2,3-Pyridinediamine, 6-methoxy-N2-methyl-, dihydrochloride: Human health tier II assessment

08 March 2019

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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

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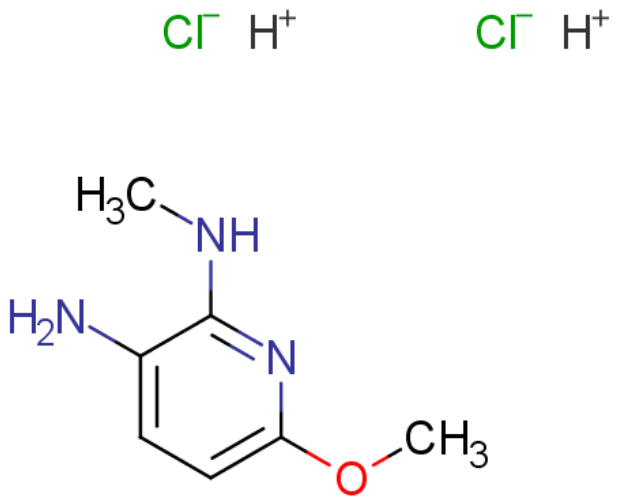
Acronyms & Abbreviations

Chemical Identity

Synonyms	6-methoxy-N2-methylpyridine-2,3-diamine dihydrochloride 6-Methoxy-2-methylamino-3-aminopyridine HCl (INCI) 2-methylamino-3-amino-6-methoxypyridine dihydrochloride 3-amino-2-methylamino-6-methoxypyridine dihydrochloride HC Blue 7
Structural Formula	
Molecular Formula	C7H11N3O.2ClH
Molecular Weight (g/mol)	226.11
Appearance and Odour (where available)	Grey to brown or grey-violet powder
SMILES	c1(NC)c(N)ccc(OC)n1_Cl_Cl

Import, Manufacture and Use

Australian

The chemical has been reported to be used in hair dyes in Australia (NICNAS, 2007).

International

The following international uses have been identified through the European Chemicals Agency (ECHA) database; eChem Portal; Galleria Chemica; the European Commission (EC) Cosmetic Ingredients and Substances (CosIng) database; the United States (US) Personal Care Products Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary; the US Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR), the EC Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers Opinion (SCCNFP, 2003); and the EC Scientific Committee on Consumer Products Opinion (SCCP, 2008).

The chemical has reported cosmetic use as a hair colourant.

In the European Union (EU) the chemical is an ingredient of oxidative and non-oxidative hair dye products at a maximum use concentration of 1 % (SCCNFP, 2003; SCCP, 2008). Prior to mixing with hydrogen peroxide, the chemical is present in oxidative hair dye products at a concentration of up to 2 % (SCCNFP, 2003).

Restrictions

Australian

No known restrictions have been identified.

International

The use of the chemical in oxidative and non-oxidative hair dye products is restricted in the EU, the Association of Southeast Asian Nations (ASEAN) and New Zealand as a ‘substance which cosmetic products must not contain except subject to restrictions laid down’ in the following (ASEAN Cosmetic Directive; CosIng; Galleria Chemica):

- EU Regulation (EC) No 1223/2009 — Annex III/203;
- ASEAN Cosmetic Directive Annex III; and
- New Zealand Cosmetic Products Group Standard—Schedule 5.

The restrictions common to both the EU and ASEAN are:

- after mixing under oxidative conditions the maximum concentration applied must not exceed 1.0 % as dihydrochloride;
- maximum concentration in finished non-oxidative products is 1.0 % as dihydrochloride;
- not to be used with nitrosating agents;
- maximum nitrosamine content of 50 µg/kg;
- to be kept in nitrite-free containers;
- to be printed on the label of oxidative hair dye products: the mixing ratio; and 'Hair colorants can cause severe allergic reactions. Read and follow instructions. This product is not intended for use on persons under the age of 16. Temporary "black henna" tattoos may increase your risk of allergy. Do not colour your hair if: — you have a rash on your face or sensitive, irritated and damaged scalp, — you have ever experienced any reaction after colouring your hair, — you have experienced a reaction to a temporary "black henna" tattoo in the past.'; and

- to be printed on the label of non-oxidative hair dye products: 'Can cause allergic reaction.'

