Phenol, 4-amino-: 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.

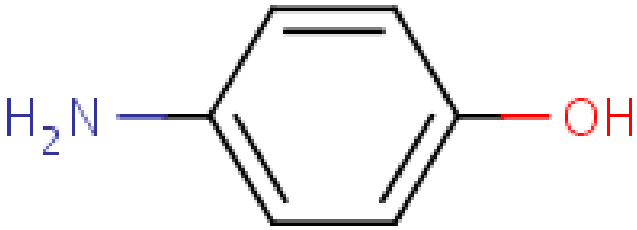
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	C.I. 76550 C.I. Oxidation Base 6 p-aminophenol 4-hydroxyaniline 1-amino-4-hydroxybenzene
Structural Formula	
Molecular Formula	C6H7NO
Molecular Weight (g/mol)	109.13
Appearance and Odour (where available)	White to pink odourless crystals
SMILES	c1(O)ccc(N)cc1

Import, Manufacture and Use

Australian

The chemical is on the 'List of chemicals used as dyes in permanent and semi-permanent hair dyes in Australia' (NICNAS, 2007).

The chemical has reported cosmetic use in permanent hair dye preparations.

International

The following international uses have been identified through the European Union (EU) Registration, Evaluation and Authorisation of Chemicals (REACH) dossiers; the Organisation for Economic Cooperation and Development (OECD) Screening information data set International Assessment Report (SIAR); Galleria Chemica; the Substances and Preparations in the Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database; the OECD High Production Volume chemical program (OECD HPV); and the Scientific Committee for Consumer Products (SCCP).

The chemical has reported cosmetic use in permanent hair dyes.

The chemical has reported commercial uses including:

- as a photographic developer;
- as an oil additive; and
- in textile dyes.

The chemical has reported site-limited uses including as:

- an intermediate for sulfur dyes; and
- a rubber antioxidant.

The chemical has a non-industrial use for pharmaceutical products.

Restrictions

Australian

No known restrictions have been identified.

International

Using the chemical in cosmetics in the European Union is subject to the restrictions described in EU Regulation Annex III. This chemical may be used in hair dyes under the following condition: after mixing under oxidative conditions the maximum concentration applied to hair must not exceed 0.9 % (CosIng).

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; R20/22 (acute toxicity)
- R68 Mut. Cat 3 (mutagenicity)

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

Toxicokinetics

The chemical is one of the three isomers of aminophenol. A gavage study in rabbits where the chemical was administered at 1000 mg/animal showed 100 % absorption from the gastrointestinal (GI) tract (Bray et al., 1952, cited in OECD, 2010).

A study in humans determined the dermal absorption of the chemical as up to 8 % of the applied dose (2–4 µg/cm^2) (Bucks et al., 1989, cited in OECD, 2010). In rats, the dermal absorption was determined to be up to 11 % of the applied dose, according to a study in female Wistar rats exposed to single doses of 0.75 % aqueous solutions of the chemical at 15, 75 or 375 µg/cm^2 (Tsomi & Kalopissis, 1982, cited in OECD, 2010).

Following subcutaneous injection of the chemical at 0, 50, 100, 200 or 400 mg/kg bw in male Fischer 344 (F344) rats, 46–76 % of the administered dose was recovered in the urine. Major metabolites were identified as conjugates of the chemical and paracetamol (acetaminophen). Unchanged chemical was also detected in the urine (OECD, 2010).

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 median lethal dose (LD50) was 671 mg/kg bw in CFY rats. Reported signs of toxicity include lethargy and piloerection, and 2/10 animals showed oedematous swelling of the salivary glands (Lloyd et al., 1977, cited in OECD, 2010).

Dermal

The chemical has low acute dermal toxicity in animals.

The LD50 in Wistar rats was reported to be >5000 mg/kg bw. No deaths were reported and the only sign of toxicity was brown discolouration in the area of application (OECD, 2010).

In a study in New Zealand White rabbits exposed to the chemical at 2000, 4000 or 8000 mg/kg bw for 24 hours, the LD50 was >8000 mg/kg bw, as all animals survived and no toxic effects were observed (REACH).

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 are inconclusive; therefore, it is not recommended that the existing hazard classification be amended.

Rats were exposed to the chemical dust at 3.42 mg/L for four hours (OECD Test Guideline (TG) 403). During the 14-day observation period no treatment-related effects were seen. The median lethal concentration (LC50) was determined to be above 3.42 mg/L (REACH).

In another study, 10 albino rats exposed to dust of the chemical at a concentration of 5.91 mg/L for one hour showed no sign of toxicity and no mortalities during the 14-day observation period that followed exposure (OECD, 2010).

