Pyridine: Human health tier II assessment

03 July 2015

CAS Number: 110-86-1

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.

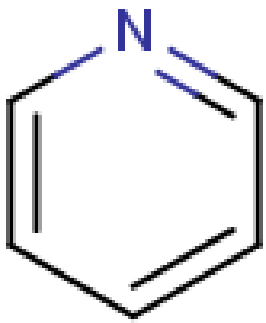
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	azabenzene azine piridina tritisan
Structural Formula	
Molecular Formula	C5H5N
Molecular Weight (g/mol)	79.10
Appearance and Odour (where available)	Colourless to yellow liquid with sharp, nauseating fish-like odour
SMILES	c1ccccn1

Import, Manufacture and Use

Australian

The total volume introduced into Australia, reported under previous mandatory and/or voluntary calls for information, was <1 tonne. No use information has been identified.

International

The following international uses have been identified through the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers; Galleria Chemica; the Substances and Preparations in Nordic countries (SPIN) database; the US Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR); the US National Library of Medicine's Hazardous Substances Data Bank (HSDB); the Agency for Toxic Substances and Disease Registry (ATSDR, 1992); and the International Fragrance Association (IFRA) Survey Transparency List.

The chemical has reported cosmetic or domestic use as a fragrance compound (IFRA Survey, 2011).

The chemical has reported site-limited uses including:

- manufacturing other chemicals, paints, dyes, adhesives and rubber products;
- as a solvent to waterproof fabrics;
- as a denaturant for alcohol and anti-freeze mixtures;
- as a dyeing auxiliary in textiles; and
- in waste treatment and processing.

The chemical has reported non-industrial uses:

- for manufacturing pharmaceuticals;
- as a food flavouring; and
- for manufacturing pesticides.

Restrictions

Australian

No known restrictions have been identified.

International

No known international restrictions have been identified.

Existing Work Health and Safety Controls

Hazard Classification

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

- Xn; R20/21/22 (acute toxicity)

Exposure Standards

Australian

The chemical has an exposure standard of 16 mg/m^3 (5 ppm) time weighted average (TWA).

International

The following exposure standards are identified (Galleria Chemica):

- a TWA of 0.9–7 mg/m^3 (up to 2 ppm) in different countries such as Canada (Alberta, British Columbia, Saskatchewan), China, Netherlands, Philippines, Poland, Russia, Spain and Sweden;
- a TWA of 15–16 mg/m^3 (5 ppm) in different countries such as Canada (Quebec, Yukon), Denmark, Egypt, Estonia, France, Greece, Hungary, Iceland, India, Indonesia, Ireland, Latvia, Malaysia, Mexico, Norway, Singapore, South Africa, Switzerland, Taiwan, Turkey, United Kingdom and USA (California, Hawaii, Minnesota, Tennessee, Vermont, Washington); and
- a short-term exposure limit (STEL) of 10–60 mg/m^3 (3–20 ppm) in different countries such as Canada (Saskatchewan, Yukon), Egypt, France, Greece, Hungary, Ireland, Mexico, South Africa, Sweden, Switzerland, United Kingdom and USA (Hawaii, Washington).

Health Hazard Information

Toxicokinetics

Pyridine is absorbed by oral, dermal and inhalation exposure. It is widely distributed in the body, with highest concentrations in the kidneys, liver, plasma and lungs. Pyridine is primarily metabolised by N-methylation or aromatic hydroxylation. It is eliminated either unchanged or as its metabolites predominantly in urine, but also by exhalation and in faeces (NTP, 2000; REACH).

Acute Toxicity

Oral

The chemical is classified as hazardous with the risk phrase 'Harmful if swallowed' (Xn; R22) in the HSIS (Safe Work Australia). The available data support this classification.

The following oral median lethal dose (LD50) values were available:

- 891 mg/kg bw in male albino rats (US EPA, 2009);
- 1580 mg/kg bw in rats (SCOEL, 2004); and
- 1500 mg/kg bw in mice (SCOEL, 2004).