The EU Regulation has the following additional restriction for products intended for colouring eyelashes:

- for professional use only; and
- to be printed on the label: the mixing ratio; and 'For professional use only. This product can cause severe allergic reactions. Eyelashes shall not be coloured if the consumer: — has a rash on the face or sensitive, irritated and damaged scalp, — has experienced any reaction after colouring hair or eyelashes, — has experienced a reaction to a temporary "black henna" tattoo in the past. Rinse eyes immediately if product comes into contact with them.'

The ASEAN Directive has the following additional restrictions:

- use for dyeing eyelashes and eyebrows is not permitted; and
- the direction for use 'wear suitable gloves' must be included in label or leaflet text.

Restrictions for the chemical in New Zealand are not substantially different from those in the EU.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is not listed on the Hazardous Chemical Information System (HCIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

Toxicokinetics

In a guideline study (Organisation for Economic Cooperation and Development (OECD) Test Guideline (TG) 428) in vitro dermal absorption of the chemical (1 % in a standard hair dye cream formulation with and without hydrogen peroxide) was determined in dermatomed pig skin (SCCP, 2008; REACH). Distribution of the test chemical 48 hours after a 30 minute exposure was as follows:

- receptor fluid—0.707 % (1.59 ± 0.757 µg/cm^2) with hydrogen peroxide and 1.57 % (3.54 ± 1.06 µg/cm^2) without hydrogen peroxide;
- epidermis and dermis—1.01 % (2.27 ± 1.49 µg/cm^2) with hydrogen peroxide and 1.37 % (3.09 ± 1.14 µg/cm^2) without hydrogen peroxide; and
- stratum corneum—0.554 % (1.25 ± 0.876 µg/cm^2) with hydrogen peroxide and 0.344 % (0.755 ± 0.895 µg/cm^2) without hydrogen peroxide.

Total absorption (receptor fluid + epidermis and upper dermis) from:

- a standard cream formulation with hydrogen peroxide was 3.9 ± 2.17 µg/cm^2 (range 1.69 to 7.59 µg/cm^2) or 1.72 % (range 0.75 to 3.36 %); and
- a standard cream formulation without hydrogen peroxide was 6.62 ± 2.05 µg/cm^2 (range 4.34 to 9.41 µg/cm^2) or 2.93 % (range 1.9 to 4.18 %).

Due to limitations in experimental design the upper limit of the range, equating to total absorption of 7.59 µg/cm^2 under oxidative conditions and 9.41 µg/cm^2 under non-oxidative conditions, was used for calculating the margin of safety (MOS) (SCCP, 2008) (see **Public risk characterisation** section).

Acute Toxicity

Oral

The chemical has moderate acute toxicity following oral exposure with median lethal doses (LD50) in the range 650–813 mg/kg body weight (bw) in rodents, warranting hazard classification (see **Recommendation** section).

In a non-guideline study (SCCNFP, 2003; SCCP, 2008; REACH), the chemical was dosed via oral gavage to Wistar rats (n= 6/sex) at 600, 700, 800 or 900 mg/kg bw, and to female CF1 mice (n=10) at 625, 700, 775, 850 or 925mg/kg bw. Observed sub-lethal effects of the chemical were reduced activity, piloerection, and diarrhoea. The LD50 was calculated as 650 mg/kg bw for female rats, 700 mg/kg bw for male rats, and 813 mg/kg bw for female mice.

Dermal

No data are available.

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

Based on the available data, although the chemical is considered to be slightly irritating to the skin, it does not warrant hazard classification.