Corrosion / Irritation

Skin Irritation

The chemical is slightly irritating to the skin.

The chemical was tested according to three standard methods: Official French Cosmetic method (OFC) occlusive patch (air and water-tight dressing) method; Association Francaise de Normalisation (AFNOR) occlusive patch method; and OECD TG 404 semiocclusive patch method. In each protocol, a dose of 0.5 g of the chemical (dry powder) was applied to the clipped skin of six male New Zealand White rabbits for four hours (according to AFNOR and OECD TG 404) or 23 hours (according to OFC). The primary cutaneous irritation indices (PCI) ranged from 0 g to 0.21 g (Guillot et al., 1982 a, cited in OECD, 2010).

The chemical was found slightly irritating to the skin of New Zealand White rabbits (study conducted in accordance to the US Consumer Product Safety Commission standards). When three New Zealand White rabbits were exposed to a 2.5 % (w/v) aqueous preparation of the chemical, one rabbit exhibited slight oedema 24 hours after exposure (Lloyd et al., 1977, cited in OECD, 2010).

Eye Irritation

The chemical is considered to be a slight eye irritant.

The chemical was tested according to three standard methods of OFC, AFNOR and OECD (Guillot et al., 1982 b, cited in OECD, 2010). In each protocol, a dose of 100 mg of the chemical was instilled into one eye of each of six male New Zealand White rabbits. Corneal opacity was not observed, but the chemical was found to slightly irritate the conjunctivae in all three test methods. All observed eye effects were reversible within two days.

A primary irritation index of 0.2 was obtained following instillation of a 2.5 % solution of the chemical into one eye of each three New Zealand White rabbits. Mild conjunctival irritation was observed in two animals, but the effects were fully reversible (Lloyd et al., 1977, cited in: SCCP, 2005 and REACH).

Sensitisation

Skin Sensitisation

The chemical is considered to be a skin sensitiser based on the positive results seen in animal tests and human data (see **Observation in humans**), warranting hazard classification.

The chemical was reported to be a skin sensitiser (Bruschweiler et al., 2014).

In a study similar to the Buehler test, Hartley guinea pigs were treated with a 0.1, 0.5, 1 or 2 % preparation of the chemical. Dose-dependent, positive skin responses were observed in 3/10, 5/10, 6/10 and 9/10 animals, respectively (Kleniewska & Maibach, 1980, cited in OECD, 2010).

Freund's complete adjuvant tests were conducted in Hartley guinea pigs using two methods of induction. In the first method, Freund's adjuvant was injected alone before 0.18 mmol/L of the chemical was topically administered twice (over two days); the chemical did not induce any skin sensitisation reaction. In the second method, Freund's adjuvant was injected with 0.18 mmol/L of the chemical (ratio 1:1) (induction), followed by a 0.09 mmol/L of the chemical 16 days later (challenge). The treatment induced positive reactions in 40 % of the animals (Dossou et al., 1985, cited in OECD, 2010).

Observation in humans

The available human data indicate that the chemical is a skin sensitiser.

The chemical gave positive skin reactions in patch tests in 25 % (1/4) and 17 % (2/12) of patients with hair dermatitis (among 13 beauticians and 33 hairdressers respectively, tested for occupational dermatitis) (Matsunaga et al., 1982, cited in OECD, 2010).

Among 24 hairdressers and eight barbers patch tested for occupational allergic contact dermatitis, the chemical induced positive reactions in 25 % (2/8) of patients with hair dermatitis (Nagaki et al., 1985, cited in OECD, 2010).

The application of the chemical at 1 % gave positive results in 3 % (11/372) of patients patch tested with the chemical (OECD, 2010).

Repeated Dose Toxicity

Oral

Based on the available data, the chemical is considered to cause some effects from repeated oral exposure, warranting hazard classification according to the Globally Harmonised System of Classification (GHS) criteria. The kidney is the target organ for repeated dose oral toxicity in rats, with nephrosis seen at doses of 30 mg/kg bw/day and above. However, there are uncertainties about the reversiblity of kidney effects in the 90-day standard study, which makes the results too inconclusive to warrant hazard classification according to the Approved Criteria from the former National Occupational Health and Safety Commission (NOHSC): 1008 (2004).

