1,2-Ethanediol: Human health tier II assessment

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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	Ethylene glycol E 600 (Glycol) Monoethylene glycol 2-hydroxyethanol Ethylene dihydrate
Structural Formula	
Molecular Formula	C2H6O2
Molecular Weight (g/mol)	62.07
Appearance and Odour (where available)	Colourless odourless liquid.
SMILES	C(O)CO

Import, Manufacture and Use

Australian

The total volume introduced into Australia, reported under previous mandatory and/or voluntary calls for information, was greater than 20 000 tonnes.

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

The chemical has reported use in cosmetics.

The chemical has reported domestic and commercial use including as a constituent of:

- cleaning/washing products;
- hydraulic brake fluids;
- anti-freeze agents; and
- corrosion inhibitors.

The chemical has reported site-limited use including:

- in the manufacture of other chemicals;
- as a stabiliser;
- as a heat transferring agent;
- as a colouring agent;
- in hydraulic fracturing;
- as a solvent; and
- as a tanning agent.

International

The following international uses have been identified through European Union Registration, Evaluation, Authorisation and Restriction of Chemicals (EU REACH) dossiers; the Organisation for Economic Cooperation and Development Screening Information Dataset Initial Assessment Report (OECD SIAR); Galleria Chemica; Substances and Preparations in the Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported cosmetic use as a:

- humectant;
- solvent; and
- viscosity controlling agent.

The chemical has reported domestic and commercial use including as a constituent of:

- cleaning/washing products;
- hydraulic brake fluids;
- anti-freeze agents; and
- corrosion inhibitors.

The chemical has reported site-limited use including:

- in the manufacture of other chemicals;

- as a stabiliser;
- as a heat transfer agent;
- in colouring agents;
- in hydraulic fracturing;
- in bleaching agents;
- as a complexing and flocculating agent;
- in electroplating;
- in manufacture of flame retardants and extinguishing agents;
- as a solvent in paints, lacquers and varnishes; and
- as a tanning agent.

The chemical has reported non-industrial use including as a constituent of pesticides.

Restrictions

Australian

The chemical is listed in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP, 2013) in Schedules 5 and 6, and Appendix C, with the following entries:

Schedule 5: Ethylene glycol (excluding salts and derivatives) in preparations containing not less than 10 mg/kg of denatonium benzoate as a bittering agent except:

(a) in paints or paint tinters;

(b) in toothpastes or mouthwashes containing more than 0.25 % of ethylene glycol; or

(c) in other preparations containing 2.5 % or less of ethylene glycol.

Schedule 6: Ethylene glycol (excluding salts and derivatives) except:

(a) when included in Section 5;

(b) in paints or paint tinters;

(c) in toothpastes or mouthwashes containing more than 0.25 % of ethylene glycol; or

(d) in other preparations containing 2.5 % or less of ethylene glycol.

Appendix C: Ethylene glycol for use in toothpastes or mouthwashes except in preparations containing 0.25 % or less of ethylene glycol.

International

The following international restrictions have been identified through Galleria Chemica.

Ethylene glycol (and mixtures containing 10 % or more by weight) is a hazardous substance under Section 3(b) of the United States Federal Hazardous Substances Act as designated by the Consumer Product Safety Commission. Ethylene glycol and mixtures containing 10 % or more by weigh require labelling with the signal word "Warning" and the statement "Harmful or fatal if swallowed".

Health advisories (HA) exist for ethylene glycol in the United States Drinking Water Standards. The health advisory is 'an estimate of acceptable drinking water levels for a chemical substance based on health effects information'. The 1-day and 10-day HAs for a 10 kg child are 20 and 6 mg/L, respectively. The lifetime HA for a 70kg adult is 14 mg/L.

Existing Work Health and Safety Controls

Hazard Classification

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

Xn; R22: Acute toxicity

Exposure Standards

Australian

Ethylene glycol (aerosol) has an exposure standard of 10 mg/m^3 time weighted average (TWA). A further exposure standard for ethylene glycol (vapour) is 52 mg/m^3 (20 ppm) TWA and a short-term exposure limit (STEL) of 104 mg/m^3 (40 ppm).