In an acute dermal irritation study in rabbits (OECD TG 404) (SCCNFP, 2003; SCCP, 2008; REACH), 0.5 g of moistened chemical was applied semi-occlusively for 4 hours to the shaved back skin of female New Zealand White (NZW) rabbits (n=3). Very slight erythema in 1 animal with a primary irritation index of 0.3 (mildly irritating) was reported. In one animal 3 brown spots with crust formation were seen. Observed irritation reversed within 7 days of exposure.

In a non-guideline study (SCCNFP, 2003), 1 or 2 drops of the chemical at a concentration of 10 % dissolved in 2 % carboxymethylcellulose and 0.5 % Cremophor in water was applied twice daily for 5 days to the back of female hr/hr mice (n=10). No signs of irritation were observed.

Eye Irritation

Based on the available data, the chemical is not irritating to the eyes.

In a non-guideline study (SCCNFP, 2003; SCCP, 2008; REACH), 0.1 mL of the chemical at a concentration of 5 % was instilled into the conjunctival sac of 1 eye each of male NZW rabbits (n=6). No effects were observed from the chemical on the cornea, iris or conjunctivae at any time point.

Observation in humans

In a non-guideline study (SCCNFP, 2003), 1 drop of the chemical at a concentration of 10 % was applied every 30 seconds for half an hour to the forearm skin of 10 human volunteers of both sexes. Two subjects reported a burning sensation accompanied by slight erythema. No signs of irritation were observed in the other 8 subjects.

Sensitisation

Skin Sensitisation

Based on the available data, the chemical is considered to be sensitising to skin, warranting hazard classification (see **Recommendation** section).

In a local lymph node assay (OECD TG 429) in female CBA/Ca OlaHsd mice, the chemical was found to be a moderate skin sensitiser (SCCP, 2008; REACH). Stimulation indices of 1.3, 2.5 and 6.4 resulted from treatment with the chemical at concentrations of 2.5 %, 5 % and 10 %, respectively. The estimated concentration of chemical needed to produce a threefold increase in lymphocyte proliferation (EC3) was calculated as 5.6 %.

In a non-guideline Magnusson and Kligman maximisation test (SCCNFP, 2003), female Pirbright White guinea pigs (n=20/group) were intradermally induced with the chemical at 5 %. One week after intradermal induction, the animals were topically induced with the chemical at 5 % under occlusive conditions for 48 hours. Two weeks later, the animals were challenged with a single topical application of the chemical at 1 %. No skin reactions were observed at challenge.

Observation in humans

A case report describes contact allergy to the chemical in a 65 year old woman with a history of colouring her hair with oxidative hair dyes 5 times a year for a period of 15 years (Sosted et al., 2009). Three days after using a hair dye, she required hospitalisation for severe oedema around the eyes and exudation around the scalp and ears. Subsequent patch testing with ingredients of the last hair dye the woman used confirmed allergic contact dermatitis to the chemical.

Repeated Dose Toxicity

Oral

The lowest observed adverse effect level (LOAEL) determined from repeated dose (28 days) and sub-chronic (90 days) toxicity studies was 50 mg/kg bw/day in rats for oral administration. Systemic effects were observed at doses of 100 mg/kg bw/day and above.

In a 90-day oral toxicity study (OECD TG 408), Wistar rats (n=10/sex/group) were dosed daily by oral gavage at 0, 50, 100 or 200 mg/kg bw/day of the chemical (SCCP, 2008; REACH). There were no deaths in any of the treatment groups. At all doses, absolute and relative liver weights were increased. The increase in absolute liver weights in males was 10 % at 50 mg/kg bw/day, 9 at 100 mg/kg bw/day and 20 % at 200 mg/kg bw/day. In females the increase in absolute and relative liver weights was 14 % at 50 mg/kg bw/day, 18 at 100 mg/kg bw/day and 37 % at 200 mg/kg bw/day. Liver alterations were confirmed by histology showing centrilobular hypertrophy of hepatocytes in treatment groups. In animals recovering from treatment, after 4 weeks there was a reduction in the severity of hypertrophy. Electrolyte and/or water balance was also altered in treated animals. Changes in liver weight during the 4 week recovery period was not included in the description of this study. Other adverse effects due to treatment with the chemical at doses above 50 mg/kg bw/day include:

