Ethanol, 2-(2,4-diaminophenoxy)-, dihydrochloride: 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.

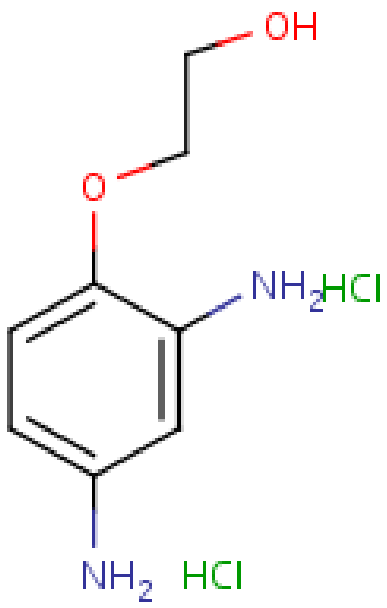
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	2,4-diaminophenoxyethanol dihydrochloride 2-(2,4-diaminophenoxy)ethanol dihydrochloride
Structural Formula	
Molecular Formula	C8H12N2O2.2ClH
Molecular Weight (g/mol)	241.117
Appearance and Odour (where available)	Odourless pale grey to pale pink-grey coloured powder
SMILES	c1(OCCO)c(N)cc(N)cc1_Cl_Cl

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, Authorization and Restriction of Chemicals (REACH) dossiers, Galleria Chemica, the European Commission 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) and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported cosmetic use as a hair dye substance in oxidative hair dye products.

Restrictions

Australian

No known restrictions have been identified.

International

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

• The Association of South East Asian Nations (ASEAN) Cosmetic Directive Annex III—Part 1: List of substances which cosmetic products must not contain except subject to restrictions and conditions laid down: ‘After mixing under oxidative conditions the maximum concentration applied to hair must not exceed 2.0% (as hydrochloride)’;

• The EU Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Annex III—List of substances which cosmetic products must not contain except subject to the restrictions laid down: ‘(a) the maximum concentration in ready for use preparation is 4.0 %; and (b) in combination with hydrogen peroxide the maximum use concentration upon application is 2.0 %. Not to be used after 31.12.2009’;

• New Zealand Cosmetic Products Group Standard—Schedule 5: Components cosmetic products must not contain except subject to the restrictions and conditions laid down: ‘In combination with hydrogen peroxide the maximum use concentration upon application is 2.0% as hydrochloride’; and

• Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient ‘Hotlist’).

Existing Work Health and Safety Controls

Hazard Classification

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

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

Toxicokinetics

The dermal absorption of the chemical was studied in female hairless Wistar rats. The chemical (20 mg/cm^2) was dermally applied to the dorsal region of the animals for 40 minutes as a pure chemical, or in a commercial formulation consisting 0.4 % of the chemical. Both solutions were mixed with an equal volume of 20 % hydrogen peroxide solution immediately before application. The penetration per cm^2 of skin was 0.84 ± 0.13 µg and 0.47 ± 0.08 µg for the pure chemical and the formulation, respectively. When the solutions were applied to the animals every 30–40 days for an unknown application duration, trace amounts of the chemical were detected in the livers but not in the thyroids of the animals (CIR, 1991; CIR, 2007).

In a separate study, the absorption of the chemical was measured using female hairless Wistar rats (six animals/group). The chemical, dissolved in a commercial vehicle at concentrations of 0.4, 0.8 or 1.2 %, was mixed with an equal volume of 20 % hydrogen peroxide. The chemical (20 mg/cm^2) was then applied immediately to the back of each animal for 40 minutes. The penetration per cm^2 of skin was 0.84 ± 0.13 µg and 1.58 ± 0.14 µg for 0.4 and 1.2 % concentrations, respectively (CIR, 1991; CIR, 2007).

