Short chain (C2-3) alkyl amines: Human health tier II assessment

01 July 2016

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
2-Propanamine	75-31-0
Ethanamine, N,N-diethyl-	121-44-8
1-Propanamine, N-propyl-	142-84-7

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

NICNAS has made every effort to assure the quality of information available in this report. However, before relying on it for a specific purpose, users should obtain advice relevant to their particular circumstances. This report has been prepared by NICNAS using a range of sources, including information from databases

ACRONYMS & ABBREVIATIONS

Grouping Rationale

The chemicals in this group are low molecular weight amines, substituted with short aliphatic alkyl chains of two to three carbon atoms in length and with molecular weights from about 59 to 102 Da. The amines may be primary, secondary or tertiary amines. These chemicals act as simple bases in aqueous solution.

Simple short-chain alkyl amines (such as the chemicals in this group) have similar base strength, regardless of the degree of substitution of the nitrogen atom. The acidity constant (p*K*a) of each chemical is >10.5; i.e. they all have high basicity. The pH of each chemical as a high concentration solution in water is >12.

The observed corrosive properties, related to the basicity of the chemicals, are the main observed effects for the human health toxicological endpoints. The degree of substitution of the nitrogen atom (primary, secondary or tertiary) is not expected significantly alter the toxicological profile of the chemicals.

Import, Manufacture and Use

Australian

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

The chemicals have reported commercial use as pH-regulating agents.

The chemical 2-propanamine (CAS No. 75-31-0) also has reported commercial use including as a solvent and with a reported use as 'other' (substances whose technical functions are not described elsewhere).

The chemicals 2-propanamine (CAS No. 75-31-0) and dipropylamine (CAS No. 142-84-7) are listed on the 2006 High Volume Industrial Chemicals List (HVICL) with a total reported volume of 1000–9999 tonnes.

International

The following international uses have been identified through the Organisation for Economic Cooperation and Development Screening information data set International Assessment Report (OECD SIAR); Galleria Chemica; the Substances and Preparations in the Nordic countries (SPIN) database; the United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary and the European Commission Cosmetic Ingredients and Substances (CosIng) database.

The chemical, 2-propanamine (CAS No. 75-31-0), is included in the CosIng database with the identified cosmetic function of buffering agent and the US INCI dictionary with the identified function of pH adjuster. The chemical had a low reported frequency of use in cosmetic products the US (<50) (ed. Bailey 2011).

Triethylamine (CAS No. 121-44-8) has reported potential domestic use including in:

- adhesives, binding agents;
- colouring agents;
- fillers;
- insulating materials;
- paints, lacquers and varnishes; and
- surface treatment.

In the US, the chemical was reported to be present in one floor polish product at a concentration of <1 % (US Household Products Database).

Triethylamine (CAS No. 121-44-8) has reported commercial use including in:

- construction materials;
- lubricants and additives;
- process regulators; and
- reprographic agents.

Triethylamine (CAS No. 121-44-8) and 2-propanamine (CAS No. 75-31-0) have reported commercial use as solvents.

The chemicals have reported site-limited use including as intermediates.

The following non-industrial uses have been identified internationally:

- non-agricultural pesticides (CAS No. 75-31-0); and
- pharmaceuticals (CAS No. 121-44-8).

Restrictions

Australian

The chemicals in this group are not specifically listed in the *Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP). However, the following general group entry in Schedule 5 of the SUSMP may apply for specific uses (which have not been definitively identified):

'AMINES for use as curing agents for epoxy resins **except** when separately specified in these Schedules' (SUSMP 2014).

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 2014)

International

The chemicals are listed on the following (Galleria Chemica):

2-Propanamine is covered by EU Cosmetics Regulation 1223/2009 Annex III—List of substances which cosmetic products must not contain except subject to the restrictions laid down.

Monoalkylamines, monoalkanolamines and their salts:

- maximum secondary amines content in the finished product: 0.5 %.
- minimum raw material purity: 99 %.
- maximum secondary amine content in the raw materials: 0.5 % (applies).
- maximum nitrosamine content 50 µg/kg.
- should not be used with nitrosating systems and should be kept in nitrite-free environments.

Dipropylamine is covered by EU Cosmetics Regulation 1223/2009 Annex II—List of substances which cosmetic products must not contain.

Secondary alkyl- and alkanolamines and their salts

Triethylamine is covered by EU Cosmetics Regulation 1223/2009 Annex III—List of substances which cosmetic products must not contain except subject to the restrictions laid down.