International

The following exposure standards are identified (Galleria Chemica):

An exposure limit (TWA) for aerosol ethylene glycol of 10 mg/m^3 in different countries such as UK, Canada (Yukon) and Netherlands. STELs reported were 10 and 20 mg/m^3 in Canada (Yukon) and UK respectively.

An exposure limit (TWA) for ethylene glycol vapour of 52–250 mg/m^3 in different countries such as UK (52 mg/m^3), Canada (Yukon 250 mg/m^3) and Taiwan (127 mg/m^3). STELs reported were 325, 4 and 104 mg/m^3 in Canada (Yukon), UK and Ireland respectively.

Health Hazard Information

The toxicity of ethylene glycol is attributed to glycolic acid and oxalic acid, major metabolites which can accumulate in the body due to their rate limiting metabolism. The accumulation of these metabolic products results in acidaemia (increased blood pH), oxalosis (due to the metabolite oxalic acid) and renal interstitial oedema. These specific effects then induce central nervous system (CNS), metabolic, cardiopulmonary and renal toxicity (TOXINZ) which are a result of the rate limiting metabolism of glycolic acid to formic acid, oxalic acid and glycine (ATSDR, 2010).

Toxicokinetics

Absorption

Ingested ethylene glycol is rapidly absorbed in rats (strain unspecified), reaching peak blood levels within 1 hour after single gavage doses of 150–20000 mg/kg bw. Similar rapid absorption was observed in mice, monkeys, dogs, and pregnant rabbits, with peak blood levels observed 1-3 hours after gavage exposure. Peak plasma concentrations were observed in rats and mice within 1-4 hours, with an absorption rate of 90–100% of the administered dose. After gavage doses of 10 and 1000 mg/kg bw ethylene glycol to rats and mice, the areas under the ethylene glycol plasma level versus time curves were similar to those observed with equivalent intravenous doses, suggesting near complete absorption of the ingested chemical in rats and mice (ATSDR, 2010; NTP, 2004).

Dermal absorption in Sprague Dawley (SD) rats was reported in the range of 26–32 % of the administered dose (occluded dermal doses of 10 or 1000 mg/kg bw ethylene glycol or 1000 mg/kg bw of a 50 % ethylene glycol solution) from radioactivity recovered in body tissues, excreta and exhaled air. CD-1 mice treated with 100 or 1000 mg/kg bw ethylene glycol or 1000 mg/kg bw of 50 % ethylene glycol showed absorption of 60–84 % (ATSDR, 2010; NTP, 2004).

Inhalation absorption in rats was estimated to be 60-90 % of the inhaled dose (32 mg/m^3 ethylene glycol vapour for 30 minutes or 184 mg/m^3 ethylene glycol aerosol for 17 minutes) (ATSDR, 2010; NTP, 2004).

Based on the available information and limited data from humans, 100 % absorption can be assumed in humans following oral, dermal or inhalation exposure.

Distribution

The analysis of tissue, plasma, and urine in humans, rats, mice, monkeys and dogs showed that ethylene glycol is readily distributed to these tissues following oral, dermal or inhalation exposure and also crosses the placenta in pregnant rabbits following oral exposure (ATSDR, 2010; NTP, 2004).

Metabolism

The metabolic pathway of ethylene glycol is similar in humans, monkeys, dogs, rabbits, rats and mice (ATSDR, 2010). The first major metabolic step is the conversion of ethylene glycol to glycoaldehyde. Glycoaldehyde has a very short half-life and is rapidly converted to glycolic acid and to a lesser extent, glyoxal. Glycolic acid is a major metabolite in humans and its potential to accumulate is of toxicological importance. The second major metabolic step is the oxidation of glycolic acid to glyoxylic acid in a rate limiting reaction. Further metabolism of glyoxylic acid leads to the formation of formic acid, glycine, and oxalic acid. In studies in rats, mice and dogs, ethylene glycol and the metabolite glycolic acid have been observed in plasma, urine and/or blood. In vitro data show that humans metabolise glycolic acid at a higher rate than rats (ATSDR, 2010; NTP, 2004).

