Benzenamine, 4-chloro-: Human health tier II assessment

04 July 2014

CAS Number: 106-47-8

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.

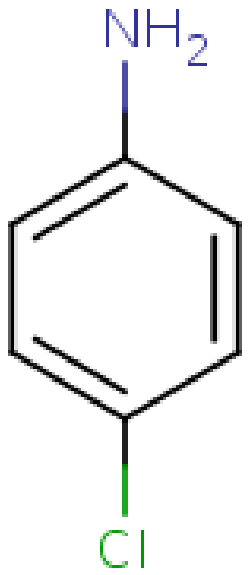
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	4-chloroaniline 4-chlorobenzenamine p-chloroaniline 4-aminochlorobenzene Aniline, p-chloro-
Structural Formula	
Molecular Formula	C6H6ClN
Molecular Weight (g/mol)	127.57
Appearance and Odour (where available)	Colourless, white, or pale-yellow crystalline solid with a characteristic sweet odour.
SMILES	c1(Cl)ccc(N)cc1

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacturing information has been identified.

International

The following international uses have been identified through European Union Registration, Evaluation, Authorisation and Restriction of Chemicals (EU REACH) dossiers; Galleria Chemica; Substances and Preparations in the Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database; United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) dictionary; the US National Library of Medicine's Hazardous Substances Data Bank (HSDB) and various international assessments (IARC, 1993; WHO, 2003).

The chemical has a site-limited use as an intermediate in manufacturing:

- azo dyes and pigments (dyeing and printing textiles); and
- cosmetic ingredients, such as chlorhexidine and triclocarban in deodorant soaps, sticks, sprays, roll-ons and mouthwashes.

The chemical is also used as a curing agent for epoxy resins, a cross-linking agent in polymer preparation and in producing urethane (Khilnani & Chandalia, 2001).

Restrictions

Australian

This chemical is not directly listed in the *Poisons Standard*—the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP). However, the chemical falls under the scope of the following group entry in Schedule 5:

'AMINES for use as curing agents for epoxy resins except when separately specified in these Schedules' (SUSMP, 2013).

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.' (SUSMP). Schedule 5 chemicals are labelled with 'Caution'.

International

The chemical is restricted under Annex XVII to REACH Regulations. ‘The chemical cannot be used in substances and preparations placed on the market for sale to the general public in individual concentrations ≥ 0.1 % ' (European Parliament and Council 1999; European Parliament and Council 2006; European Parliament and Council 2008).

The chemical is listed on the following (Galleria Chemica):

- Chile List of Substances Hazardous to Health; and
- United Arab Emirates Restricted Chemicals.

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):

- R45 Carc. Cat. 2 (carcinogenicity);
- R43 (skin sensitisation); and
- T; R23/24/25 (acute toxicity).

Exposure Standards

Australian

No specific exposure standards are available. The *Workplace exposure standards for airborne contaminants* advises that 'exposure to carcinogens should be eliminated or minimised so far as is reasonably practicable' (Safe Work Australia).

International

The following exposure standards are identified (Galleria Chemica).

An exposure limit (OEL) of 0.2 mg/m^3 in different countries such as Switzerland, Germany, Austria, Hungary; and 0.3 mg/m^3 in countries such as Bulgaria, Russia, and Poland. A short-term exposure limit (STEL) of 0.8 mg/m^3 is listed in Hungary.

Health Hazard Information

Data for the chemical benzenamine (CAS No. 62-53-3) are included in this report. The chemical shares a number of similarities with benzenamine including structure, metabolic and toxicological profiles. Therefore benzenamine is considered a suitable analogue where the available data are limited.

Toxicokinetics

The chemical can enter the body through oral and inhalation routes. It is readily absorbed by the skin and rapidly absorbed in the gastrointestinal tract. The chemical is also rapidly metabolised in the liver and eliminated through urinary, faecal and biliary excretion (IARC, 1993; WHO, 2003). In laboratory animals, the chemical is widely distributed throughout the body including in the muscle, fat, skin, blood, liver, spleen and kidneys. Within three hours of a single intraperitoneal (i.p.) administration in rats, the highest tissue concentration of the chemical was found in the liver (94 %). Twenty-one hours after administration, the tissue concentration was highest in the kidney medulla, followed by the spleen, then the liver.