Trialkylamines, trialkanolamines and their salts:

- maximum concentration of 2.5 % in leave-on products.

For use in leave-on and rinse-off products:

- Do not use with nitrosating systems
- Minimum raw material purity: 99 %
- Maximum secondary amine content: 0.5 % (applies to raw materials)
- Maximum nitrosamine content: 50 µg/kg
- should not be used with nitrosating systems and should be kept in nitrite-free environments.

Existing Worker Health and Safety Controls

Hazard Classification

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

2-Propanamine (CAS No. 75-31-0): Xi; R36/37/38

Dipropylamine (CAS No. 142-84-7): Xn; R20/21/22, C; R35 (corrosive)

Triethylamine (CAS No. 121-44-8): Xn; R20/21/22, C; R35 (corrosive)

Exposure Standards

Australian

Triethylamine (CAS No. 121-44-8) has an exposure standard of 8 mg/m^3 (2 ppm) time weighted average (TWA) and 17 mg/m^3 (4 ppm) short-term exposure limit (STEL).

2-Propanamine (CAS No. 75-31-0) has an exposure standard of 12 mg/m^3 (5 ppm) TWA and 24 mg/m^3 (10 ppm) STEL.

International

The following exposure standards are identified (Galleria Chemica).

2-Propanamine (CAS No. 75-31-0) has an exposure standard of 12 mg/m^3 (5 ppm) TWA and 24 mg/m^3 (10 ppm) STEL in different countries such as Canada, China, Denmark, France, Germany, Latvia, Russia, Singapore, Taiwan and USA. The American Conference of Governmental Industrial Hygienists (ACGIH) recommends a threshold limit value (TLV) of 5 ppm (12 mg/m^3) (TWA) and 10 ppm (24 mg/m^3) (STEL). 'This is to minimize the potential for respiratory and ocular irritation, including a temporal visual disturbance...' (ACGIH 2011).

Triethylamine (CAS No. 121-44-8) has an exposure standard of 4.2–100 mg/m^3 (1–25 ppm) TWA and 5–60 mg/m^3 (2–40 ppm) STEL in different countries such as Canada, China, Europe, Latvia, Russia, Singapore, Taiwan, United Kingdom and USA. The ACGIH recommends a TLV of 1 ppm (4.1 mg/m^3) (TWA) and 3 ppm (12.4 mg/m^3) (STEL). 'The TLV TWA is intended to minimize the potential for corneal change causing visual disturbances such as hazing, blurring, and halo vision reported among workers at 3 to 4 ppm but not at 1 to 1.25 ppm. The TLV STEL is recommended to minimize transient visual disturbances observed at higher concentrations...' (ACGIH 2011)

Dipropylamine (CAS No. 142-84-7) has an exposure standard of 1–2 mg/m^3 TWA in different countries such as Latvia and Russia.

Health Hazard Information

Toxicokinetics

The chemicals in this group are rapidly absorbed through the skin, except when they are present in a charged form, which hinders absorption. The main routes of metabolism of short chain primary amines may involve processes including oxidation, conjugation, and other enzyme-catalysed reactions leading to detoxification and excretion. Additionally, *N*-acetylation may occur, but this represents a minor pathway in the metabolism of aliphatic amines (Benya, TJ & Harbison, RD 1994). The main routes of the biotransformation of aliphatic amines is *N*-dealkylation or oxidative deamination followed by *N*-oxidation (Benya, TJ & Harbison, RD 1994). Lower molecular weight secondary amines are largely excreted unchanged (Benya, TJ & Harbison, RD 1994).

Pharmacokinetic studies in humans with triethylamine (CAS No. 121-44-8) demonstrate that the chemical is readily absorbed following inhalation and oral exposure. The majority of the absorbed dose was excreted in the urine unchanged or as triethylamine *N*-oxide (Benya, TJ & Harbison, RD 1994; ACGIH 2011).

Acute Toxicity

Oral

Based on the available data, the chemicals in this group had moderate to high acute toxicity (concentration dependent) in animal tests following oral exposure, in undiluted and in dilute preparations. Dipropylamine (CAS No. 142-84-7) and triethylamine (CAS No. 121-44-8) are classified as hazardous with the risk phrase ‘Harmful if swallowed’ (Xn; R22) in the HSIS (Safe Work Australia). The available data for dilute preparations support this classification for all the chemicals in this group. The greater effect seen for undiluted chemicals can be attributed to corrosivity.