In an in vitro dermal absorption study conducted according to the Organisation for Economic Co-operation and Development Test Guideline (OECD TG) 428, an oxidative hair dye formulation containing 2 % of the chemical (corresponding to 428 µg/cm^2 when mixed equally with hydrogen peroxide) or a non-oxidative formulation containing 2 % of the chemical (corresponding to 428 µg/cm^2 when mixed equally with water) was applied to the dermatomed skin obtained from seven female human subjects and left for 30 minutes before being washed off. Approximately 90 % and 94 % of the applied chemical in oxidative and non-oxidative conditions, respectively, was removed following skin washing. The mean dermal absorptions were 1.74 ± 1.08 and 6.55 ± 4.72 µg/cm^2 under oxidative and non-oxidative conditions, respectively (SCCP, 2006; CIR, 2007).

Acute Toxicity

Oral

The chemical is considered to have moderate acute toxicity based on results from animal tests following oral exposure, warranting hazard classification. The median lethal dose (LD50) was approximately 1000 mg/kg bw (inducing death in 1/5 male and 3/5 females) in Sprague Dawley (SD) rats and 1160 mg/kg bw in Swiss albino mice. Observed sub-lethal effects included hypoactivity, piloerection, lateral recumbency, tonic-clonic convulsions, dyspnoea and unsteady gait (CIR, 1991; SCCP, 2006; CIR, 2007; REACH).

Dermal

No data are available.

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

Limited data are available. The chemical is not considered to be a skin irritant.

In a separate skin irritation study conducted according to OECD TG 404 with three female New Zealand White rabbits, the undiluted chemical was applied non-occlusively to a clipped area of the right flank in each animal for four hours. Slight erythema was observed in one animal at 48 hours after treatment. The chemical was concluded to be non-irritating to the skin (SCCP, 2006; CIR, 2007; REACH).

In a skin irritation study with albino Bouscat rabbits (three animals/sex), the chemical (4 % solution) was applied to the shaved intact and abraded skin of each animal. The chemical was minimally irritating to the rabbit skin with a primary irritation index of 0.08/8 (CIR, 1991; CIR, 2007).

Eye Irritation

Limited data are available. The chemical is considered to be an eye irritant, warranting hazard classification.

In an eye irritation study conducted according to OECD TG 405 with three female New Zealand White rabbits, the undiluted chemical was instilled into the conjunctival sac of the left eye of each animal. The eyes were not rinsed following instillation of the chemical. Moderate to marked chemosis, slight to moderate conjunctival redness, slight to moderate corneal opacification and slight iridial lesions were observed in the animals. These effects were not fully reversed at the end of the study (day 15). The undiluted chemical was concluded to be irritating to rabbit eyes (SCCP, 2006; CIR, 2007; REACH).

In a separate eye irritation study conducted according to OECD TG 405 with three male New Zealand White rabbits, the chemical (4 % solution) was instilled into the conjunctival sac of the left eye of each animal. The eyes were not rinsed following instillation of the chemical. Slight chemosis and conjunctival redness were observed in two animals for the first two days following treatment. The diluted chemical at 4 % solution was concluded to be non-irritating to rabbit eyes (SCCP, 2006; CIR, 2007; REACH).

In an eye irritation study with albino Bouscat rabbits (three animals/sex), the chemical (4 % solution) was instilled into the conjunctival sac of one eye of each animal. The eyes were not rinsed following instillation of the chemical. The chemical at 4 % solution was concluded to be ‘practically not irritating’ to rabbit eyes (CIR, 1991; CIR, 2007).

Sensitisation

Skin Sensitisation

The chemical is considered to be a moderate skin sensitiser, warranting hazard classification.