In laboratory animals, the chemical is rapidly metabolised, primarily via C-hydroxylation, N-oxidation (N-hydroxylation) and N-acetylation. The major metabolic products include 2-amino-5-chlorophenylsulfate, which is formed by C-hydroxylation of the chemical in the ortho position. It is rapidly N-acetylated to 4-chloroacetanilide, which is predominantly found in blood, muscle, skin, fat, and the liver. The 4-chloroacetanilide is further transformed into 4-chloro-glycoanilide and then to 4-chlorooxanilic acid, which is excreted in the urine. The chemical can also undergo N-oxidation to form 4-chloro-phenylhydroxylamine, then to 4-chloronitrosobenzene, which is found in the red blood cells. These metabolic products were also recovered in dog and rabbit urine following intravenous and i.p. exposures (Wiley VCH, 1990). Intragastric and nasogastric intubation studies have demonstrated that N-hydroxylation of the chemical in a number of species, including C3H mice, rhesus monkeys and Fischer 344 (F344) rats, is catalysed by the microsomal cytochrome P450 enzymes in the liver, including those that are inducible by phenobarbital (IARC, 1993).

The chemical is primarily excreted in the urine. The elimination of the chemical or its metabolites occurs in two phases (biphasic). Compared with mice and rats, the retention of the metabolites was longer in monkeys. In humans, the chemical and a metabolite, 2-amino-5-chlorophenol, were detectable in the urine on days three and four after an acute poisoning incident (IARC, 1993).

Binding of the chemical to haemoglobin has been observed in animals and in humans. Of all the chlorinated anilines, this chemical possesses the strongest potential to bind to haemoglobin, resulting in adduct formation. The active metabolite responsible for covalent binding is 4-chloronitrosobenzene, which forms a hydrolysable sulfinic acid amide adduct (93 % of total haemoglobin adducts). These play a significant role in the development of blood disorders associated with the chemical exposure (see **Repeated dose toxicity**). Binding to protein in the kidney and liver has also been observed (IARC, 1993; WHO, 2003).

Acute Toxicity

Oral

The chemical is classified as hazardous with the risk phrase ‘Toxic if swallowed’ (T; R25) in HSIS (Safe Work Australia).While the available data do not support this classification, in the absence of more comprehensive information, there is insufficient evidence to support a recommendation to amend the existing classification.

The acute oral toxicity of the chemical was investigated in rats, mice and cats. The reported median lethal dose (LD50) values from the oral gavage studies in Wistar and Sprague Dawley (SD) rats were 340–380 mg/kg bw for males and 300–370 mg/kg bw for females. Methaemoglobin formation and the resulting methaemoglobinaemia was observed in Wistar rats, along with clinical changes such as restlessness, tremors, respiratory difficulties, cyanosis and a more advanced stage of intoxication (REACH). Similar effects were reported from another oral gavage study in F344 rats and B6C3F1 mice. In cats, exposure to 8 mg/kg bw of the chemical resulted in increased methaemoglobin formation within the first five hours of exposure (WHO, 2003; REACH).

Dermal

The chemical is classified as hazardous with the risk phrase ‘Toxic in contact with skin’ (T; R24) in HSIS (Safe Work Australia). The limited available data (LD50—335 mg/kg bw rat; LD50—360 mg/kg bw rabbit) support this classification (REACH).

Dermal application of the chemical (doses not specified) to cats produced clinical changes such as cyanosis, dilated pupils, increased respiration rate and unsteady gait. Treatment-related lethality was observed following application of 1 g of the chemical. Discolouration of lungs was also noted at histological analysis (Wiley VCH, 1990).

Inhalation

The chemical is classified as hazardous with the risk phrase ‘Toxic by inhalation’ (T; R23) in HSIS (Safe Work Australia). While the available animal data do not support this classification, in the absence of more comprehensive information, there is insufficient evidence to support a recommendation to amend the existing classification. However, one death was reported following exposure of a factory worker to the chemical (see **Observation in humans**).

There is limited information on the acute inhalation toxicity of the chemical. However one available study reported a median lethal concentration (LC50) of 2340 mg/m^3. In this investigation, male Crl:CD rats were exposed to the chemical by 'head only' exposure for four hours. The concentrations tested were 0, 1690, 1810, 1920, 2101, 2380, 2660 mg/m^3 and the animals were observed for 14 days after exposure. Cyanosis and lethargy were noted in rats from all treated groups 24 hours after exposure. Other treatment-related changes include weight loss and clouding of the cornea for up to 14 days. The study also reported some animal deaths (REACH; Wiley VCH, 1990).

Similar investigations conducted in mice, cats and albino rats reported an increased formation of Heinz bodies (aggregates of denatured haemoglobin) in the erythrocytes following inhalation exposure to 22.5, 21.4 and 36 mg/m^3 of the chemical (WHO, 2003).