In a test conducted similarly to OECD Test Guideline (TG) 425, 2-propanamine (CAS No. 75-31-0) was toxic by the oral route in rats (REACH a). The median lethal dose (LD 50) in rats was <173 mg/kg bw (undiluted) and 730 mg/kg bw (10 % aqueous solution). Reported signs of toxicity include lethargy, laboured breathing, piloerection, and prostration.

In tests conducted similarly to OECD TG 401, dipropylamine (CAS No. 142-84-7) was toxic by the oral route in rats. The LD50 in rats was reported from 495 (4 % solution in water and tragacanth) to 933 mg/kg bw (5 % in corn oil). The study authors reported that, when the chemical was administered undiluted, deaths occurred at doses as low as 92.5 mg/kg bw. Reported signs of toxicity include intermittent respiration, dyspnoea, ruffled fur, squatting posture, calmness, trembling gait, and watery mouth discharge (REACH b).

In a test considered comparable to the OECD TG 401, triethylamine was administered to rats by gavage as solution in olive oil at various concentrations and doses. Three out of five rats receiving a dose of 929 mg/kg bw at a concentration of 10 % died. No mortality was observed in rats receiving lower doses (230, 366, 580 mg/kg bw) at this same concentrations (10 %). An LD50 of 730 mg/kg bw was reported (REACH c). Undiluted triethylamine (CAS No. 121-44-8) had a reported oral LD50 of 460 mg/kg (ACGIH 2011).

Dermal

The chemicals in this group had moderate acute toxicity in animal tests following dermal exposure, in undiluted and in dilute preparations. Dipropylamine (CAS No. 142-84-7) and triethylamine (CAS No. 121-44-8) are 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 for all the chemicals in this group.

In a GLP compliant study conducted in accordance with OECD TG 402, 2-propanamine (CAS No. 75-31-0) showed toxicity in rats following dermal exposure. The LD50 in rats was >400 mg/kg bw when applied as a 10 % aqueous solution. Necrosis of the skin was observed at the application site. Reported signs of toxicity include dyspnoea, apathy, staggering, spastic gait, tremor, piloerection, exophthalmia and poor general state (REACH a). An LD50 in rats of 380 mg/kg bw was also reported, but the study details were not available (REACH a). An LD50 in rats of 403 mg/kg bw was reported for the analogue chemical, propylamine (CAS No. 107-10-8) (REACH d).

In a study conducted similarly to OECD TG 402, dipropylamine (CAS No. 142-84-7) was acutely toxic in rats following dermal exposure. The LD50 in rats was 925 mg/kg bw when the chemical was applied undiluted. Necrosis of the skin was observed at the application site. At necropsy, internal organs (not specified) appeared pale or opaque. The lungs of animals that died during the study had haemorrhaged (REACH b).

In a study conducted similarly to OECD TG 402, triethylamine (CAS No. 121-44-8) was acutely toxic in rats following dermal exposure. The LD50 in rats was 580 mg/kg bw when applied undiluted. Necrosis of the skin and scab formation were observed at the application site. Following necropsy, darkening of the lungs and kidneys, mottled livers and pale livers and spleens were observed (REACH c). A dermal LD50 in rabbits of 420 mg/kg bw has also been reported (ACGIH 2011).

Inhalation

The chemicals in this group had moderate acute toxicity in animals tested following inhalation exposure. Dipropylamine (CAS No. 142-84-7) and triethylamine (CAS No. 121-44-8) are classified as hazardous with the risk phrase ‘Harmful by inhalation’ (Xn; R20) in the HSIS (Safe Work Australia). The available data support this classification for all the chemicals in this group.

In a GLP-compliant study conducted in accordance with OECD TG 403, 2-propanamine (CAS No. 75-31-0) vapour was acutely toxic in rats following inhalation exposure. The median lethal concentration (LC50) in rats was 8.7 mg/L-4h. Reported signs of toxicity included laboured breathing, lacrimation, nasal discharge, reduced activity, and closed eyes. In surviving animals, respiratory distress and nasal discharge persisted for the first week following exposure (REACH a).