- reduced body weight gain in males;
- alterations in haematological parameters, including reticulocyte count and maturity index;
- blood lipid metabolism;
- haemosiderin deposits in the red pulp of the spleen;
- higher incidence and severity of tubular basophilia in the kidneys of males; and
- macroscopic and microscopic alterations of the thyroid and microscopic alterations of the pituitary.

Based on these findings the LOAEL for this study was considered to be 50 mg/kg bw/day (SCCP, 2008). The magnitude of the change in liver weight for male animals at 50 and 100 mg/kg bw/day is borderline indicative of an adverse effect (=10% for an adverse effect), and there is also evidence for the reversibility of liver effects in both sexes. Considering that only an effect on the liver was evident at the dose of 50 mg/kg bw/day, the effect of the chemical at this dose may represent an adaptive reversible effect and not an adverse health effect. Consequently there is some uncertainty as to whether 50 mg/kg bw/day is a suitable LOAEL for this study.

In a 28-day oral toxicity study (OECD TG 407), Wistar rats (n=5/sex/group) were dosed with the chemical daily by gavage at 0, 80, 160 or 360 mg/kg bw/day (SCCP, 2008; REACH). No deaths resulted from treatment with the chemical. Adverse effects observed from treatment were:

- hypersalivation and reduced thymus weights in all dose groups, although the biological significance of the change in thymus weight is unclear;
- body weight gain was reduced and liver weights were increased in males at 160 mg/kg bw/day and in males and females at 360 mg/kg bw/day; and
- at 360 mg/kg bw/day the kidneys showed a higher incidence and severity of tubular basophilia in both sexes.

The no-observed adverse effect level (NOAEL) for this study was considered to be 80 mg/kg bw/day (SCCP, 2008).

In a non-guideline 90-day oral toxicity study, Wistar rats (n=10/sex/group) were dosed 5 days per week for 90 days by gavage with 0 or 50 mg/kg bw/day of the chemical (SCCNFP, 2003). No animals died from treatment with the chemical. There was an increase in the number of thrombocytes in animals treated at 50 mg/kg bw/day with the chemical. The LOAEL for this study was considered to be 50 mg/kg bw/day (SCCNFP, 2003). In the absence of any other haematological effects observed in this study, the biological significance of the observed increase in thrombocytes is unclear.

In a non-guideline 21-day oral toxicity study, Wistar rats (n=15/sex/group) were dosed 5 days per week for 21 days by gavage with 0, 75, 150 or 300 mg/kg bw/day of the chemical (SCCNFP, 2003). No deaths resulted from treatment with the chemical. Adverse effects from treatment with the chemical were observed at doses of 75 mg/kg bw/day and above, and include haematological alterations, macroscopic and microscopic changes in the thyroid, and alterations in thyroid hormones. The LOAEL for this study was 75 mg/kg bw/day.

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

The chemical is not considered to be genotoxic based on the weight of evidence from the available in vitro and in vivo studies. The chemical gave positive results in several in vitro assays, and was negative in the remaining in vitro and in vivo studies.

In vitro

In a bacterial gene reverse mutation assay (OECD TG 471), the chemical induced dose-dependent increases in revertant colonies of *Salmonella typhimurium* strains TA98 and TA1535 without metabolic activation at 3–5000 µg/plate (SCCP, 2008; REACH). No mutagenic activity was observed in the other tester strains (*S. typhimurium* TA100, TA102 and TA1537) without metabolic activation, and in any of the tester strains with metabolic activation. The study concluded that the chemical is mutagenic in bacteria under these test conditions.