Reported signs of toxicity included weakness, uncoordinated muscle movement, excess salivation and unconsciousness (SCOEL, 2004).

Dermal

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

The following dermal LD50 values were available:

- between 1000 and 2000 mg/kg bw in albino rabbits (US EPA, 2009);
- 1121 mg/kg bw in rabbits (RTECS); and
- 1000 mg/kg bw in guinea pigs (RTECS).

Reported signs of toxicity included weakness, uncoordinated muscle movement, excess salivation and unconsciousness (SCOEL, 2004).

Inhalation

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

The following median lethal concentration (LC50) values were available (US EPA, 2009):

- between 15 mg/L and 18 mg/L in male Sprague Dawley (SD) rats exposed (nose only) to the chemical vapour for four hours;
- approximately 29 mg/L in male and female SD rats exposed (whole body) to the chemical vapour for one hour;
- <12 mg/L in rats exposed to the chemical vapour for four hours.

Reported signs of toxicity included weakness, uncoordinated muscle movement, excess salivation and unconsciousness (SCOEL, 2004).

Observation in humans

Inhalation is the primary route of exposure to the chemical (NTP, 2000) and acute exposure affects the central nervous system (IARC, 2000). The estimated lethal dose of the chemical is reported to be between 0.5 and 5.0 g/kg bw, and an air concentration of approximately 10.8 mg/L (3600 ppm) was reported to be an immediate threat to life (SCOEL, 2004).

Acute narcosis was reported in a man who had cleaned a tank that previously contained the chemical. 'A 29-year-old man who accidentally swallowed half a cup of pyridine (approximately 125 mL) experienced nausea, dizziness, abdominal pain and lung congestion followed by death within two days' (SCOEL, 2004).

Corrosion / Irritation

Corrosivity

Based on the available data, the chemical is considered to be corrosive, warranting hazard classification (see **Recommendation** section). Corrosive chemicals are also considered to cause irreversible effects on the eyes. The available eye irritation studies for the chemical indicate severe irritation or eye damage, supporting the hazard classification.

In New Zealand White rabbits (n = 3 females), 0.5 mL of the undiluted chemical was applied to intact and abraded skin for four hours, and animals were observed at 24 and 72 hours post-exposure. Irreversible damage to the skin was reported, and it was concluded that the chemical was corrosive (REACH).

In albino rabbits (n = 6), 0.5 mL of the undiluted chemical was applied to intact and abraded skin, and animals were observed at 24 and 72 hours post-exposure. The chemical was reported to be corrosive (US EPA, 2009).

In male New Zealand White rabbits, mild oedema and mild to severe erythema with some necrosis was observed when the chemical was applied to intact skin. A cutaneous primary irritation index value of 4.8/8 was reported for this study (HSDB). Skin necrosis was reported in rabbits when the chemical was applied to damaged skin (SCOEL, 2004). However, other studies reported no or mild skin irritation in rabbits (SCOEL, 2004; ATSDR, 1992; REACH; RTECS).

Several eye irritation studies in rabbits indicated the chemical to be a severe eye irritant. The chemical was reported to be severely irritating to the eyes of albino rabbits (n = 6), when 0.1 mL was administered into the eyes with observation at 24, 48 and 72 hours (US EPA, 2009). Rabbits exposed to commercial grade chemical (90 % solution) showed severe eye damage, with corneal opacity (due to permanent stromal opalescence), conjunctival scarring and subepithelial vascularisation (HSDB). Moderate ocular irritation (injury score of 7/10, 24 hours post-exposure) was also reported in rabbits when administered the undiluted chemical (ATSDR, 1992; HSDB).

Observation in humans

The chemical was reported to be a skin, eye and mucous membrane irritant in humans (SCOEL, 2004).

Sensitisation

Skin Sensitisation

Based on the limited data available, the chemical is not considered to be a skin sensitiser.

In a dermal sensitisation test in guinea pigs, the chemical was reported as not sensitising (US EPA, 2009). Study details were not available.