In a GLP-compliant study conducted in accordance with OECD TG 403, triethylamine (CAS No. 121-44-8) vapour was acutely toxic in rats following inhalation exposure. The LC50 in rats was 3496 ppm-1h (approximately 7.2 mg/L-4h). Reported signs of toxicity included laboured breathing, tremors and increased salivation. In surviving animals, one animal from each of the mid- and low-dose groups showed corneal opacity in both eyes (REACH c). In another study, all six rats exposed to 2000 ppm (8.2 mg/L) for four hours died, with death occurring in one out of six rats exposed to 1000 ppm (4.1 mg/L) (ACGIH 2011).

No documented study data are available for dipropylamine (CAS No. 142-84-7), although an LC50 has been reported as 4.4 mg/L-4 h in rat (REACH b).

Observation in humans

Short-term exposure to unspecified concentrations of triethylamine was reported to disrupt the central nervous system (ACGIH 2011). Effects on the eyes, nose, throat and skin have also been reported (see **corrosion/irritation** section).

Corrosion / Irritation

Corrosivity

The chemicals in this group were corrosive in animal tests following exposure to the skin and eyes. Dipropylamine and triethylamine are classified as hazardous with the risk phrase 'Causes severe burns' (C; R35) in the HSIS (Safe Work Australia). The available data support this classification for all the chemicals in this group.

Studies were performed in accordance with, or similarly to, OECD TG 404. The results showed that the chemicals in this group were corrosive to rabbit skin following 1 minute exposure. Following exposure to 2-propanamine, necrosis was observed within 3 minutes, and eschar within 24 h (REACH a). Following exposure to dipropylamine, necrosis was observed in animals within 1 hour in washed and unwashed groups. Eschar was observed within 24 hours (REACH b). Following exposure to triethylamine, marked oedema and haemorrhagic areas were observed on the day of application, which remained almost unchanged for 1 week (REACH c). At the end of observation period (14–26 days), scar formation was observed in most animals for all the chemicals in this group.

In animal studies performed in accordance with, or similarly to, OECD TG 405, severe corneal damage was observed for all the chemicals (REACH a-c). Severe damage was also produced in the eyes of cats following exposure to triethylamine vapours with the degree and reversibility of effects dependent on exposure time (ACGIH 2011).

There is no evidence of destruction of respiratory tract tissue following single, limited inhalation exposure although respiratory irritant effects have been observed (see **Respiratory irritation**).

Respiratory Irritation

The chemicals in this group may cause respiratory irritation at non-corrosive concentrations. The chemical, 2-propanamine (CAS No. 75-31-0), is classified as hazardous with the risk phrase 'Irritating to respiratory system' (Xi; R37) in the HSIS (Safe Work Australia). The available data support an amendment of this

classification (See **Corrosivity**). The available data support the classification for all the chemicals in this group under the GHS (2009), as 'May cause respiratory irritation' (specific target organ toxicity, single exposure, Category 3).

The chemicals in this group were reported to cause upper airway irritation in mice, following 15-min oronasal exposure of the amines in study similar to the American Society for Testing and Materials (ASTM) test for estimating sensory irritancy of airborne chemicals (Gagnaire et al. 1989). The RD50 (exposure concentration producing a 50 % respiratory rate decrease) for 2-propanamine (CAS No. 75-31-0) was 157 mL/m^3 (ppm). The RD50 values for dipropylamine and triethylamine were reported as 92 ppm and 156 ppm respectively. The study noted that previous studies with several chemicals have shown that RD50 values may be used to estimate acceptable industrial exposure limits (such as TLV). At 0.1 RD50, humans would experience some slight discomfort when exposed to the chemicals.

Skin Irritation

The chemical, 2-propanamine (CAS No. 75-31-0), is classified as hazardous with the risk phrase 'Irritating to skin' (Xi; R38) in the HSIS (Safe Work Australia). The available data support an amendment of this classification (See **Corrosivity**).

Eye Irritation

The chemical, 2-propanamine (CSA No. 75-31-0), is classified as hazardous with the risk phrase 'Irritating to eyes' (Xi; R36) in the HSIS (Safe Work Australia). The available data support an amendment of this classification (See **Corrosivity**).

Observation in humans

Ocular injuries consisting of corneal opacities have been reported in workers exposed to triethylamine. Visual disturbances (foggy vision, blue haze and halo phenomena) were reported in workers exposed to a TWA concentration of 3 to 4 ppm. No effects were observed in workers exposed to 1 to 1.25 ppm. No permanent eye damage was reported in these workers. Similar effects were reported in other studies at concentrations around 5 ppm (ACGIH 2011).