In a local lymph node assay (LLNA) conducted according to OECD TG 429, the chemical at dilutions of 0.5, 1.0, 2.5, 5.0 or 10 % was applied to the ears of CBA/J mice (four females/group) for three consecutive days. The mean stimulation indices (SIs) were 0.92, 1.56, 1.17, 4.21 and 7.42 for the 0.5, 1.0, 2.5, 5.0 and 10 % dilutions, respectively. The estimated concentration needed to produce a three-fold increase in lymphocyte proliferation (EC3) was calculated to be 3.2 %, indicating a moderate sensitising potential. In the absence of local irritation, these responses were attributed to delayed contact hypersensitivity following exposure to the chemical (SCCP, 2006; CIR, 2007; REACH).

In a Buehler test conducted according to OECD TG 406 using Dunkin-Hartley guinea pigs (10 animals/sex), sensitisation was induced by three, weekly, occlusive topical applications of the undiluted chemical to the anterior left flank of each animal for six hours. Following a two-week rest period after the third topical treatment, a topical challenge was performed with an application of the undiluted chemical to the right flank of each animal. Purple discolouration of the skin was observed in the treated animals. Very slight erythema in 2/20 treated animals was reported at the 48-hour observation. The chemical was concluded to be a non-sensitiser to the skin in this study (SCCP, 2006; CIR, 2007; REACH).

In a separate skin sensitisation study using 10 female Hartley guinea pigs, two intradermal injections of Freund's complete adjuvant (FCA) were administered to an area of deeply abraded skin of each animal. The undiluted chemical was then applied occlusively for 48 hours. On day seven, a second dermal application, 25 % of the chemical was administered occlusively for 48 hours. On day 21, a challenge was performed by applying the chemical at a 25 % concentration to an untreated skin area occlusively for 24 hours. Erythema was observed in 3/10 animals, but was reversed within five days. It was concluded that the chemical could have a low skin sensitising potential (CIR, 1991; CIR, 2007).

Repeated Dose Toxicity

Oral

The available data suggest that the chemical has harmful effects following repeated oral dosing, based on results from animal tests. However, the effects were not sufficient to warrant hazard classification.

In a repeated dose toxicity study conducted according to OECD TG 408, SD rats (10 animals/sex/group) were administered the chemical at concentrations of 0, 4, 20 or 100 mg/kg bw/day by oral gavage, daily for 13 weeks. Recovery animals (six animals/sex/group) were added to the control and 100 mg/kg bw/day groups, then had a further four-week treatment-free period. No treatment-related mortalities were observed in the study. Excessive salivation was observed in the animals of the 100 mg/kg bw/day group. Urinary changes were also observed in these animals, including the presence of bilirubin, nitrites, glucose and marked colouration in the urine. These effects were reversed after the treatment-free period. Deposition of brown pigment in the thyroids and spleen haemosiderosis (iron overload) were observed in the animals of the 100 mg/kg bw/day group. These effects were not reversed after the treatment-free period. A no observed adverse effect level (NOAEL) of 20 mg/kg bw/day was established for this study (SCCP, 2006; CIR, 2007; REACH).

In a separate repeated dose toxicity study, BDF1 mice and Fischer 344 (F344) rats (10 animals/strain/sex/group) were administered the chemical at concentrations of 0, 0.01, 0.03, 0.05, 0.1 or 0.2 % in tap water, *ad libitum*, for 12 weeks. No treatment-related mortalities were observed. In the 0.1 and 0.2 % groups, decreased body weight gains were observed in the male mice and feed consumption was decreased for both male and female mice. Dose-dependent decreases in mean body weight gains were observed in all treated rats while feed consumption was decreased in the rats of the 0.2 % group. Water intake was also decreased in all treated mice and rats. Kidney abnormalities, pneumonia lesions and deposition of pigment in the thyroid follicles were observed in the mice of the 0.2 % group. Pigment deposits in the thyroid follicles were also observed in the rats of the 0.2 % group (CIR, 1991; CIR, 2007).