Excretion

The elimination of ethylene glycol from plasma in humans and laboratory animals was reported to be rapid following oral exposure. The elimination half-lives in blood ranged from 1–4 hours in rats, mice, monkeys and dogs, and the main excretion pathways were exhaled air and urine, independent of the exposure route. Human elimination data of the chemical, mostly sourced from cases of accidental poisonings, reports half-lives in blood ranging from 2.5–8.4 hours, and minimal concentrations of the chemical can be detected in urine or tissue after 24–48 hours (ATSDR, 2010; NTP, 2004).

Acute Toxicity

Oral

The chemical is classified as hazardous with the risk phrase ‘Harmful if swallowed’ (Xn; R22) in HSIS (Safe Work Australia). While the available animal data do not support this classification, poisoning (deliberate/accidental) data from humans (refer to **Acute Toxicity—Observations In Humans**) indicate that the chemical has moderate toxicity by the oral route of exposure.

The chemical had low acute toxicity in animal tests following oral exposure. The median lethal dose (LD50) in rats was greater than 2000 mg/kg bw. Observed sub-lethal effects included central nervous system (CNS) depression, metabolic acidosis, cardiopulmonary effects and renal toxicity. Oral LD50s for ethylene glycol were 4000–10020 mg/kg bw in rats, 6610–8200 mg/kg

bw in guinea pigs, 5500-8350 mg/kg bw in mice, 5000 mg/kg bw in rabbits, and >8000 mg/kg bw in dogs (NTP, 2004; WHO, 2002).

Dermal

The chemical had low acute toxicity in animal tests following dermal exposure. The median lethal dose (LD50) in rabbits was 10600 mg/kg bw. No further details are available (WHO, 2002).

Inhalation

The chemical had low acute toxicity in animal tests following inhalation exposure. The lethal concentration in rats and mice was >200 mg/m^3 after a two-hour inhalation exposure. No further details are reported (WHO, 2002). A further study conducted in CD rats and mice reported an LC50 of >2.5 mg/L after a six-hour inhalation exposure. No adverse effects were reported (REACH).

Observation in humans

Mortality has been observed in humans following intentional or accidental ingestion of ethylene glycol, with the lethal oral dose estimated to be 1400–1600 mg/kg bw (NTP, 2004). The lethal dose in humans is variable and is reported to be 100 mL of pure ethylene glycol, although mortality has been reported in cases where 30 mL of ethylene glycol was ingested (TOXINZ). The estimated range of acute lethal doses is uncertain since the ingested amount is generally not quantified in cases of accidental and/or intentional ingestion.

The American Association of Poison Control Centres (AAPCC) reported 25 mortalities related to ingestion of ethylene glycol for 2005. A case study of five deaths of accidental or intentional poisoning reported the ingestion of ethylene glycol ranging from 150–1500 mL (2379–23786 mg/kg). The minimum lethal dose of ethylene glycol (95 %) reported in humans is 1.4 mL/kg (1330 mg/kg bw) (ATSDR, 2010).

Toxic effects have been characterised by stages that possibly overlap. During the first stage (0.5–12 hours after intake), symptoms include central nervous system depression with ataxia, slurred speech, somnolence, convulsions and gastrointestinal upset. During the second stage (12–72 hours after intake), symptoms include metabolic acidosis with reductions in blood pH and bicarbonate levels and cardiopulmonary effects such as tachypnoea, hyperpnoea, tachycardia, cyanosis, pulmonary oedema and cardiac failure. During the third stage (24–72 hours after intake) renal toxicity is observed possibly from deposition of calcium oxalate crystals in the kidney. Histological investigation of the kidneys has shown tubular necrosis and presence of oxalate crystals. A possible fourth stage (six or more days after intake) included symptoms of deafness, facial paralysis and other neurologic effects (NTP, 2004; TOXINZ).

