0.4 or 4 % propionic acid in their feed. Ten rats from each group were euthanised after 20 weeks. All remaining animals were fed on their respective diets until death. Histopathological examination of the stomach showed hyperplasia and hyperkeratosis in the group on the 0.4 % diet, both in animals euthanised at 20 weeks and those euthanised after two years. Six out of ten rats on the 4 % propionic acid diet showed elevations in the forestomach mucosa in the limiting ridge area. No treatment-related mortality was reported. Marked squamous hyperplasia of the epidermis with incipient ulceration and hyperplasia of the mucosal papillae were observed in the animals that were euthanised at 20 weeks and those euthanised after two years. One animal euthanised at two years displayed hyperplasia with ulceration and unspecified 'carcinomatous changes' along with some erosive changes in the glandular region of the stomach (OECD SIDS, 2007).

Dermal

With repeated dermal exposure to the chemical, skin irritation is seen at high doses.

In a repeated dermal exposure study, CD-1 (ICR)BR female mice (10 animals/dose) were exposed to 8, 10 or 14 % of the chemical (equivalent to 136.9, 169.0 or 237.4 mg/kg bw/day) on the shaved skin of the interscapular area once a day for five days a week for 90 days. As there was no sign of the expected irritation effects at the initial low dose of 6 %, the dose was increased to 14 % after three weeks (in the pilot study). No severe skin irritation effects were observed at the 8 % concentration. Skin changes at the application site included erythema and crust formation at concentrations of 10 % and 14 %. All treated groups showed histological changes including acanthosis and fibrous condensation of the corium connective tissue along with the skin losing its ability to fold normally. No mortality was reported in any treatment group. The LOAEL was established as 136.9 mg/kg bw/day (OECD SIDS, 2007; REACH).

Inhalation

No data are available. However, based on the acute toxicity study on inhalation exposure, there is a concern that respiratory irritation could result, with reduced respiratory frequency and slight to increased intermittent respiration.

Genotoxicity

Based on the available data, the chemical is not genotoxic. Both in vitro and in vivo assays gave negative results.

In vitro studies

In an Ames test conducted according to OECD TG 471, propionic acid was tested at 0, 100, 333, 1000, 3333 or 10,000 µL per plate in *Salmonella typhimurium* strains TA 97, 98, 100, 102, 104, 1535, 1537 and 1538 with or without metabolic activation. The chemical had no mutagenic activity in any of the strains tested (OECD SIDS, 2007; REACH).

In another bacterial test, propionic acid was tested in *Escherichia coli* Sd4-73 without metabolic activation in a broth containing 20 µg/mL of streptomycin. No effects indicating mutagenicity were seen (REACH).

In an SOS-Chromotest conducted in bacterial strain *E.Coli* PQ37, propionic acid was tested at 0, 0.3, 1.0, 3.3, 10 or 33.3 mM (equivalent to 0, 22.2, 74.1, 222.3, 741 or 222.3 µg/mL), both in presence and absence of S9 from male Wistar rats and male Syrian hamsters. The chemical was not genotoxic, both in presence and absence of metabolic activation (OECD SIDS, 2007; REACH).

In a sister chromatid exchange assay in mammalian cells conducted similarly to OECD TG 479, propionic acid was tested in Chinese hamster lung fibroblast (V79) cells with and without metabolic activation at concentrations of 0.1, 0.3, 1.0, 3.3, 10 or 33.3 mM. Cytotoxicity was seen at concentrations $\geq$10 mM without metabolic activation. All concentrations tested showed no cytotoxicity and/or genotoxicity with or with metabolic activation (OECD SIDS, 2007; REACH).

Propionic acid has been tested in several other in vitro assays, including a DNA damage and repair assay in bacteria, yeast gene mutation assay and chromosome aberration, Ames test and sister-chromatid exchange (SCE) in mammalian cells. In all cases no positive results have been observed.

In vivo studies

In a chromosomal aberration assay, Chinese hamsters (12 animals/sex/dose) were exposed to 124 mg/kg of the chemical once intra-peritoneally (i.p.) and the other were controls. Four animals out of the 24 treated animals died, but no significant treatment-related increase in micronucleated polychromatic erythrocytes was observed in the surviving animals. The chemical showed no clastogenic activity (OECD SIDS, 2007; REACH).

Carcinogenicity

Based on the available data, the chemical is not a carcinogen.

In a lifetime study, Wistar male rats (30 males/dose) were exposed to the chemical at concentration of 0, 264 or 2640 mg/kg bw/day for 20 weeks or their lifetime. Ten animals from each group were euthanised at week 20 and the remaining animals were fed their respective diet until death. No treatment-related effects were seen in animals dosed with 264 mg/kg bw/day. In rats fed 2640 mg/kg bw/day, forestomach epithelial changes such as hyperplasia and hyperkeratosis were noted at 20 weeks. Other permanent effects included hyperplasia with ulceration, dyskeratosis and papillomatous elevations. One animal euthanised after two years displayed hyperplasia with ulceration and unspecified 'carcinomatous changes', along with some erosive changes in the glandular region of the stomach (OECD SIDS, 2007; REACH). This was reported to be due to chronic irritation and inflammation, and the associated hyperplastic proliferative repair response (OECD SIDS, 2007).

Reproductive and Developmental Toxicity

There are limited data for fertility and developmental effects. Based on this, the chemical is concluded to have no specific reproductive or developmental toxicity.

In a repeated dose oral toxicity study, male and female beagle dogs were exposed to propionic acid at 0, 196, 660 or 1848 mg/kg bw/day for males and 0, 210, 696 or 1832 mg/kg bw/day for females in the diet for approximately 100 days. The animals were euthanised at approximately 100 days for necropsy. No changes were observed in the reproductive organs (testes and

ovaries) of male and female rats. The LOAEL was 1848 mg/kg bw/day for males and 1832 mg/kg bw/day for females; the NOAEL was 660 and 696 mg/kg bw/day for male and female dogs respectively (OECD SIDS, 2007).

In a developmental toxicity study, pregnant mice and rats were fed the calcium salt of propionic acid (calcium propionate) on days 6–15 of gestation at 3–300 mg/kg bw/day. No treatment-related effects on maternal or foetal survival, or foetal/litter size were observed. No foetal abnormalities were observed in any species (OECD SIDS, 2007; REACH).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include corrosivity and acute toxicity from oral and dermal exposure.

Public Risk Characterisation

The irritant and corrosive effects are not expected from the use of the chemical in cosmetic or domestic products, as they are not used under conditions of very low pH.

Occupational Risk Characterisation

During product formulation, dermal, ocular and inhalation exposure might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. 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 health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise dermal and ocular exposure 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 the appropriate controls.

The data available support an amendment to the hazard classification in the HSIS (Safe Work Australia) (refer to **Recommendation** section.

NICNAS Recommendation

Assessment of the chemical is considered to be sufficient, provided that the recommended amendment to the classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Public Health

Products containing the chemical should be labelled in accordance with state and territory legislation (SUSMP, 2015).

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 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 if swallowed - Cat. 4 (H302) Toxic in contact with skin - Cat. 3 (H311)
Irritation / Corrosivity	Causes burns (C; R34)*	May cause respiratory irritation - Specific target organ tox, single exp Cat. 3 (H335) Causes severe skin burns and eye damage - Cat. 1B (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 industry

Control measures

Control measures to minimise the risk from oral, dermal and ocular 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 help meet 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.

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Last update 01 July 2016

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