Observation in humans

In a Kligman maximisation test, pyridine was rated 1/5 and reported to be a 'low' skin sensitising agent (SCOEL, 2004).

Repeated Dose Toxicity

Oral

Based on the available data, the chemical is considered to cause severe health effects (e.g. liver lesions) following repeated oral exposure, warranting hazard classification (see **Recommendation** section).

Several 13-week studies in rodents were available. In an 89-day oral study (similar to the Organisation for Economic Cooperation and Development (OECD) test guideline (TG) 408), SD rats (n = 10/sex/dose) were administered the chemical by oral gavage at 0, 0.25, 1, 10, 25 or 50 mg/kg bw/day. Terminal body weights were significantly reduced, despite increased food intake in male rats at 50 mg/kg bw/day, compared with controls. Absolute liver weights were significantly increased in female rats at 10 and 50 mg/kg bw/day. In male and female rats, the overall incidence of inflammatory liver lesions (infiltrate around the bile ducts, bile duct proliferation, enlarged and vacuolated hepatocytes, hepatocyte death) was reported to be up to 70 % and 20 %, respectively, compared with 10 % incidence in controls. However, no dose-response was observed. The no observed adverse effect level (NOAEL) was reported to be 1 mg/kg bw/day, based on increased liver weights in the female rats at 10 mg/kg bw/day (US EPA, 2009; SCOEL, 2004; US EPA IRIS; REACH). Based on this NOAEL, an oral reference dose (RfD) of 1 µg/kg bw/day was determined ('daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime') (US EPA IRIS).

In a 13-week oral study, Fischer 344/N (F344/N) rats (n = 10/sex/dose) were exposed to the chemical in drinking water at 0, 50, 100, 250, 500 or 1000 ppm (equivalent to doses of 0, 5, 10, 25, 55 and 90 mg/kg bw/day). Two female rats died at 1000 ppm. Terminal body weights were significantly decreased in male rats (by 15 %) at 1000 ppm and in female rats (by 6–9 %) at ≥500 ppm, compared with controls. Absolute liver weights were significantly increased in male rats at ≥250 ppm and in female rats at ≥100 ppm, with significantly increased incidence of liver lesions (pigmentation, centrilobular degeneration, hypertrophy, chronic inflammation) in male rats at ≥500 ppm and in females rats at ≥250 ppm, compared with controls. Males at 1000 ppm had significantly increased nephropathy (granular casts, hyaline droplets) (NTP, 2000). The NOAEL was 5 ppm (5 mg/kg bw/day), based on significantly increased absolute liver weights in female rats at 100 ppm (10 mg/kg bw/day).

Male Wistar rats (n = 10/dose) were administered the chemical in drinking water at 0, 50, 100, 250, 500 or 1000 ppm (equivalent to doses of 0, 5, 10, 30, 60 and 100 mg/kg bw/day) for 13 weeks. One rat died at 500 ppm. Significantly increased incidences of liver lesions (pigmentation, centrilobular degeneration, hypertrophy, chronic inflammation) were observed at ≥500 ppm, compared with controls (NTP, 2000). Body weights were significantly decreased from 250 ppm, and a NOAEL of 100 ppm (10 mg/kg bw/day) can be determined based on this.

In another 13-week study, F344 rats (n = 10/sex/dose) were administered the chemical by oral gavage at 0, 12.5, 25, 50, 100 or 200 mg/kg bw/day. Four animals died during the study (one male at 100 mg/kg bw/day and one male and two females at 200 mg/kg bw/day). Liver lesions (necrosis, enlarged liver cells, bile duct hyperplasia, fat infiltration) at ≥100 mg/kg bw/day and inflamed heart muscle at 200 mg/kg bw/day were observed. The NOAEL was reported to be 50 mg/kg bw/day, although decreased bodyweights (by 11–14 %, compared with the control group) were observed in all treated females (US EPA, 2009).