Corrosion / Irritation

Respiratory Irritation

Based on the available information a classification for respiratory irritation is warranted (refer to **Repeated dose toxicity—observation in humans**).

Skin Irritation

The available data show that the chemical is a mild skin irritant in animals. Mild dermal irritation was reported in rabbits and guinea pigs. No dermal effects were reported in female CD-1 mice exposed to 3549 mg/kg bw/day ethylene glycol under occlusive conditions for 6 hours/day on gestation days 6-15 (NTP, 2004; WHO, 2002).

Eye Irritation

The available data indicate that the chemical is a mild eye irritant in animals.

In a study conducted in six New Zealand White rabbits, 0.05 mL of the chemical (4 or 40 %) applied to one eye (while the other eye served as a control) at 10 minute intervals for a total of 35 applications in a six hour period was reported to cause chemosis, swelling and conjunctival redness. All eyes exposed to the chemical were reported to be normal on day seven of observation and no evidence of systemic toxicity was reported (REACH).

Sensitisation

Skin Sensitisation

The chemical was not found to induce dermal sensitisation when tested according to OECD Test Guideline (TG) 406 (REACH).

Repeated Dose Toxicity

Oral

Considering the lowest observed adverse effect levels (LOAELs) available from 13–104 week studies (300–3000 mg/kg bw/d) (ATSDR, 2010), and based on the treatment-related effects reported in various repeated dose toxicity studies, the chemical is not considered to cause serious damage to health from repeated oral exposure. However, there is evidence of cumulative effects, as the nephropathy observed at high doses in acute toxicity studies also occurs after repeated exposure at lower doses.

The National Toxicology Program (NTP) conducted a 13 week and a two year study in B6C3F1 mice. In the 13 week study, 10 male and 10 female mice were administered 0, 3200, 6300, 12500, 25000 or 50000 ppm ethylene glycol incorporated into feed. There were no reported deaths and no chemical-related clinical findings were reported. Histopathology showed chemical-related kidney and liver lesions, which were significantly elevated in the 25000 and 50000 ppm male mice. These lesions included nephropathy and centrilobular hepatocellular hyaline degeneration (NTP, 1993).

The two year study used 60 male mice dosed with the chemical at 0, 6250, 12500 or 25000 ppm and 60 females dosed at 0, 12500, 25000 or 50000 ppm in feed. The doses in ppm were reported as being equivalent to: males - 0, 1500, 3000 or 6000 mg/kg bw/d and females - 0, 3000, 6000 or 12000 mg/kg bw/d. There were no significant differences in survival although male mice in the high dose (6000 mg/kg bw/d) group had to be housed separately after week 54 due to excessive fighting. Survival of mice was not affected by ethylene glycol administration at all doses. As with the 13 week study, mice did not show any adverse clinical signs. Histopathology showed hepatocellular degeneration in the mid and high dose male and high dose female mice. Pulmonary arterial hyperplasia occurred at a higher incidence in female mice than male mice exposed to the chemical. Some male mice in the high dose group had oxalate-like crystals and/or calculi in the renal system (NTP, 1993).

Mice appear to be less sensitive than rats to ethylene glycol. A two-year study conducted in Fischer-344 (F344) rats found that administration of the chemical (40, 200 or 1000 mg/kg bw/d) resulted in excessive mortality in male rats in the high dose group after nine months. All male rats in the high dose group (1000 mg/kg bw/d) were reported dead by 15 months of the study. Survival was significantly reduced in male rats in the 1000 mg/kg bw/d group only. (Cruzan et al., 2004; DePass et al., 1986). Pathology investigation of the male rats concluded that extensive kidney damage was the reason for increased mortality in the 1000 mg/kg bw/d group. The NOAEL for male rats was reported as 200 mg/kg bw/d in this study (DePass et al., 1986).