Observation in humans

Cyanosis and methaemoglobinaemia have been reported in workers exposed to the chemical. These symptoms were also observed in incubated premature infants exposed to small amounts of the chemical resulting from the break down of chlorhexidine gluconate in incubators (WHO, 2003).

Increased levels of methaemoglobin can lead to fatigue, headache, nausea, loss of consciousness, tachycardia and, in some cases, death. There has been one reported death of a worker accidentally sprayed in the face and upper body with a heated form of the chemical (WHO, 2003).

Humans may be more susceptible than rats and mice to methaemoglobinaemia due to lower methaemoglobin reductase activity (WHO, 2003).

Corrosion / Irritation

Skin Irritation

The chemical is considered to be, at most, a slight skin irritant. Effects are not sufficient to warrant a hazard classification.

The chemical produced no skin irritation in a study performed in accordance with OECD Test Guideline (TG) 404 (WHO, 2003: REACH). A single application (100-900 mg) of the chemical was reported to induce dermatitis in rabbits or cats after 3–5 days of exposure. The effects were reversible within 15–24 days (Wiley VCH, 1990).

Eye Irritation

The chemical was reported to slightly irritate the eyes when tested according to OECD TG 405. The average scores for cornea/iris/conjunctivae (redness)/conjunctivae (chemosis) were given as 0.3/0.3/1.7/0.6 respectively. The effects were reversible within seven days after exposure. Effects were not considered sufficient to warrant a hazard classification (REACH).

Sensitisation

Skin Sensitisation

The chemical is classified as hazardous with the risk phrase ‘May cause sensitisation by skin contact’ (R43) in HSIS (Safe Work Australia). The available data support this classification.

In a guinea pig maximisation test (OECD TG 405-compliant), 50–60 % of the animals showed positive sensitisation reactions following intradermal and topical induction at 0.3 and 10 % respectively and were challenged with 2.5 % of the chemical under occlusive conditions (WHO, 2003).

Results from an inter-laboratory mouse local lymph node assay (LLNA), conducted in accordance with OECD TG 429, also indicated a sensitising potential. The chemical, at test concentrations of 2.5, 5.0, and 10 % (in olive oil), were applied to the animals for three consecutive days. In addition, animals were injected with 20 µCi of the radiolabelled [^{3}H]methyl thymidine (^{3}HTdR) five days after the exposure initiation to determine the sensitising strength of the chemical. The results showed a

slightly positive sensitisation reaction in one laboratory. By contrast, this effect was not observed in other two laboratories (REACH).

Repeated Dose Toxicity

Oral

Considering the lowest observed-effect levels (LOELs) available from 13-week studies in rats and mice (5–7.5 mg/kg bw/day), classification for serious damage to health from repeated oral exposure, is considered warranted (refer **Recommendation** section). The targets for toxicity are the blood, liver, spleen and kidneys.

The toxic effects of the chemical from repeated oral exposure were investigated in a number of well-conducted studies (OECD TG 408) in B6C3F1 mice and Fischer 344 rats. The results demonstrated not only chemically-induced development of multi-site tumours (see **Carcinogenicity** section) but also non-cancer effects. Repeated exposure of rats and mice to the chemical (2–103 weeks at concentrations of 2–2600 mg/kg bw) also resulted in a number of pathologies including:

- decreased survival rate;
- cyanosis;
- formation of abnormal type of haemoglobin (methaemoglobinaemia) from 2 mg/kg dose;
- premature destruction and removal of red blood cells from the bloodstream (haemolytic anaemia);
- increased iron deposition (haemosiderosis) in the spleen and kidney (5 mg/kg bw);
- enlarged spleen (5 mg/kg bw) with plaque formation;
- congested renal cortex;
- blood cells formed and developed outside the bone marrow (extramedullary haematopoiesis);
- lethargy;
- Heinz body formation;
- decreased body weight gain (mice only); and
- dystrophic changes in the liver and kidney.

The LOEL values are 5 mg/kg bw for 13 weeks and 2 mg/kg bw for 26–103 weeks in rats and 7.5 mg/kg bw for 13 weeks and 3 mg/kg bw for 26–103 weeks in mice (Wiley VCH, 1990; WHO, 2003; REACH).

Toxicity of the chemical was also reported in guinea pigs and beagle dogs. Beagle dogs exposed to 5–15 mg/kg bw of the chemical for 90 days resulted in cyanosis, Heinz body formation and increased numbers of immature red blood cells (reticulocytes). Histological changes were also observed in the liver and the spleen. Other chemically-induced pathologies include extramedullary haematopoiesis, erythoid hyperplasia of bone marrow and renal haemosiderosis. In addition, dystrophic changes also occurred in the liver and kidneys of guinea pigs gavaged with 0.5 and 5 mg/kg bw of the chemical (REACH).