In a 28-day gavage study (OECD TG 407), the chemical was administered at doses of 0, 4, 20, 100 or 500 mg/kg bw/day to groups of Sprague Dawley (SD) rats (n = six/sex/dose). One male in the highest dose group died on day four from serious renal damage, attributed to the chemical. Most of the statistically significant adverse effects were observed at the 500 mg/kg bw/day dose. Anaemia-related effects included decreased red blood cell counts in both sexes, decreased haematocrit in females, increased reticulocyte counts in females and increased mean corpuscular haemoglobin (MCH) in males. Inflammatory cell infiltration in the interstitium (2/5) and mineralisation at the corticomedullary junction in males' kidneys (1/5), dark reddish spleen in all females (6/6) and a white streak at the renal corticomedullary junction in three males and all females were reported at the 500 mg/kg bw/day dose. Increases in liver, kidney and spleen weights were also observed at the highest dose. A few significant effects were observed from 100 mg/kg bw/day, including an increase of absolute kidney weights, basophilic tubules in the kidneys and changes in urinalysis parameters. Most of the effects had not reversed after a 14-day recovery period. A no observed adverse effect level (NOAEL) of 20 mg/kg bw/day was reported (MHW, 1998a, cited in OECD, 2010).

In a 13-week study (OECD TG 408), groups of SD rats (n = 10/sex/dose) were treated with the chemical at 0, 10, 30 or 100 mg/kg bw/day by gavage. The major effect observed was tubular nephrosis, characterised by the degeneration of the tubular epithelium, with exfoliation of the tubular cells in the tubular lumen, dilated tubules and/or denuded basement membrane. Minimal to marked tubular nephrosis was observed in 5/10 males and 2/10 females at 30 mg/kg bw/day and in 9/10 males and 10/10 females at the highest dose, compared with none in the control group. The dose of 10 mg/kg bw/day was chosen as the no observed effect level (NOEL) in this study (CIT, 1995, cited in SCCP, 2005 and REACH). However, there was no indication of the reversibility of kidney effects, as no recovery period was mentioned in the study summaries.

A NOAEL of 20 mg/kg bw/day for systemic toxicity was determined after administration of the chemical to SD rats by gavage at doses of 20, 100 or 500 mg/kg bw/day for 40–60 days in a reproductive and developmental toxicity study (see **Reproductive and developmental toxicity**). Adverse effects at 500 mg/kg bw/day included significantly decreased food consumption, brown urine, acute renal failure that caused the death of six animals, and histopathological changes. At 100 mg/kg bw/day, food consumption was reduced in females and both sexes had brown coloured urine (MHW, 2007a cited in OECD, 2010).

In a six-month feeding study in SD rats, the chemical was administered at 0, 0.07, 0.2 or 0.7 % in the diet (equivalent to ca. 0, 47, 133 and 467 mg/kg bw/day). Based on nephrosis observed during the histopathological examination at the 47 mg/kg bw/day dose after 13 and 27 weeks of exposure, the lowest observed adverse effect level (LOAEL) was reported to be 47 mg/kg bw/day (Burnett et al., 1989, cited in OECD, 2010).

Dermal

Only limited data are available.

In a 13-week study, three hair dye formulations containing 0.04, 0.2 or 1 % of the chemical were applied topically to the clipped skin of rabbits, twice a week, after mixing with hydrogen peroxide. No treatment-related effects were reported (Burnett et al., 1976, cited in SCCP, 2005).

Inhalation

No data are available.

Genotoxicity

The chemical is classified as a Category 3 mutagenic substance with the risk phrase ‘Possible risk of irreversible effects’ (Xn; R68) in the HSIS (Safe Work Australia). The available data support this classification.

Several in vitro assays conducted using the chemical showed both positive and negative results. These included:

- negative results in a bacterial gene mutation test (OECD TG 471) at concentrations up to 5000 µg/plate, with or without metabolic activation (MHW, 1998b, cited in OECD, 2010);
- mutations in L5178Y mouse lymphoma cells at 7 µg/mL, without metabolic activation (Oberly et al., 1993, cited in OECD, 2010);
- no mutations in Chinese hamster ovary (CHO) cells exposed to the chemical up to 16 µg/mL, with or without metabolic activation (Oberly et al., 1993, cited in OECD, 2010);
- structural aberrations in chromosomes including gaps, in Chinese hamster lung cells (OECD TG 473) at 0.0025, 0.005 and 0.01 mg/mL with 24 or 48 hours exposure and at 0.013 and 0.025 mg/mL with six hours exposure, without metabolic activation (MHW, 1998c, cited in OECD, 2010);
- positive results in a sister chromatid exchange (SCE) assay in V79 Chinese hamster cells at doses up to 0.1 mM, without metabolic activation (Holme et al., 1988, cited in OECD, 2010);
- negative results in another SCE assay in human fibroblasts exposed to doses up to 0.2 mM, without metabolic activation (Wilmer et al., 1981, cited in OECD, 2010);
- no unscheduled DNA synthesis in F344 rat hepatocytes exposed to doses up to 1000 nmol/mL (Thompson et al., 1983, cited in OECD, 2010).