A further study indicates that the Wistar rat strain is more sensitive than the F344 strain. In a 16-week study, 10 male rats of each strain were exposed to the chemical (0, 50, 150, 500 or 1000 mg/kg bw/d) by incorporation in a normal diet. Mortality was reported in two Wistar rats at the highest dose and significant weight loss was observed in Wistar rats administered 500 and 1000 mg/kg bw/d, respectively. Both strains of rats treated with ≥ 500 mg/kg bw/d had increased calcium oxalate crystals in the kidney tubules as well as crystal associated nephropathy; this was reported as being more severe in the Wistar rat strain (Cruzan et al., 2004).

Further repeated dose studies conducted in rodents have reported no observed adverse effect levels (NOAELs) in the range of 150–2000 mg/kg bw/d depending on species and strain studied. Overall, repeated oral exposure to ethylene glycol is consistently associated with adverse effects on the kidney such as crystal nephropathy in rodents (ATSDR, 2010).

Dermal

In a study conducted according to OECD TG 410, five male Beagle dogs per group were dermally exposed (60 % of the total body surface area) to 0.5, 2.0 or 8 mL/kg bw/d Glysantin G 105 (automotive coolant which contains ≥ 92.5 % ethylene glycol and ≥1.4 % p-tert.-butyl benzoate (PTBBA)) daily for four weeks. Mortality (4/5 animals) was reported at the highest dose (8 mL/kg). Prior to death, animals showed signs of toxicity including staggering gait, vomiting, diarrhoea and reduced food intake. Clinical analysis showed increased creatinine and urea levels and increased incidence of calcium oxalate crystals. Pathology investigation reported oxalate nephrosis, testicular atrophy and uraemic gastroenteritis. Similar pathology findings were reported at the mid dose (2 mL/kg), but only in one animal. No mortality or any further clinical or pathological adverse effects were reported at the mid and lower doses. Further studies conducted comparing pure ethylene glycol to Glysantin G105 showed that the testicular atrophy was associated with the presence of PTBBA in Glysantin G105 and not ethylene glycol (REACH). PTBBA has known testicular toxicity (NICNAS).

Inhalation

Mortality was reported in 1/15 rats, 3/15 guinea pigs, 1/3 rabbits, 0/3 dogs and 0/3 monkeys after exposure to 12 mg/m^3 of ethylene glycol aerosol for 90 days. Apart from mortality, no specific signs of clinical toxicity were reported. In a further study, no mortality or toxicity was observed in the same range of animal species exposed to either 10 or 57 mg/m^3 ethylene glycol. The authors noted that as the exposure was whole body, further oral intake from grooming may have occurred, and therefore a reliable LOAEL could not be established (ATSDR, 2010).

Observation in humans

In a study conducted with 19 human volunteers, the tolerance to ethylene glycol aerosol was assessed in a repeat dose study. The volunteers were exposed to the chemical (on average 23–30 mg/m^3) for 20–22 hours/day for 30 days. During the last 10 days of the study, the concentration of aerosol was gradually increased to determine the threshold of discomfort. At 140 mg/m^3 most of the volunteers reported upper respiratory and/or nasal irritation. At higher doses the chemical was only tolerable for a few minutes or even 'a couple of breaths' (15 minutes at 188 mg/m^3, two minutes at 244 mg/m^3 and a couple of breaths at 308 mg/m^3). At the highest exposure dose volunteers reported intense respiratory discomfort with a burning sensation in the trachea and a burning cough. While some volunteers reported having a headache, no further adverse effects were reported (ATSDR, 2010).

Genotoxicity

Based on the weight of evidence from the available in vitro and in vivo genotoxicity studies the chemical is not considered to be genotoxic.

An Ames assay conducted according to OECD TG 471 reported that the chemical did not induce bacterial mutations in *Salmonella typhimurium* strains TA 1535, TA 1537, TA 98, TA 100 and *Escherichia coli* WP2 at a concentration up to 5000 μg/plate with or without metabolic activation (REACH). Further in vitro genotoxicity tests conducted with bacterial and mammalian cell lines were all negative for gene mutations and DNA strand breaks respectively (ATSDR, 2010).