When B6C3F$_1$ mice (n = 10/sex/dose) were exposed to the chemical in drinking water at 0, 50, 100, 250, 500 or 1000 ppm (equivalent to doses of 0, 10, 20, 50, 85 and 160 mg/kg bw/day for males and 0, 10, 20, 60, 100 and 190 mg/kg bw/day for females) for 13 weeks, one female died at 250 ppm. Absolute liver weights were significantly increased in males at ≥100 ppm (by 11–22 %) and in females at 250 or 500 ppm only (by 15 % and 21 %, respectively), compared with controls. There were no histopathological changes in the liver or in other organs (NTP, 2000).

Dermal

No data are available.

Inhalation

Only limited data are available and are insufficient to make a conclusion on the repeated dose inhalation toxicity of the chemical.

Male F344/N rats (n = 5/dose and n = 10 for controls) were exposed (nose only) to the chemical vapour at 0, 5 or 444 ppm for six hours per day for four days and euthanised 18–20 hours after the last exposure. Olfactory epithelium in the nasal mucosa of all exposed animals showed vacuole damage in sustentacular (supporting) cells; weakening of the epithelium; neuron loss, indicated by reduced neuronal cell nuclei; and intraepithelial luminal structures (indicative of degenerating cells). The lesions were slightly increased in severity at 444 ppm (SCOEL, 2004; REACH).

In rats exposed to the chemical vapour at 10 or 50 ppm (32 or 162 mg/m^3) for seven hours a day, five days per week for six months, increased liver weights were reported. There were no mortalities and no effects on growth rate (SCOEL, 2004; US EPA IRIS). No further details were available.

Observation in humans

Workers exposed to the chemical vapour at approximately 125 ppm (0.405 mg/L) for four hours per day for up to two weeks reported headaches, dizziness, insomnia, nausea and anorexia (IARC, 2000; NTP, 2000).

In a chemical plant where workers were exposed to the chemical at 6–13 ppm (duration of exposure not stated), seven cases of poisoning were reported and symptoms included headaches, occasional dizziness, nervousness, insomnia and some nausea with vomiting (SCOEL, 2004).

Two patients were treated with the chemical for epilepsy and were administered oral doses of 1.9–2.4 mL daily for 10–30 days. Fatigue, nausea, headache, and severe liver and kidney damage were reported. One patient (a 32-year-old man) died, but death could not be attributed specifically to the chemical because other medications (e.g. phenobarbital, magnesium sulfate, sodium bromide) were being taken concurrently (ATSDR, 1992; SCOEL, 2004).

Two workers were exposed to the chemical contaminated with its methyl derivatives. A chemist exposed for 6 months (dose not stated), suffered from disordered balance, facial paralysis and bouts of fainting which ceased after he stopped working with the chemical. The other, who was exposed for two years (dose not stated), developed symptoms resembling Wernicke's encephalopathy—a neurological disorder associated with thiamine deficiency and characterised by ataxia, confusion and eye disturbances (SCOEL, 2004).

Genotoxicity

Based on the available data, the chemical is not considered to be genotoxic.

A number of in vitro genotoxicity assays gave negative results for the chemical (US EPA, 2009; NTP, 2000; REACH), including:

- DNA damage/repair assay using *Escherichia coli* strains 343/113 polA$^+$ and KMBL1787 polA$^-$ at 10 µg/plate, without metabolic activation;
- several bacterial reverse mutation assays using *Salmonella typhimurium* strains TA98, TA100, TA102, TA1535, TA1537 and TA1538 at 0.05–100 µL/plate or 100–10000 µg/plate, with or without metabolic activation;
- gene mutations in L5178Y mouse lymphoma cells at up to 5000 µg/mL, with or without metabolic activation;
- gene mutations in Chinese hamster lung cells (V79) at up to 9.25 µL/mL, with or without metabolic activation;
- chromosomal aberrations in V79 cells up to 10 µL/mL with or without metabolic activation, and up to 506 mg/L without metabolic activation;
- chromosomal aberrations in Chinese hamster ovary (CHO) cells at up to 2.3 mg/mL without metabolic activation, and at up to 5 mg/mL with metabolic activation;
- a sister chromatid exchange (SCE) assay in CHO cells at 1, 2 and 5 mM without metabolic activation, and up to 5020 µg/mL with or without metabolic activation.

