2-Propanol, 1-amino-: Human health tier II assessment

12 September 2013

CAS Number: 78-96-6

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.

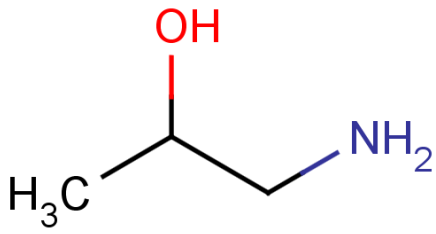
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	Isopropanolamine Monoisopropanolamine 1-Amino-2-hydroxypropane 2-Hydroxypropanamine 1-Methyl-2-aminoethanol
Structural Formula	
Molecular Formula	C3H9NO
Molecular Weight (g/mol)	75.11
Appearance and Odour (where available)	Colourless liquid with a mild ammoniacal odour.
SMILES	C(C)(O)CN

Import, Manufacture and Use

Australian

The total volume introduced into Australia, reported under previous mandatory and/or voluntary calls for information, was 100–1000 tonnes. The following Australian industrial uses were reported:

The chemical has reported commercial use including in:

- corrosion inhibitors;
- solvents; and
- lubricants and additives.

International

The following international uses have been identified through European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers; Substances and Preparations in the Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database; United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported cosmetic use:

- as a buffering agent; and
- in pH regulation.

The chemical has reported domestic use including in:

- cleaning and washing agents; and
- paints, lacquers and varnishes.

The chemical has reported commercial use including:

- as a welding and soldering agent;
- in metal cutting solutions;
- in surface treatments;
- in reprographic agents; and
- in solvents.

The chemical has reported site-limited use including:

- as a plasticiser;
- in asphalt aggregation;
- as a gas-scrubber in natural and refinery gas operations;
- as a concrete grinding aid; and
- as a fuel additive.

It should be noted that while international cosmetic and domestic use has been identified through some sources, the Compilation of Ingredients used in Cosmetics in the United States does not report any occurrences of the chemical (MIPA) and few occurrences of MIPA salts (CIUCUS, 2011). Furthermore, the chemical is not listed on the U.S Department of Health & Human Services Household Products Database or on the Consumer Product Information Database (whatsinproducts.com).

Restrictions

Australian

No known restrictions have been identified.

International

International restrictions include:

European Union:

The chemical is listed in Annex III (List of substances which cosmetic products must not contain except subject to the restrictions laid down) under the category of monoalkylamines, monoalkanolamines and their salts with the following restrictions:

- maximum secondary amine content: 0.5%;
- do not use with nitrosating systems;
- maximum secondary amine content: 5% (applies to raw materials);
- maximum nitrosamine content: 50 µg/kg; and
- keep in nitrite-free containers.

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):

Corrosive; R34 (Causes burns).

Exposure Standards

Australian

No specific exposure standards are available.

International

The following exposure standards are identified (Galleria Chemica):

In Germany, an exposure time weighted average (TWA) limit of 2 ppm is recommended.

Health Hazard Information

Toxicokinetics

No specific toxicokinetic data are available for this chemical.

It is expected that this chemical will have similar toxicokinetic properties to other alkanolamines and dialkanolamines such as monoethanolamine (MEA) (CAS No. 141-43-5) and diisopropanolamine (DIPA) (CAS No. 110-97-4).

Toxicokinetic data available for DIPA indicate that 25 % of ^{14}C labelled DIPA applied (19.5 mg/kg) to the skin of four female Fischer 344 (F344) rats was absorbed through the skin after 48 hours (CIR, 1987). Almost half (12.5 %) of the absorbed chemical was excreted in urine and the other half remained in the tissues of the animals, although, no accumulation was detected in fat. In a further study, intravenous administration of carbon-14 labelled DIPA (19 mg/kg) to four female F344 rats showed a fast elimination rate with 70 % of the radioactivity cleared from the blood within six hours. The majority (90 %) of the dose was excreted as the parent chemical and no metabolites were identified in the urine within 12 hours (CIR, 1987).

Acute Toxicity

Oral

The chemical was of moderate acute toxicity in animal tests following oral exposure. The median lethal dose (LD50) in rats is 1715 mg/kg bw. The LD50 ranged from 2100–4260 mg/kg bw in mice, guinea pigs and rabbits. Observed sub-lethal effects included lethargy, watery eyes, diarrhoea and rough coats. The available data support a hazard classification (refer to **Recommendation** section).

Rats (unspecified strain) orally administered 500–3500 mg/kg bw showed signs of lethargy and diarrhoea (BIBRA, 1999). In a further study rats (unspecified strain) orally administered a single dose of the chemical (194–6208 mg/kg bw) showed signs of bronchitis, bowel irritation, and red discolouration of the abdominal lining. The LD50 was determined to be 2813 mg/kg bw (REACH).

Dermal

The chemical was of moderate acute toxicity in animal tests following dermal exposure. The median lethal dose (LD50) in rabbits was determined to be 1851 mg/kg bw (CIR, 1987).