In another repeated dose toxicity study, SD rats (10 animals/sex/group) were administered the chemical at concentrations of 0 or 56 mg/kg bw/day by oral intubation for three months. Dull appearance of the fur, light brown areolas and brown discolouration of the urine, thyroid glands and trachea were observed in the treated animals. No other significant treatment-related effects were observed (CIR, 1991; CIR, 2007).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on the weight of evidence from the available in vitro and in vivo genotoxicity studies, the chemical is not considered to be genotoxic. Positive results were seen in some in vitro genotoxicity tests, but all in vivo tests were negative.

In vitro studies

A bacterial gene mutation assay was conducted according to OECD TG 471 in five *Salmonella typhimurium* strains (TA98, TA100, TA102, TA1535 and TA1537) up to a maximum concentration of 5000 µg/plate of the chemical, in the absence and presence of a rat liver metabolic activation system. The chemical induced mutations in strain TA98 in the presence of the metabolic activation (SCCP, 2006; CIR, 2007; REACH).

A bacterial gene mutation assay was conducted in four *S. typhimurium* strains (TA97, TA98, TA100 and TA1538) and *Escherichia coli* strain WP2uvrA (pKM101) up to a maximum concentration of 100 µg/plate of the chemical, in the absence and presence of a rat liver metabolic activation system. This study produced negative findings except for strains TA97, TA98 and TA1538 in the presence of the metabolic activation, where significant increases in mutations were observed (CIR, 1991; CIR, 2007; HSDB).

In six separate bacterial gene mutation assays, *S. typhimurium* strains (TA98, TA100, TA1535, TA1537 or TA1538), *E. coli* strains (WP2, WP2uvrA or WP2uvrA/recA) or *Saccharomyces cerevisiae* strains (D4 or XV185-14C) were tested up to a maximum concentration of 6000 µg/plate of the chemical in the absence and presence of a rat liver metabolic activation system. Negative findings were reported in these studies (CIR, 1991; CIR, 2007; HSDB).

A fluctuation test using two *S. typhimurium* strains (TA98 and TA1538) in the presence of a rat liver metabolic activation system produced statistically significant dose-dependent increases in mutations, while negative findings were reported in the absence of the metabolic activation (CIR, 1991; CIR, 2007).

A mammalian cell gene mutation assay was conducted according to OECD TG 476 in the mouse lymphoma L5178Y cell line (hypoxanthine-phosphoribosyl-transferase (hprt) locus). The chemical was tested up to a maximum concentration of 2410 µg/mL in the absence and presence of a rat liver metabolic activation system. The chemical was considered to be non-mutagenic in this study (SCCP, 2006; CIR, 2007; REACH).

An in vitro mammalian chromosome aberration test was conducted according to OECD TG 473 in cultured human peripheral blood lymphocytes up to maximum concentrations of 120.9 or 2200 µg/mL in the absence or presence of a rat liver metabolic activation system, respectively. The chemical induced an increase in chromosome aberrations in the presence of the metabolic activation, indicating clastogenic potential of the chemical (SCCP, 2006; CIR, 2007; REACH).

In a separate chromosome aberration test conducted in Chinese hamster ovary (CHO) cells, the chemical was tested at concentrations of 0.6 or 1.2 mg/mL in the absence or presence of a rat liver metabolic activation system. No increases in chromosome aberrations were observed in this study (CIR, 1991; CIR, 2007; HSDB).

An in vitro micronucleus test was conducted according to OECD TG 487 in cultured human peripheral blood lymphocytes up to maximum concentrations of 361.3 or 2410 µg/mL in the absence or presence of a rat liver metabolic activation system, respectively. The chemical induced an increase in the frequencies of micronucleated binucleated (MNBN) cells in the absence and presence of the metabolic activation, indicating genotoxic potential of the chemical (SCCP, 2006; CIR, 2007; REACH).