Several in vivo genotoxicity assays gave negative results for the chemical (US EPA, 2009; SCOEL, 2004; REACH):

- a chromosomal aberrations assay in bone marrow cells of male B6C3F$_1$ mice (n = 10/dose) exposed to the chemical by intraperitoneal (i.p.) injection at 400, 500 or 600 mg/kg bw and euthanised at 17 or 36 hours after exposure;
- a bone marrow micronucleus assay in male B6C3F$_1$ mice (n = 5/dose) exposed to the chemical by i.p. injection at 31.25, 62.5, 125, 250 or 500 mg/kg bw/day for three days and euthanised 24 hours after the last exposure;
- an unscheduled DNA synthesis (UDS) assay in hepatocytes from male mice administered the chemical once by oral gavage at 175, 350 or 700 mg/kg bw and euthanised two or 16 hours after the last exposure;
- negative or equivocal results in sex-linked recessive lethal mutation assays in *Drosophila melanogaster* (administered the chemical in feed up to 730 ppm or by injection up to 7000 µg/mL, respectively);
- a reciprocal translocations assay in germ cells of male *D. melanogaster* exposed to the chemical by injection at 4300 ppm.

Carcinogenicity

The animal data available on the carcinogenicity of the chemical are not conclusive. In rat carcinogenicity studies, it was reported that only kidney tubule adenomas and testicular interstitial cell adenomas developed in males, whereas mononuclear cell leukaemia developed in females. Non-neoplastic lesions were also observed in the livers of rats at doses up to 36 mg/kg bw/day. However, the carcinogenicity study in mice reported hepatocellular adenomas and carcinomas including metastasis (reported in the NTP studies but not discussed in the International Agency for Research on Cancer (IARC) report (2000)). Therefore, the chemical was not recommended to be classified as a carcinogen.

The IARC has evaluated the chemical as '*not classifiable as to its carcinogenicity to humans*' (Group 3), based on inadequate evidence for carcinogenicity in humans, and limited evidence for carcinogenicity in experimental animals (IARC, 2000).

In a two-year carcinogenicity study, F344/N rats (n = 50/sex/dose) were exposed to the chemical in drinking water at 0, 100, 200 or 400 ppm (equivalent to doses of 0, 7, 14 and 33 mg/kg bw/day). Significantly increased kidney tubule adenomas and glandular stomach mineralisation were observed in males at the highest dose. In females at ≥14 mg/kg bw/day, significantly increased incidence of mononuclear cell leukaemia was reported. Non-neoplastic lesions were observed in the livers of all treated rats (NTP, 2000).

In a carcinogenicity study, male Wistar rats (n = 50/sex/dose) were exposed to the chemical in drinking water at 0, 100, 200 or 400 ppm (equivalent to doses of 0, 8, 17 and 36 mg/kg bw/day) for two years. The survival rate was significantly decreased at ≥17 mg/kg bw/day. At the highest dose, there was significantly increased incidence of testicular interstitial cell adenomas, compared with controls. Moderately severe nephropathy was reported in all animals, including in the control group, but extra-renal lesions indicative of severe nephropathy (glandular stomach mineralisation and parathyroid gland hyperplasia) were observed in rats at 8 and 17 mg/kg bw/day. Non-neoplastic lesions including centrilobular degeneration, necrosis and fibrosis were observed in the livers of all treated rats (NTP, 2000).