In a mouse lymphoma assay (OECD TG 476), the chemical did not induce a biologically relevant increase in mutant frequency at the tk locus at 0.8–54 µg/mL, and it was concluded that the chemical was not mutagenic under the experimental conditions used (SCCP, 2008; REACH).

In an unscheduled DNA synthesis (UDS) in vitro test (OECD TG 482), at 0.0064–500 µg/mL there was a statistically significant and dose-dependent increase in unscheduled DNA synthesis, both in the presence and absence of metabolic activation (SCCNFP, 2003). The study concluded that the chemical was genotoxic in the assay system.

In a non-guideline mammalian cell gene mutation test, the chemical did not induce a biologically relevant increase in mutation at 5 and 20 µg/mL, and was not considered mutagenic (SCCNFP, 2003).

In a non-guideline mammalian cell transformation test, the chemical did not induce a statistically or biologically significant increase in the number of transformed colonies at 1–100 µg/mL, and was considered negative for the ability to induce cell transformation (SCCNFP, 2003).

In vivo

In a bone marrow micronucleus test (OECD TG 474), NMRI mice were administered single gavage doses of the chemical at 0, 62.5, 125 or 250 mg/kg bw. Bone marrow cells were collected at 24 and 48 hours after dosing (SCCP, 2008; REACH). No increases were observed in micronucleated polychromatic erythrocytes (PCEs) at any of the test doses.

In a bone marrow chromosome aberration test (OECD TG 475), Wistar rats were administered single gavage doses of the chemical at 0 or 50 mg/kg bw. Bone marrow cells were collected at 24 and 48 hours after dosing (SCCNFP, 2003; SCCP, 2008; REACH). No increases were observed in the number of bone marrow cells with chromosomal aberrations in animals treated with the chemical.

In an unscheduled DNA synthesis (UDS) test (OECD TG 486), negative results were reported in male Wistar rats when the chemical was administered via gavage at doses of 0, 250, 500 or 1000 mg/kg bw (SCCP, 2008; REACH). Hepatocytes were collected for analysis at two time points, 2–4 hours or 12–16 hours after administration of the chemical. No increases were observed in mean net nuclear grain count or percentage of cells in repair in any of the dosed groups for both 2–4 hour, and the 12–16 hour treatment times.

Carcinogenicity

No data are available.

Reproductive and Developmental Toxicity

Based on the available data, the chemical is not expected to cause specific developmental toxicity. No data are available for reproductive toxicity. Any developmental effects were only observed secondary to maternal toxicity.

In a prenatal development toxicity study (OECD TG 414), a maternal NOAEL of 50 mg/kg bw/day and a foetal NOAEL of 200 mg/kg bw/day were determined for the chemical in female rats dosed at 0, 50, 100 or 200 mg/kg bw/day on days 6–20 after mating (SCCP, 2008; REACH). There were no animal deaths. At doses of 100 mg/kg bw/day and above ruffled fur and signs of discomfort were noted after treatment with the chemical on most days. Mean food consumption and body weight gain was also dose-dependently reduced in pregnant females at these doses. No treatment-related effects were observed on foetal development. The chemical produced maternal toxicity at 50 mg/kg bw but was not embryotoxic or teratogenic at any of the doses tested.

In a non-guideline prenatal development toxicity study, female rats were dosed at 0, 100, 200 or 400 mg/kg bw/day on days 6–20 after mating (REACH). Mean food consumption and body weight gain was reduced in all pregnant females treated with the chemical. At a dose of 400 mg/kg bw/day, foetal weights were significantly reduced. No other foetal parameters examined were altered by treatment. The chemical resulted in maternal toxicity at all doses tested.

In a non-guideline prenatal developmental toxicity study, female rats were dosed at 0, 5, 15 or 30 mg/kg bw/day on days 6–15 after mating (SCCNFP, 2003). There was a non-significant decrease in food consumption of pregnant females at 30 mg/kg bw/day. No treatment-related effects were observed on foetal development. The chemical did not produce either maternal or foetal toxicity at any of the doses tested.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation are systemic acute effects (acute toxicity from oral exposure) and local effects (skin sensitisation).