Rabbits exposed dermally to the chemical (630–5000 mg/kg bw) showed sub-lethal effects of marked redness, moderate swelling, skin necrosis and lethargy at all doses (CIR, 1987). Anorexia and diarrhoea was observed at doses of 630 and 1300 mg/kg bw. At necropsy, no treatment related systemic changes were observed (CIR, 1987).

Inhalation

The chemical was of low acute toxicity in animal tests following inhalation exposure with no deaths or toxic effects observed (REACH).

Corrosion / Irritation

Corrosivity

The chemical is classified as hazardous with the risk phrase ‘Causes Burns’ (C; R34) in HSIS (Safe Work Australia). The available data from skin and eye irritation studies support this classification (REACH).

A skin irritation/corrosion study performed in Vienna White rabbits showed that occlusive application of undiluted chemical for 1–15 minutes or 20 hours resulted in severe skin corrosion. Bleeding at the application site was noted in animals treated for five minutes or longer. Animals treated for 20 hours developed severe oedema, erythema and a grey-blackish necrosis that extended beyond the application site. Effects noted in animals treated for five minutes or longer were not reversible within the

eight-day observation period. Scale and crust formation and necrosis was observed in animals treated for 20 hours at the end of the observation period (REACH).

Corrosive chemicals are also considered to cause irreversible effects on the eyes; the available eye irritation data for the chemical support this finding.

Vienna White rabbits instilled with 50 µL of the chemical showed severe eye corrosion consisting of irreversible severe corneal opacity, severe erythema, crusty eyelids, staphyloma and iritis 24–48 hours after application (REACH).

Sensitisation

Skin Sensitisation

In a modification of the Draize repeat insult patch test a 2 % aqueous solution of the chemical did not induce allergic or photoallergic dermatitis in humans (BIBRA, 1999).

Repeated Dose Toxicity

Oral

Based on treatment-related effects reported in a repeated dose toxicity study, the chemical is not considered to cause serious damage to health from repeated oral exposure. The available data do not warrant a hazard classification.

In a seven-week oral gavage study conducted in accordance with OECD Test Guideline (TG) 422, Wistar rats were administered isopropanolamine as its hydrochloride salt (CAS No. 7780-04-3) at doses of 0, 100, 300 or 1000 mg/kg bw/day. No observed adverse effect levels (NOAEL) of 300 and 1000 mg/kg bw/day in males and females, respectively were reported. Toxic effects were noted at doses ≥300 mg/kg bw/day; this included transient salivation in all males and most females after week one and decreased haemoglobin by 5 %, and haematocrit levels by 6 %, in males at 1000 mg/kg bw/day (REACH).

Dermal

No data are available.

Inhalation

Based on the available information, no hazard classification for repeated dose inhalation toxicity is recommended.

In a 45-day repeated dose inhalation toxicity study in male and female $B6C3F_1$ mice and F344 rats, exposure to 25–75 ppm of the chemical for six hours a day did not produce local or systemic toxicity (CIR, 1987).

Genotoxicity

The chemical tested negative in several in vitro (Ames test, in vitro mammalian cell gene mutation assay and in vitro mammalian chromosome aberration test) and in vivo (*Drosophila melanogaster* gene mutation test) tests for gene mutation and clastogenicity (REACH).

Carcinogenicity

No data are available.

Reproductive and Developmental Toxicity

Based on the information available, the chemical does not show reproductive or developmental toxicity.

In a study conducted according to OECD TG 422, a hydrochloride salt of isopropanolamine was used (CAS No. 7780-04-3) to assess the reproductive and/or developmental toxicity of the chemical. Male and female Wistar rats were orally administered the chemical (100, 300 or 1000 mg/kg bw/day) for at least 13 days before mating and throughout gestation. There were no reproductive or developmental effects noted up to the highest dose administered (REACH).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic acute effects (acute toxicity from oral and dermal routes of exposure) and local effects (corrosivity).

Under certain conditions, the chemical may give rise to the formation of nitrosamines that are potent carcinogens (CIR,1987; SCCS, 2012).

Public Risk Characterisation

Available data suggest that the chemical is used in a category of products which may have domestic use in Australia and possibly in cosmetic products overseas. The information on uses in the US indicates that domestic and cosmetic use in Australia is unlikely. Furthermore, any cosmetic use is expected to be at low concentrations of free MIPA, leading to low public risk.

Occupational Risk Characterisation

During product formulation, dermal, occular and inhalation exposure of workers to the chemical may occur, particularly where manual or open processes are used. These may include transfer and blending activities, quality control analysis, and cleaning and maintenance of equipment. Worker exposure to the chemical at lower concentrations may 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 systemic acute and local health effects, the chemical may 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.

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

NICNAS Recommendation

Assessment of the chemical is considered to be sufficient provided that risk management recommendations are implemented and all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

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 if swallowed - Cat. 4 (H302) Harmful in contact with skin - Cat. 4 (H312)
Irritation / Corrosivity	Causes burns (C; R34)*	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 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 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 may 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;
- 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.

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