The chemical gave mostly positive results for in vivo genotoxicity assays, but negative results were reported in a germ cell mutagenicity assay, confirming the validity of the existing hazard classification. These included:

- a significant increase in micronucleated polychromatic erythrocytes and inhibition of bone marrow cell proliferation in male CD1 mice orally administered the chemical at 125, 250 or 500 mg/kg bw in a micronucleus test (OECD TG 474) (MHW, 2007b, cited in OECD, 2010);
- positive results in four other micronucleus tests in mice receiving doses of the chemical up to 214.5 mg/kg bw (oral) or 872 mg/kg bw (intraperitoneal (i.p.)) (OECD, 2010);
- positive results for somatic mutations and recombinations (SMAR) in *Drosophila melanogaster* fed with 20 mmol/L of the chemical (Eiche et al., 1990, cited in OECD, 2010);
- negative results in sex-linked recessive lethal (SLRL) test in *D. melanogaster* administered the chemical at doses up to 130 mmol/L (oral) or 30 mmol/L (injection) (Eiche et al., 1990, cited in OECD, 2010); and
- negative results in a dominant lethal test in male SD rats fed with the chemical at doses up to 467 mg/kg bw/day for 20 weeks (Burnett et al., 1989, cited in OECD, 2010).

Carcinogenicity

Based on the limited information available, the chemical is not expected to be carcinogenic.

The OECD report (2010) stated that there were no reliable data to assess carcinogenicity potential of the chemical.

However, the SCCP report (2005) considered one oral study in rats as reliable enough to conclude that the chemical is not expected to be carcinogenic. In a carcinogenicity study (OECD TG 451) SD rats (n=50/sex/dose) received the chemical by oral gavage at doses of 0, 2, 5, 12 or 30 mg/kg bw/day for 102 weeks. The only effects reported include a marginal increase in the number of malignant lymphomas in males at 30 mg/kg bw/day, lower survival of the high-dose females and coloured urine in all animals at the highest dose (CIT, 1998, cited in SCCP, 2005 and REACH).

In a two-generation reproduction study, SD rats received topical applications of hair dye formulations containing the chemical at 1 %, mixed with an equal volume of hydrogen peroxide, twice a week for 24 months. No compound-related neoplastic effects were observed (Burnett et al., 1988, cited in SCCP, 2005).

In Swiss Webster mice painted with three hair dye formulations containing the chemical at 0.04, 0.2 or 1 % for up to 23 months, no significant differences in tumour incidences were found between treated and control groups (Burnett et al., 1980, cited in SCCP, 2005).

Reproductive and Developmental Toxicity

Based on the available data, the chemical is not expected to have reproductive or developmental toxicity. The foetal effects observed in rats at high doses are considered secondary to maternal toxicity.

In a reproductive and developmental toxicity study (OECD TG 421), SD rats (n=12/sex/dose) were administered the chemical by oral gavage at doses of 0, 20, 100 or 500 mg/kg bw/day, starting 14 days before mating and through the mating period and gestation periods, for a total of 49 days for males and 40–60 days for females. Mortalities were observed at the highest dose (four males and two females). Also, decreased spermatocytes and spermatid levels, decreased sperm counts, and some histopathological changes (necrosis of spermatocytes in the testis, vacuolation of Sertoli cells) in males were observed, without affecting the reproductive performance. A NOAEL of 100 mg/kg bw/day was established for reproductive toxicity, based on 'terminated oestrus and longer gestation period' (OECD, 2010) in females at 500 mg/kg bw/day. The developmental NOAEL was also reported to be 100 mg/kg bw/day 'based on decreased delivery index, increased number of stillborn pups, lowered pup weight and decreased viability of pups at 500 mg/kg bw/day' (OECD, 2010). However the observed effects at the highest dose were thought to be secondary to maternal toxicity (MHW, 2007a and Harada et al., 2008, cited in OECD, 2010 and SCCP, 2005).