Human workers exposed briefly to 2-propanamine (CAS No. 75-31-0) at 10 to 20 ppm experienced irritation of the nose and throat. Workers complained of transient visual disturbances (halos around lights) following an 8 h exposure to the chemical; probably due to mild corneal oedema, which cleared within 3 to 4 h (Benya, TJ & Harbison, RD 1994; ACGIH 2011).

Sensitisation

Skin Sensitisation

Based on the data available, the chemicals in this group are not dermal sensitisers.

The chemical, 2-propanamine (CAS No. 75-31-0) was not found to induce dermal sensitisation when tested according to OECD TG 406. However, in the dermal pre-test, necrosis was observed in 25 % of the animals tested. Additionally, after induction, necrosis in the treated group was observed (REACH a).

Dipropylamine (CAS No. 142-84-7) and triethylamine (CAS No. 121-44-8) were not found to induce dermal sensitisation when tested according to the mouse ear swelling test (Gad, SC et al. 1986). However, after induction in the test with dipropylamine, necrosis at the test site was observed in the treated group.

Repeated Dose Toxicity

Oral

There are limited data available. The chemicals in this group are not considered to cause serious damage to health from repeated oral exposure at non-corrosive concentrations.

In a 14-day dietary study in Sprague Dawley (SD) rats, performed similarly to OECD TG 407, dipropylamine was administered at dosages of 0, 75, 150 or 300 mg/kg bw/day (REACH a). There was a slight dose-related decrease in body weight gain and decrease in mean food consumption. The largest decrease in body weight gain was about 20 % in males in the high dose group. Gross pathology reported kidney changes, including dilation of the pelvis, cystic areas in the cortex and darkening of the medulla. A no-observed adverse effect level (NOAEL) for systemic effects of 300 mg/kg bw/day was reported based on the reduced body weight gain.

In a six week study in rats with triethylamine (oral dose of 0, 5, 15, 30 and 60 mg/kg bw three times a week), there were no significant changes in haematological parameters and histopathological examination revealed no abnormalities except for local corrosion. Although deaths were observed at 60 mg/kg bw/day, this is considered due to the corrosive effects of the chemicals (ACGIH 2011).

Dermal

There are no data are available.

Inhalation

Based on the available data, the chemicals in this group are not considered to cause serious damage to health from repeated inhalation exposure at non-corrosive concentrations.

In a 125-day study in SD rats, conducted in accordance with OECD TG 413, 2-propanamine (CAS No. 75-31-0) vapour was administered at concentrations of 20, 101 or 500 mg/m^3. Limited results were reported in the study summary (REACH a). Slight reductions in male body weights (<7 %) and female serum-glucose levels were observed in the high dose group. Inflammation of the nasal mucosa was observed in females in the high dose group. A no-observed adverse effect concentration (NOAEC) for systemic effects of 500 mg/m^3 was reported. A NOAEC for local effects of 100 mg/m^3 was reported.

In a 90-day study in Fischer 344 (F344) rats, conducted similarly to OECD TG 413 and OECD TG 452, triethylamine (CAS No. 121-44-8) vapour was administered at concentrations of 0, 25 or 247 ppm (0, 103 or 1020 mg/m^3) for 6 hours/day, 5 days/week, whole body exposure. There were no statistically significant treatment-related effects on body weight gain, organ weights, haematology, and clinical chemistry reported. There were no gross or histopathological lesions in any of the organs examined, including the nasal passages, which were attributed to the chemical by the study authors. In the high dose group, signs of irritation including closed eyes and noses buried in fur were reported. A NOAEC for systemic effects of 1020 mg/m^3 was reported. A NOAEC for local effects (eye and nose irritation) of 103 mg/m^3 was reported (REACH c). Pulmonary irritation has been observed in other studies in rabbits and rats exposed to triethylamine (ACGIH 2011).

Genotoxicity

Based on the weight of evidence from the available in vitro and in vivo genotoxicity studies, the chemicals in this group are not considered to be genotoxic. Several in vitro (bacterial gene mutation, mammalian gene mutation test) and in vivo (chromosomal aberration) tests for gene mutation and clastogenicity were negative (REACH a-c).

Negative results were reported in bacterial reverse mutation tests for mutagenicity in *Salmonella typhimurium* (strains included TA1535, TA1537, TA98 and TA100), for the chemicals, with and without metabolic activation. The highest non-toxic dose tested was 3333 mg/plate (32.94 mmol/plate) (REACH a-c).