An in vivo study in mice reported no chromosomal aberrations in Swiss mice exposed to 638 mg/kg bw/day for two days (WHO, 2002). Negative results were found for dominant lethal mutations in F344 rats after administration of up to 1000 mg/kg bw/d ethylene glycol in a 155-day multi-generational study.

Carcinogenicity

Based on the available data, ethylene glycol is not considered to be a carcinogen.

Histopathological investigations showed no evidence of carcinogenicity in studies conducted in various rodent species. No tumours were reported in SD rats administered up to 3000 mg/kg bw/day in the diet for two years, F344 rats administered 1000 mg/kg bw/day in the diet for one year, B6C3F1 mice administered up to 12000 mg/kg bw/day in the diet for two years and CD-1 mice administered up to 1000 mg/kg bw/day in the diet for two years (NTP, 2004; WHO, 2002).

A limited number of epidemiological studies have reported that exposure to the chemical does not increase the risk of cancer. Ethylene glycol exposure (inhalation) in 1666 chemical plant employees was not found to increase the odds ratio (OR) for any type of cancer (ATSDR, 2010).

Reproductive and Developmental Toxicity

The available data from rat studies suggest that developmental effects were only observed secondary to maternal toxicity, so the chemical does not show specific developmental toxicity. The chemical is not toxic to reproduction.

Having reviewed the available data the Centre for the Evaluation of Risks to Human Reproduction (CERHR) expert panel concluded that there are sufficient data to conclude that the chemical is not toxic to reproduction in rats orally exposed to 1000 mg/kg bw/day in diet (NTP, 2004). A study in mice gave negative results at doses up to 2826 mg/kg bw/day via drinking water.

The expert panel also concluded that exposure of CD-1 mice to the chemical by the dermal route for 6 hours/d on gestation days (GD) 6-15 resulted in no evidence of developmental toxicity up to a dose of 3549 mg/kg bw/d. Developmental toxicity was also not observed in rabbits exposed orally via gavage on GD 6-19 to doses as high as 2000 mg/kg bw/d. Severe maternal toxicity was observed at the high dose with maternal deaths as well as oxalate crystals in the kidney.

Data suggested that oral exposure to high doses of the chemical (≥500 mg/kg bw/d in CD-1 mice and ≥1000 mg/kg bw/d in SD rats) on GD 6-15 causes developmental effects in mice and rats such as axial skeletal malformations, external malformations, reduced body weights and increased post-implantation loss (NTP, 2004). The CERHR expert panel concluded that developmental toxicity may not be attributed directly to the chemical but from the accumulation of glycolic acid, which is a metabolic breakdown product of ethylene glycol. The developmental effects are seen at doses that exceed saturation of glycolic acid metabolism. Observations from rat studies suggest that oral doses resulting in developmental toxicity (1000 mg/kg bw/d) are greater than those associated with maternal and renal toxicity at 500 mg/kg bw/d.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation of this chemical includes systemic acute effects particularly acute toxicity by the oral route of exposure, which has led to a number of human fatalities. The chemical also causes respiratory irritation.

Public Risk Characterisation

The chemical is currently listed in Appendix C of the SUSMP for toothpaste and mouthwash uses at above 0.25 %. For other domestic and cosmetic products it is listed in Schedule 5 or 6, depending on whether it is treated with a bittering agent to make it unpalatable. When the chemical is in Schedule 5 or 6, a number of warning statements, first aid instructions and safety directions apply. The current controls are considered adequate to minimise the risk to public health posed by domestic and cosmetic products containing the chemical, therefore, the chemical is not considered to pose an unreasonable risk to public health.

Occupational Risk Characterisation

During product formulation, dermal, ocular 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 oral 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 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).

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 if swallowed - Cat. 4 (H302)
Irritation / Corrosivity	Irritating to respiratory system (Xi; R37)	May cause respiratory irritation - Specific target organ tox, single exp Cat. 3 (H335)

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

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

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

Advice for consumers

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

Advice for industry

Control measures

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

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

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

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

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

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

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

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

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

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