Mice (B6C3F$_1$, n = 50/sex/dose) were exposed to the chemical in drinking water at 0, 250, 500 or 1000 ppm for males (equivalent to 0, 35, 65 and 110 mg/kg bw/day) and at 0, 125, 250 or 500 ppm for females (equivalent to 0, 15, 35 and 70 mg/kg bw/day) for two years. Significantly increased incidence of hepatocellular adenomas (29/50, 40/50, 34/49 and 39/50 in males at control, low, mid and high dose groups, respectively), carcinomas (15/50, 35/50, 41/49 and 40/50 in males and 13/49, 23/50, 33/50 and 41/50 in females at control, low dose, mid dose and high dose groups, respectively), and hepatoblastoma (2/50, 18/50, 22/49 and 15/50 in males and 1/49, 2/50, 9/50 and 16/50 in females at control, low dose, mid dose and high dose groups, respectively) were observed in all treated mice (IARC, 2000; NTP, 2000). The NTP also reported metastases (development of secondary malignant growths) of liver tumours to the lungs or to adjacent lymph nodes (NTP, 2000).

Reproductive and Developmental Toxicity

No reproductive or developmental toxicity studies on the chemical are available. The information available from repeated dose toxicity studies are insufficient to make a conclusion on the reproductive and developmental toxicity of the chemical.

Rats (F344/N; n = 10/sex/dose) exposed to the chemical in drinking water at 1000 ppm (equivalent to 90 mg/kg bw/day) for 13 weeks showed significantly prolonged oestrus cycle in females and significantly reduced epididymides and testes weights in males, compared with controls. In a 13-week study in B6C3F$_1$ mice (n = 10/sex/dose), significantly decreased sperm motility was reported in male mice treated with the chemical at 250, 500 or 1000 ppm in drinking water (equivalent to 50, 85 and 160 mg/kg bw/day) (NTP, 2000).

Injection of the chemical into chicken embryos at 10 or 20 mg/egg resulted in abnormal chick development. Incompletely developed or underdeveloped muscle (15 % and 67 % incidence in low and high doses, respectively); defective beaks (4.9 % incidence in the high dose); and short or twisted necks (1.1 % incidence in the high dose) were observed in chicks (ATSDR, 1992).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation are:

- local effects (corrosivity);
- harmful systemic effects following repeated oral exposure; and
- systemic acute effects from oral, dermal or inhalation exposure.

Although the carcinogenicity data were equivocal overall, the potential for carcinogenicity can not be ruled out.

Public Risk Characterisation

Although use in cosmetic or domestic products in Australia is not known, the chemical is reported to be used in cosmetics and domestic products as a fragrance compound (IFRA Survey, 2011). However, the maximum concentration of the chemical in these products is not available, although the highly unpleasant smell of pyridine at high concentrations suggests that maximum use concentrations must be low.

Currently, there are no restrictions on using this chemical in Australia. In the absence of any regulatory controls, the characterised critical health effects have the potential to pose an unreasonable risk if used at high concentrations. Considering the consumer exposure to the chemical only as a fragrance ingredient and noting the introduction volume into Australia (<1 tonne), high concentrations of the chemical in consumer products are not expected. Therefore, the public risk from this chemical is not considered to be unreasonable.

Occupational Risk Characterisation

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

The data available support an amendment to the hazard classification in the HSIS (Safe Work Australia) (see **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

Public Health

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

Work Health and Safety

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

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22)* Harmful in contact with skin (Xn; R21)* Harmful by inhalation (Xn; R20)*	Harmful if swallowed - Cat. 4 (H302) Harmful in contact with skin - Cat. 4 (H312) Harmful if inhaled - Cat. 4 (H332)
Irritation / Corrosivity	Causes burns (C; R34)	Causes severe skin burns and eye damage - Cat. 1C (H314)
Repeat Dose Toxicity	Harmful: danger of serious damage to health by prolonged exposure if swallowed (Xn; R48/22)	May cause damage to organs through prolonged or repeated exposure - Cat. 2 (H373)

[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 the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from oral, dermal, ocular 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 that could minimise the risk include, but are not limited to:

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

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

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

Obligations under workplace health and safety legislation

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

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the 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 the chemical has not been undertaken as part of this assessment.

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Last update 03 July 2015

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