Negative results were reported for 2-propanamine (CAS No. 75-31-0) in a hypoxanthine-guanine phosphoribosyl transferase (HPRT) assay in mouse lymphoma cells, conducted in accordance with OECD TG 476, with and without metabolic activation. Dose-related cytotoxicity was reported (REACH a).

Negative results were reported for 2-propanamine (CAS No. 75-31-0) in a chromosomal aberration test, conducted in accordance with OECD TG 473. In the absence of metabolic activation, cytotoxicity was observed at the highest evaluated concentration. With metabolic activation, no cytotoxicity was observed up to the highest evaluated concentration (REACH a).

Triethylamine (CAS No. 121-44-8) did not induce in vivo chromosomal damage in rat bone marrow cells, after repeated inhalation exposure (30- and 90-days) at concentrations of 1 or 10 mg/m^3 per day. The incidence of cells with chromosomal breakage did not exceed controls but the incidence of aneuploid cells was significantly higher at 1 mg/cm^3 after 30 days. There was no incidence of aneuploidy in the 10 mg/m³ dose group. There was no decrease in mitotic activity reported (REACH c).

Carcinogenicity

Limited data are available.

Primary, secondary and tertiary amines can all be nitrosated, in the presence of nitrosating agents such as nitrites, to generate nitrosamines which are of concern for carcinogenicity. Secondary amines are considered the most reactive (SCCS 2012).

No tumours were observed in a two year study in rats in which animals were exposed to triethylamine (CAS No. 121-44-8) and sodium nitrite in the diet (each at 5000 ppm) (ACGIH 2011). No data were available for the secondary amine, dipropylamine (CAS No. 142-84-7).

Reproductive and Developmental Toxicity

Based on the limited information available, the chemicals in this group do not show specific reproductive or developmental toxicity.

In a one generation reproduction study (GLP-compliant, non-guideline study), SD rats were exposed to 2-propanamine (CAS No. 75-31-0) at analytical concentrations of 20, 100 or 499 mg/m^3 for 6 h per day (5 days/week) by inhalation (whole body exposure). Clinical signs included incidental fur discolouration and focal hair loss. There were no significant differences in mating and fertility parameters, number of corpora lutea, implantations and resorptions. The was a reduction in mean body weight gain in males in the high dose group. A reported NOAEC of 499 mg/m^3 was determined for maternal and developmental toxicity (REACH a).

In 90 day studies in F344 rats and B6C3F1 mice, with the structurally related chemical diethylamine, a dose-related decrease in the motility of sperm was observed at 0.096, 0.19 or 0.37 mg/L (OECD 2013). There are no data to evaluate the impact of this on reproductive toxicity.

No effects on reproductive parameters were reported in a three generation study in rats exposed to up to 500 ppm triethylamine in drinking water (ACGIH 2011). Foetotoxic effects have been reported in rabbits and chick embryos following injection of triethylamine although the relevance of this to other routes of exposure has not been investigated (ACGIH 2011).

Risk Characterisation

Critical Health Effects

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

Although the acute toxicity of the chemicals in this group is related to the corrosive properties of the chemicals, there is sufficient evidence to demonstrate that the chemicals may be harmful by acute exposure to dilute preparations. The chemicals in this group may also cause respiratory irritation following inhalation exposure.

The potential for the chemicals to indirectly give rise to the formation of nitrosamines which are of concern for carcinogenicity is considered greatest for dipropylamine (CAS No. 142-84-7).

Public Risk Characterisation

Although use in domestic and cosmetic products in Australia is not known, some of the chemicals are reported to be used in domestic (triethylamine) and cosmetic products (2-propanamine) overseas. Cosmetic use of dipropylamine and triethylamine has not been identified. Based on the identified function (pH adjuster), the chemicals are expected to be used at low concentrations and exist largely as charged salts. As such, acute toxicity and corrosive effects are not expected and, therefore, the risk to public health is not considered to be unreasonable. In addition, at these low concentrations, the risk relating to nitrosamine formation for the primary amine 2-propanamine is considered to be low. The secondary amine dipropylamine (CAS No. 142-84-7), which has a greater concern for nitrosamine formation, has not been identified to have cosmetic uses. Overall, further risk management is not considered necessary for public safety.