In a six-month feeding study, groups of SD rats were fed with the chemical at doses of 0, 0.07, 0.2 or 0.7 % in the diet (approximately 0, 47, 133 and 467 mg/kg bw/day). After 13 weeks of exposure, 25 females were mated with untreated males and treated until gestation day (GD) 20. Based on a significant decrease in maternal weight gain at 133 mg/kg bw/day, a NOAEL of 47 mg/kg bw/day was determined for maternal toxicity, but there were no reproductive toxicity effects. There were no significant malformations in the foetuses, but the number of foetal variations was increased at the 133 and 467 mg/kg bw/day doses due to maternal toxicity. A NOAEL of 47 mg/kg bw/day for developmental toxicity was determined, based on postimplantation loss at higher doses, but this was considered to be secondary to maternal toxicity (Burnett et al., 1989, cited in OECD, 2010).

Dermal applications of three hair dye formulations containing the chemical at 0.04, 0.2 or 1 % to pregnant Charles River rats on GD 1, 4, 7, 10, 13, 16 and 19 did not induce any treatment-related effects (Burnett et al., 1976, cited in SCCP, 2005).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include:

- systemic long-term effects (mutagenicity);
- systemic acute effects (acute toxicity from oral and inhalation exposure); and
- local effects (skin sensitisation).

The chemical can also cause harmful effects following repeated oral exposure.

Public Risk Characterisation

The chemical is reported to be used in permanent hair dyes in Australia. The European Union has restricted the use of this chemical in hair dyes (maximum concentration applied to hair should not exceed 0.9 % after mixing under oxidative conditions).

If the chemical is included in cosmetic products containing N-nitrosating agents, carcinogenic N-nitrosamine compounds could be formed (SCCS, 2012).

Currently, there are no restrictions in Australia on using this chemical in hair dyes. In the absence of any regulatory controls, the characterised critical health effects, particularly skin sensitisation and mutagenicity, have the potential to pose an unreasonable risk under the identified use. The risk could be mitigated by implementing restrictions for the use of the chemical in hair dyes.

The international uses indicate that the chemical is used in textile dyes or as an intermediate to manufacture dyes to be used in textiles. The public could be exposed to the chemical as an impurity in, or through release of the chemical from dyes manufactured using the chemical, including by:

- dermal contact with the chemical from prolonged exposure to articles of clothing and leather goods containing the dye; and
- oral exposure by young children sucking articles and textiles containing the dye.

The risk to the public from oral and dermal exposure from use in textile dyes will be considered in subsequent IMAP assessments of the relevant dye and pigment chemicals.

Occupational Risk Characterisation

During product formulation, oral, dermal and inhalation exposure might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the 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 health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise 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) (refer to **Recommendation** section).

NICNAS Recommendation

Further risk management is required. Sufficient information is available to recommend that risks to public health and safety from the potential use of the chemical in hair dyes be managed through changes to poisons scheduling, and risks for workplace health and safety be managed through changes to classification and labelling.

The chemical is also recommended for a Tier III assessment as part of the assessment of 'Azo dyes that cleave to aromatic amines of potential toxicological concern' (NICNAS, 2015).

Regulatory Control

Public Health

Given the risk characterisation, it is recommended that the chemical be included in Schedule 6 of the *Poisons Standard* (the *Standard for the Uniform Scheduling of Medicines and Poisons*) for use in hair dyes.

Consideration should be given to the following:

- the chemical is a skin sensitiser in humans;
- it has mutagenic properties;
- there are overseas restrictions for use of this chemical in hair dyes (see **International restrictions**); and
- that, as many hair dye formulations come under Schedule 6 due to p-phenylenediamine (a strong skin sensitiser) content, inclusion in Schedule 6 with a cut-off is not likely to give an effective upper concentration limit for the chemical.

For use in textile dyes, further regulatory controls for public health may be determined as part of a Tier III assessment for 'Azo dyes that cleave to aromatic amines of potential toxicological concern' (NICNAS, 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 by inhalation (Xn; R20)*	Harmful if swallowed - Cat. 4 (H302) Harmful if inhaled - Cat. 4 (H332)

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Sensitisation	May cause sensitisation by skin contact (Xi; R43)	May cause an allergic skin reaction - Cat. 1 (H317)
Repeat Dose Toxicity		May cause damage to organs through prolonged or repeated exposure through the oral route - Cat. 2 (H373)
Genotoxicity	Muta. Cat 3 - Possible risk of irreversible effects (Xn; R68)*	Suspected of causing genetic defects - Cat. 2 (H341)

[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 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 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;
- 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 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.

References

Approved Criteria for Classifying Hazardous Substances [NOHSC: 1008(2004)] Third edition. Accessed at http://www.safeworkaustralia.gov.au/sites/SWA/about/Publications/Documents/258/ApprovedCriteria_Classifying_Hazardous_Substances_NOHSC1008-2004_PDF.pdf

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