Public Risk Characterisation

The chemical is reported to be used in hair dyes in Australia (NICNAS, 2007). Currently, there is no restriction on using the chemical in cosmetic products in Australia.

The EU, ASEAN and New Zealand have restricted the use of the chemical in oxidative and non-oxidative hair dyes to a maximum use concentration of 1.0 % (see **Restrictions: International** section). Hair dye products in Australia are expected to contain the chemical at similar concentrations.

Following a safety evaluation, the SCCP concluded that the use of the chemical as an oxidative and non-oxidative hair dye ingredient at a maximum on-head concentration of 1.0 % does not pose a risk to the health of the consumer, apart from sensitising potential (SCCP, 2008).

A margin of safety (MOS) of 555 for oxidative hair dye products and 455 for non-oxidative hair dye products was calculated for the chemical. Dermal absorption values of 7.59 μg/cm^2 and 9.41 μg/cm^2 were used for oxidative and non-oxidative products respectively (see **Toxicokinetics** section). Since a NOAEL was not available the LOAEL of 50 mg/kg bw/day from the 90 day oral toxicity study (OECD TG 408) was used instead (see **Repeated dose toxicity: Oral** section). Although calculated based on an LOAEL, the MOS was still considered indicative that hair dye products containing the chemical were safe for use as indicated. A cosmetic ingredient with a MOS of at least 100 is generally considered safe for use (SCCS, 2016). This is further supported by the effect used to define a LOAEL being of uncertain adversity.

The chemical is a secondary amine and thus prone to nitrosation and formation of carcinogenic nitrosamines (SCCP, 2008). The EU Cosmetics Regulation entry for this chemical restricts the nitrosamine content to 50 μg/kg (equivalent to 50 ppb); does not allow use with nitrosating agents; and mandates storage in nitrite-free containers. These measures are considered appropriate and should be considered by formulators and importers of hair dyes containing the chemical.

In the absence of any regulatory controls in Australia, the characterised critical health effects, particularly skin sensitisation, have the potential to pose an unreasonable risk to the public under the identified use. The risk could be mitigated by implementing restrictions for the use of the chemical in hair dyes.

Occupational Risk Characterisation

During product formulation, dermal, oral and inhalation exposure may 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 systemic acute and potential local health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise dermal exposure are implemented. Oral exposure can be prevented by good hygiene practices. 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 hazard classification in HCIS (Safe Work Australia) (see **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 cosmetics be managed through changes to poisons scheduling, and risks for workplace health and safety be managed through changes to classification and labelling.

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

Given the risk characterisation, it is recommended that the chemical be included in the Poisons Standard (the *Standard for the Uniform Scheduling of Medicines and Poisons*—SUSMP) for use in hair dyes, to ensure appropriate restrictions and labelling.

Consideration should be given to the following:

- the known use of the chemical in hair dye products available in Australia;
- the chemical is acutely toxic by the oral route and a moderate skin sensitiser;
- lack of data on acute or repeated dermal and inhalation toxicity; and
- the chemical is restricted for cosmetic use overseas. Restrictions on the use of the chemical in cosmetic products in other countries (see **Restrictions: International** section) are considered appropriate in Australia, to mitigate the risk.

Work Health and Safety

The chemical is recommended for classification and labelling aligned with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below. This does not consider classification of physical hazards and environmental hazards.

From 1 January 2017, under the model Work Health and Safety Regulations, chemicals are no longer to be classified under the Approved Criteria for Classifying Hazardous Substances system.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Not Applicable	Harmful if swallowed - Cat. 4 (H302)
Sensitisation	Not Applicable	May cause an allergic skin reaction - Cat. 1B (H317)

[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 and dermal 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;
- 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.

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