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 chemicals at lower concentrations could also occur while using formulated products containing the chemicals. 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 chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise dermal, ocular and inhalation exposure are implemented. The chemicals 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 (refer to **Recommendation** section).

NICNAS Recommendation

Assessment of these chemicals is considered to be sufficient, provided that the recommended amendments to the classifications are 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 chemicals should be labelled in accordance with state and territory legislation (SUSMP 2014).

Work Health and Safety

The chemicals are 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.

The acute toxicity and corrosivity classification are the existing classifications for dipropylamine (CAS No. 142-84-7) and triethylamine (CAS No. 121-44-8) and, therefore, will require a classification amendment for 2-propanamine (CAS No. 75-31-0).

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)*	May cause respiratory irritation - Specific target organ tox, single exp Cat. 3 (H335) 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 chemicals should be used according to the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from dermal, ocular and inhalation exposure to the chemicals 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 chemicals are 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 chemicals 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 chemicals.

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 chemicals 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 these chemicals has not been undertaken as part of this assessment.

References

Bailey, JE (ed.) 2011, Compilation of Ingredients Used in Cosmetics in the United States (CIUCUS), 1st Edition, Personal Care Products Council, Washington, D.C.

Benya, TJ& Harbison, RD 1994, 'Aliphatic and Alicyclic Amines', in Clayton, GD and Clayton, FE (eds), Patty's Industrial Hygiene and Toxicology (4th Edition), Vol. 2, Part B, Wiley, pp. 1087-175.

Cosmetic Ingredients and Substances (CosIng). Accessed January 2015 at **http://ec.europa.eu/consumers/cosmetics/cosing/**

Gagnaire, F, Azim, S, Bonnet, P, Simon, P, Guenier, JP& De Ceaurriz, J 1989, 'Nasal irritation and pulmonary toxicity of aliphatic amines in mice', Journal of Applied Toxicology, vol. 9, no. 5, pp. 301-4.

Galleria Chemica. Accessed January 2015 at **http://jr.chemwatch.net/galleria/**

Globally Harmonised System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third edition. Accessed at **http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html**

OECD 2013, SIDS Initial Assessment Profile Report (SIAR): Aliphatic secondary amines, for CoCAM4 Paris, France April 16-18, 2013 (unpublished).

REACH Dossier (REACH a) Isopropylamine (CAS No. 75-31-0), viewed January 2015, **http://echa.europa.eu/information-on-chemicals/registered-substances**.

REACH Dossier (REACH b) Dipropylamine (CAS No. 142-84-7), viewed January 2015, **http://echa.europa.eu/information-on-chemicals/registered-substances**.

REACH Dossier (REACH c) Triethylamine (CAS No. 121-44-8), viewed January 2015, **http://echa.europa.eu/information-on-chemicals/registered-substances**.

REACH Dossier (REACH d) Propylamine (CAS No. 107-10-8), viewed January 2015, **http://echa.europa.eu/information-on-chemicals/registered-substances**.

Safe Work Australia (SWA). Approved Criteria for Classifying Hazardous Substances, 3rd Edition [NOHSC: 1008 (2004)]. Accessed January 2015 at **http://www.safeworkaustralia.gov.au/sites/SWA/about/Publications/Documents/258/ApprovedCriteria_Classifying_Hazardous_Substances_NOHSC1008-2004_PDF.pdf**

Safe Work Australia (SWA). Hazardous Substances Information System (HSIS). Accessed January 2015 at **http://hsis.safeworkaustralia.gov.au/HazardousSubstance**