In vivo studies

An in vivo micronucleus assay in bone marrow cells was conducted according to OECD TG 474 in Crl:CD SD (BR) rats (five animals/sex/group). The chemical was administered at concentrations of 0, 375, 750 or 1500 mg/kg bw by oral gavage. Bone marrow cells were collected 24 hours (or 48 hours for the 1500 mg/kg bw group) after the chemical was administered and the polychromatic erythrocytes (PCEs) for each rat were examined. No increases in micronucleated PCEs were found; thus, the chemical was concluded to be non-mutagenic in this study (SCCP, 2006; CIR, 2007; REACH).

In a micronucleus test conducted in CD-1 mice, the chemical was orally administered at concentrations of 0, 25, 50 or 100 µg/mL in two separate doses, 24 hours apart. The animals were euthanised six hours following administration of the second dose. Although bone marrow toxicity was observed, no increases in micronucleated PCEs were found in the animals. The chemical was concluded to be non-mutagenic in this study (CIR, 1991; CIR, 2007; HSDB).

In an unscheduled DNA synthesis (UDS) test with rat hepatocytes conducted according to OECD TG 486 in male Crl:CD SD (BR) rats (four animals/group/sacrifice time), the chemical was administered at concentrations of 0, 375, 750 or 1500 mg/kg bw by oral gavage. The animals were euthanised 2–4 or 14–16 hours after treatment. No significant UDS responses were observed; thus, the chemical was concluded to be non-mutagenic in this study (SCCP 2006; CIR, 2007; REACH).

In a dominant lethal assay, the chemical was dermally applied at concentrations ranging from 15 to 1500 mg/kg bw/day to the shaved dorsal skin of male T-strain mice (two animals/group) for five consecutive days. Following treatment, each male was housed with two virgin C57B1/6 female mice for seven days. These females were then replaced by two new virgin female mice and this process was repeated for seven weeks. No treatment-related effects were observed and the chemical was concluded to not induce dominant lethal mutations in this study (CIR, 1991; CIR, 2007).

Negative findings were reported in a *Drosophila melanogaster* sex-linked recessive lethal mutation assay following oral administration of the chemical. Concentrations used in the study were not reported (CIR, 1991; CIR, 2007; HSDB).

Carcinogenicity

Limited data are available. Based on the available data, the chemical is not considered to be carcinogenic.

A study was conducted to determine the carcinogenicity potential of the chemical using F344 rats (50 animals/sex/group). The animals were administered the chemical in tap water, *ad libitum*, at concentrations of 0, 0.05 or 0.1 % (corresponding to intake levels of 0, 20.9 or 35.5 mg/kg bw/day for males and 0, 27.8 or 60.9 mg/kg bw/day for females) for 104 weeks. In the 0.1 % group, dosing was suspended in the males during weeks 12–16 and 32–36 and in the females during weeks 32–36 due to marked decreases in body weight gain of the animals. The overall survival rate of the animals was 71 %. Deposition of pigment in the thyroid follicles was observed in the animals of the 0.1 % group. An increase in C-cell adenomas in the thyroid glands was observed in male rats. However, C-cell adenomas were reported to be frequently observed in aged F344 rats, more commonly in males than in females (Capen et al., 2002). Thus, it was not possible to conclude if the increases in these tumours were treatment-related (CIR, 1991; SCCP, 2006; CIR, 2007; REACH).

In the same study, BDF1 mice (50 animals/sex/group) were administered the chemical in tap water, *ad libitum*, at concentrations of 0, 0.04 or 0.07 % (corresponding to intake levels of 0, 35.8 or 62.8 mg/kg bw/day for males and 0, 44.6 or 81.4 mg/kg bw/day for females) for 104 weeks. The overall survival rate of the animals was 72 %. No significant differences in the target organs or tumour incidences were observed between the control and treated animals. Deposition of pigment in the thyroid follicles was observed in the animals of the 0.07 % group with no other details provided. No other treatment-related effects were observed. The chemical was considered to be non-carcinogenic in mice (CIR, 1991; SCCP, 2006; CIR, 2007; REACH).