Dermal

No data are available. Given the ready absorption of the chemical through the skin and similarity in acute toxicities following oral and dermal exposure, the chemical is considered to have the potential to cause serious damage to health from repeated dermal exposure.

Inhalation

Limited data are available. Effects are consistent with those observed in the repeated dose oral toxicity studies.

The chronic inhalation toxicity potential of the chemical was tested in CD rats. In this study, the animals were exposed to 0, 12, 53, and 120 mg/m^3 of the chemical five days a week for two weeks. Changes in haematological profiles such as a decrease red blood cell count and increased level of methaemoglobin formation (reversible) were observed in the lowest dose group (12 mg/m^3). In this group, animals also displayed changes in the spleen, extramedullary haematopoiesis and haemosiderosis. Mild to moderate cyanosis was detected in animals exposed to 53 mg/m^3 of the chemical, while changes in breathing, irreversible clouding of the cornea and loss of hair were reported in the 120 mg/m^3 dose group. The reported LOAEL for this study was 12 mg/m^3 (REACH). In a non-guideline six-month study in rats, increased methaemoglobin levels (up to 22 % after three months) and an increase in the number of reticulocytes and Heinz bodies were observed at 15 mg/m³ (REACH). The animals from this group also displayed reduced haemoglobin levels.

Genotoxicity

The chemical is considered genotoxic based on the weight of evidence from available, well-documented (guideline-compliant) in vitro and in vivo genotoxicity studies. The available data support classification (refer to the **Recommendation** section).

In vitro, the chemical was tested positive in the following tests:

- Pol A test (DNA damage) and gene mutations in *Aspergillus nidulans*;
- mutagenicity assay in L5178Y mouse lymphoma cells with or without metabolic activation; and
- cell transformation activity in Rauscher leukaemia virus-infected rat embryo cells and in C3H/10T1/2 cells.

The results from several in vitro assays for the chemical such as bacterial reverse mutation tests (Ames tests), chromosomal aberration (CA), sister chromatid exchange (SCE) in Chinese hamster ovary cells and induction of DNA repair in rat hepatocytes were not consistent. However, positive results were reported including several tests repeatedly producing weak positive results in *Salmonella typhimurium* strains TA98, TA100 and TA1538 with metabolic activation.

In *Drosophila melanogaster*, the chemical was genotoxic both in repair-proficient and in excision repair-defective larvae in a wing somatic mutation and recombination test, demonstrating its potential for point mutations, chromosome breakages and mitotic recombination (Graf & Hall, 1990; WHO, 2003).

In B6C3F1 mice, a significant increase in micronucleus frequency was also reported following exposure to 300 mg/kg bw of the chemical (highest dose tested). A negative finding with respect to induction of micronuclei was found in another study at lower doses of the chemical (180 mg/kg bw) (WHO, 2003).

The genotoxicity profile of the chemical is similar to the analogue chemical benzenamine (CAS No. 62-53-3), which is classified as hazardous, Category 3 mutagenic substance with the risk phrase ‘Possible risk of irreversible effects’ (Xn; R68) in HSIS (NICNAS).

Carcinogenicity

The chemical is classified as hazardous (Category 2 carcinogenic substance) with the risk phrase ‘May cause cancer’ (T; R45) in HSIS (Safe Work Australia). The available data support this classification.

The carcinogenic potential of the chemical has been documented in several long-term oral studies in rats and mice. These studies reported a number of chemically-induced tumours primarily in the spleen, subcutaneous tissues, kidney, adrenal gland, liver and blood, although effects were also reported in other sites. Male rats and mice were more susceptible to the carcinogenic effects of the chemical than females.

Oral exposure of F344 rats to 250 or 500 ppm of the chemical in the diet for six weeks resulted in mesenchymal tumours of the spleen or splenic capsule in both sexes. Reduced survival rate was also noted in the exposed animals. Similar cancer-related effects in the spleen were observed in a well-conducted study (OECD TG 451) following exposure of F344 rats to 2, 6 or 18 mg/kg bw of the chemical via gavage, five days a week for 103 weeks. The results showed a significant increase in the incidence of tumours of the spleen such as fibroma, fibrosarcoma, osteosarcoma, haemangiosarcoma and sarcoma in male rats at the top dose. Proliferative mesenchymal lesions and fatty metamorphosis were observed in both sexes at the top dose. Fibrosis of the spleen (potential pre-neoplastic lesion) was seen in all dose groups. In addition, significant increases in adrenal phaeochromocytomas were observed in male rats at the top dose (IARC, 1993; WHO, 2003: REACH).