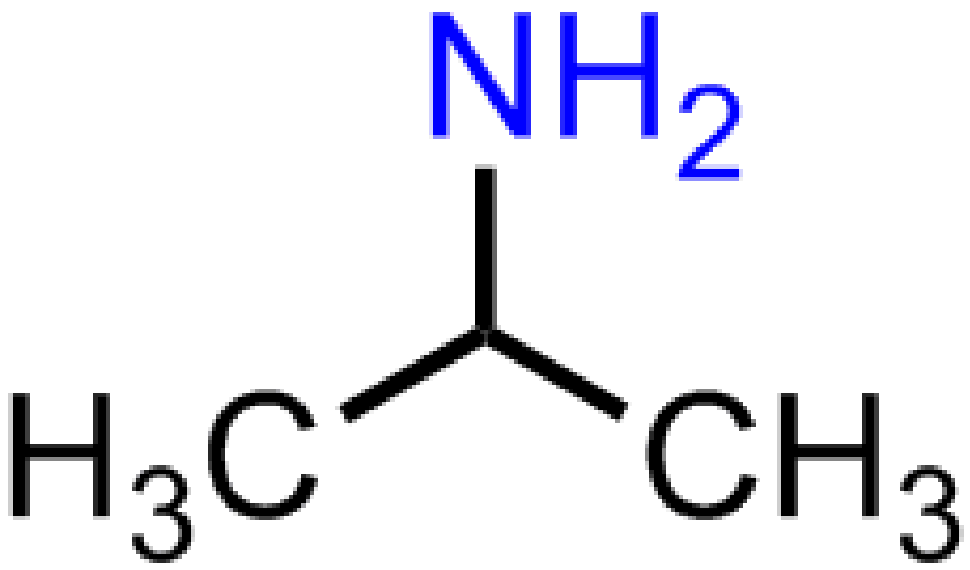
Substances in Preparations in Nordic Countries (SPIN). Accessed January 2015 at **http://188.183.47.4/dotnetnuke/Home/tabid/58/Default.aspx**

The Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)) 2014. Accessed January 2015 at **http://www.comlaw.gov.au/Details/F2014L01343**

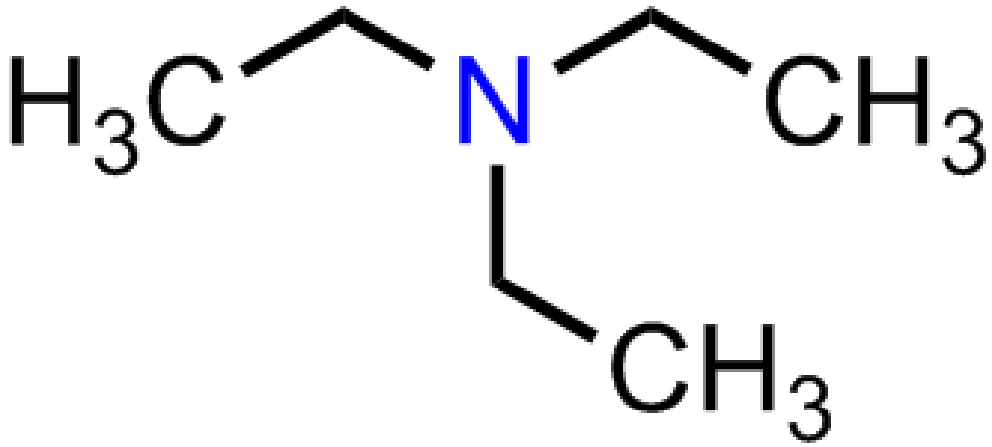
US Household Products Database. US Department of Health and Human Services. Accessed January 2015 at **http://householdproducts.nlm.nih.gov/advancedsearch.htm**

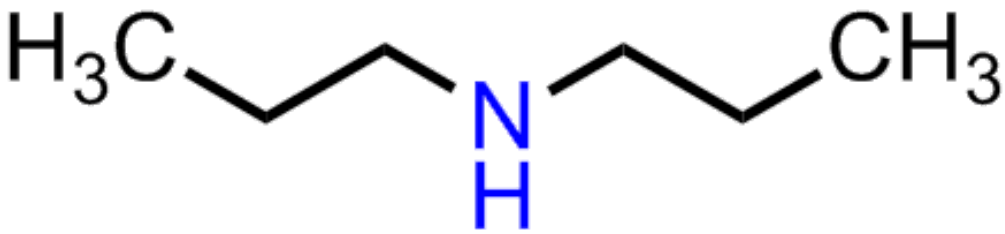
Last Update 01 July 2016

Chemical Identities

Chemical Name in the Inventory and Synonyms	**2-Propanamine** isopropylamine 2-aminopropane
CAS Number	75-31-0
Structural Formula	
Molecular Formula	C3H9N
Molecular Weight	59.11

Chemical Name in the Inventory and Synonyms	**Ethanamine, N,N-diethyl-** triethylamine

CAS Number	121-44-8
Structural Formula	
Molecular Formula	C6H15N
Molecular Weight	101.19

Chemical Name in the Inventory and Synonyms	**1-Propanamine, N-propyl-** di-n-propylamine n-dipropylamine
CAS Number	142-84-7
Structural Formula	
Molecular Formula	C6H15N
Molecular Weight	101.19

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