Reproductive and Developmental Toxicity

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

In a prenatal development toxicity study conducted according to OECD TG 414, pregnant SD rats (24 animals/group) were orally administered the chemical at concentrations of 0, 4, 20 or 125 mg/kg bw/day on gestational days (GD) 6–19. The animals were euthanised on GD 20. Excessive salivation, significantly reduced body weight gain and significantly reduced mean food consumption were observed in the female rats treated with 125 mg/kg bw/day of the chemical. A significant reduction in the mean foetal weight associated with a significantly increased incidence of foetuses with incomplete ossification of the thoracic vertebra centrum or supernumerary short 14^{th} rib was observed in the 125 mg/kg bw/day group. A NOAEL of 20 mg/kg bw/day was established for maternal and developmental toxicity in this study (SCCP, 2006; CIR, 2007; REACH). The developmental effects observed in this study could be secondary to maternal toxicity.

In a separate reproductive and developmental toxicity study, pregnant specific pathogen-free rats (20 animals/group) were orally administered the chemical at concentrations of 0, 50, 100 or 200 mg/kg bw/day on GD 6–15. The animals were euthanised on

GD 20. Excessive salivation, urine discolouration and loss of fur were observed in the animals of the 200 mg/kg bw/day group. Decreased body weight gain was observed in the animals of the 100 and 200 mg/kg bw/day groups. Significant increases in the incidence of skeletal anomalies and variations were observed in the foetuses of the 200 mg/kg bw/day group. The authors concluded that the increase was 'probably related to a general nonspecific retardation of embryo/foetal development during gestation' (CIR, 1991; CIR, 2007).

In a study with pregnant C57B1/6 mice (10 animals/group; 18 animals/high dose group), the chemical was topically applied at concentrations of 0, 15, 150 or 1500 mg/kg to the shaved back of each animal. No significant effects were observed in this study (CIR, 1991; CIR, 2007).

Risk Characterisation

Critical Health Effects

The critical health effect for risk characterisation is skin sensitisation. The chemical can also cause harmful systemic effect (acute toxicity from oral exposure) and eye irritation.

Public Risk Characterisation

The chemical is reported to be used in permanent hair dye preparations in Australia (NICNAS, 2007).

The ASEAN, Canada, New Zealand and the EU have restricted the use of this chemical in cosmetics. Following a safety evaluation, the Scientific Committee on Consumer Products (SCCP) concluded that the use of the chemical 'as an oxidative hair dye at a maximum concentration of 2.0 % in the finished cosmetic product (after mixing with hydrogen peroxide) does not pose a risk to the health of the consumer, apart from its sensitising potential' (SCCP, 2006).

Currently, there are no restrictions in Australia on using this chemical in cosmetic products. The risks could be mitigated by implementing concentration limits for use in hair dyes to address the risk of skin sensitisation.

Occupational Risk Characterisation

During product formulation, dermal and ocular 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 and local health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise dermal and ocular 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 cosmetic products (hair dye preparations) be managed through changes to the Poisons Standard, 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 should be included in the Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons) with an appropriate concentration cut-off (exemption) for hair dye use.

Consideration should be given to the following:

- the chemical has moderate oral acute toxicity;
- the chemical is an eye irritant;
- the chemical is a moderate skin sensitiser;
- overseas restrictions for use of the chemical in hair dyes where the maximum concentration allowed in the finished cosmetic product is 4.0 % and the maximum use concentration upon application is 2.0 % (after mixing with hydrogen peroxide); and
- the risk could be controlled by including warning statements on the label of hair dye formulations containing the chemical at any concentration.

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 if swallowed - Cat. 4 (H302)
Irritation / Corrosivity	Irritating to eyes (Xi; R36)	Causes serious eye irritation - Cat. 2A (H319)
Sensitisation	May cause sensitisation by skin contact (Xi; R43)	May cause an allergic skin reaction - Cat. 1 (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 dermal and ocular 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;
- 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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