In B6C3F1 mice, exposure to the chemical through the diet for 78 weeks (dose: 2500 or 5000 mg/kg) resulted in multi-organ haemangiosarcomas and vascular tumours in both sexes. In a similar study, female mice were less affected by the chemical at low doses. Exposure to 3, 10, or 30 mg/kg of the chemical via oral gavage for five days a week for 103 weeks produced significant increases in the incidence of hepatocellular adenomas, carcinomas and haemangiosarcomas of the liver and spleen in male mice. The cancer-related effects in females were not considered significant (IARC, 1993). By contrast, tumourgenic activity was not observed in the Strain A mouse pulmonary tumour test at doses 25, 57.5, or 60 mg/kg bw (intraperitoneally administered), three times a week for 10 weeks (IARC, 1993; WHO, 2003: REACH).

There is a lack of evidence in humans for the carcinogenicity of the chemical. Overall, the International Agency for Research on Cancer (IARC) has reviewed and subsequently concluded that it is ‘possibly carcinogenic to humans’ (Group 2B).

The mode of action for the carcinogenicity is not clear. It has been suggested that the spleen tumours may be a progression from fibrosis or a result of erythrocyte toxicity. For the analogue, benzenamine, it has been proposed that carcinogenicity is induced by damaged erythrocytes leading to an iron overload or oxidative damage to macromolecules (proteins, DNA or lipids) in the spleen by direct binding. Evidence for and against a genotoxic mechanism of carcinogenicity has also been discussed (NICNAS).

Reproductive and Developmental Toxicity

No data are available. The analogue chemical, benzenamine, does not show specific reproductive or developmental toxicity. Any reproductive or developmental effects were only observed secondary to maternal toxicity (NICNAS).

Risk Characterisation

Critical Health Effects

The chemical could be a carcinogen following long-term repeated exposure. A genotoxic mode of action cannot be excluded. The critical health effects for risk characterisation also include systemic acute and chronic effects by all routes of exposure (refer to **Acute and repeated dose toxicity** sections). The chemical can also cause skin sensitisation.

Public Risk Characterisation

Based on the current information available, the intentional inclusion of the chemical in consumer products is not expected. Hence, the public risk from this chemical is not considered to be unreasonable.

However, the public could be exposed to the chemical through the following scenarios:

- as an impurity in cosmetic ingredients such as chlorhexidine and triclocarban;
- by release of the chemical from the heat-induced breakdown of chlorhexidine gluconate (see **Acute toxicity: Observation in humans**); and
- release of the chemical from dyes and pigments manufacured using the chemical.

The risk to the public from these routes of exposure will be considered in subsequent IMAP assessments of the relevant chemicals.

Occupational Risk Characterisation

During product formulation, dermal, ocular and inhalation exposure of workers to the chemical might occur, particularly where manual or open processes are used. These can include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

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

Guidance on the interpretation of workplace exposure standards for airborne contaminants provides advice that 'exposure to carcinogens should be eliminated or minimised so far as is reasonably practicable' (Safe Work Australia, 2013).

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.

However, the public could be exposed to the chemical due to its presence as an impurity in, or release due to breakdown of, other chemicals (see **Public risk characterisation**). The risk to the public from these routes of exposure will be considered in subsequent IMAP assessments of the relevant chemicals.

Regulatory Control

Work Health and Safety

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

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Toxic if swallowed (T; R25)* Toxic in contact with skin (T; R24)* Toxic by inhalation (T; R23)*	Toxic if swallowed - Cat. 3 (H301) Toxic in contact with skin - Cat. 3 (H311) Toxic if inhaled - Cat. 3 (H331)
Sensitisation	May cause sensitisation by skin contact (Xi; R43)*	May cause an allergic skin reaction - Cat. 1 (H317)

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Repeat Dose Toxicity	Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed (T; R48/23/24/25)	Causes damage to organs through prolonged or repeated exposure - Cat. 1 (H372)
Genotoxicity	Muta. Cat 3 - Possible risk of irreversible effects (Xn; R68)	Suspected of causing genetic defects - Cat. 2 (H341)
Carcinogenicity	Carc. Cat 2 - May cause cancer (T; R45)*	May cause cancer - Cat. 1B (H350)

[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, 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 which may minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- 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 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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