1,4-Benzenediamine: Human health tier II assessment

07 February 2014

CAS Number: 106-50-3

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.

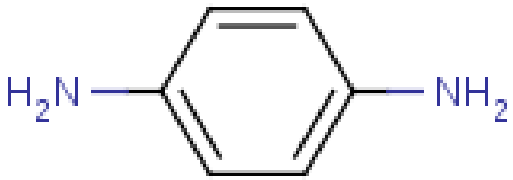
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	p-phenylenediamine 1,4-phenylenediamine 1,4-diaminobenzene 4-aminoaniline PPD
Structural Formula	
Molecular Formula	C6H8N2
Molecular Weight (g/mol)	108.14
Appearance and Odour (where available)	White to slightly red crystals
SMILES	c1(N)ccc(N)cc1

Import, Manufacture and Use

Australian

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

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

International

The following international uses have been identified through European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers; Galleria Chemica; the European Commission Cosmetic Ingredients and Substances (CosIng) database; United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary; eChemPortal: the US Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR), the US National Library of Medicine's Hazardous Substances Data Bank (HSDB); and the National Cancer Institute (NCI) technical report (NCI, 1979).

The chemical has reported cosmetic use:

- in permanent hair dyes

The chemical is used in oxidative hair dye products at a maximum concentration of 4 %. After mixing with hydrogen peroxide at 1:1 ratio, the maximum concentration applied to hair is 2 % (SCCP, 2006).

The chemical has reported commercial use including:

- in dyes;
- as a photographic developing agent;
- as an antioxidant in rubber compounds; and
- as a vulcanising accelerator.

The chemical has reported site-limited use including:

- as an intermediate in chemical and dye manufacturing; and
- as a laboratory reagent.

Restrictions

Australian

This chemical is not individually listed in the Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons—SUSMP). However, there is a group entry in Schedule 6 and Appendix C of the SUSMP that includes this chemical:

Schedule 6

- 'PHENYLENEDIAMINES and alkylated phenylenediamines not elsewhere specified in these Schedules:

(a) in preparations packed and labelled for photographic purposes;

(b) in preparations packed and labelled for testing water except tablets containing 10 mg or less of diethyl-para-phenylenediamine or dimethyl-para-phenylenediamine in opaque strip packaging provided the directions for use include the statement, "Do not discard testing solutions into the pool";

(c) in hair dye preparations except when the immediate container and primary pack are labelled with the following statements: KEEP OUT OF REACH OF CHILDREN, and WARNING - This product contains ingredients which may cause skin irritation to certain individuals. A preliminary test according to the accompanying directions should be made before use. This product must not be used for dyeing eyelashes or eyebrows; to do so may be injurious to the eye.

written in letters not less than 1.5 mm in height; or

(d) in eyelash and eyebrow tinting products when the immediate container and primary pack are labelled with the following statement: WARNING - This product contains ingredients which may cause skin irritation to certain individuals, and when used for eyelash and eyebrow tinting may cause injury to the eye. A preliminary test according to the accompanying directions should be made before use.

written in letters not less than 1.5 mm in height.'

Schedule 6 chemicals are labelled with 'Poison'. These are substances with a moderate potential for causing harm, the extent of which can be reduced by using distinctive packaging with strong warnings and safety directions on the label.

Appendix C:

- 'PHENYLENEDIAMINES in preparations for skin colouration and dyeing of eyelashes or eyebrows except when included in Schedule 6.'

Appendix C chemicals are substances of such danger to health as to warrant prohibition of sale, supply and use.

International

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

- EU Cosmetics Regulation 1223/2009 Annex III—List of substances which cosmetic products must not contain except subject to the restrictions laid down;
- 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 the restrictions laid down;

- New Zealand Cosmetic Products Group Standard—Schedule 5—Components cosmetic products must not contain except subject to the restrictions and conditions laid down;
- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient "Hotlist").

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):

- T; R23/24/25 (acute toxicity)
- Xi; R36 (irritation)
- R43 (sensitisation)

Exposure Standards

Australian

The chemical has an exposure standard of 0.1 mg/m³ time weighted average (TWA).

International

The following exposure standards are identified (Galleria Chemica):

- An occupational exposure limit (OEL) or TWA of 0.1 mg/m³ in countries such as USA, Canada, Norway, France, Germany and Switzerland.

Health Hazard Information

HSIS indicates similar hazard classifications for the chemical and its hydrochloride salt. Considering the ready pH-dependent inter-conversion of the chemical and its hydrochloride salt, when there are no hazard data or insufficient hazard data available on the chemical, data on the hydrochloride salt of the chemical (CAS No. 624-18-0) are used in this assessment.

Toxicokinetics

On administration of the chemical intraperitoneally to rats—following OECD Test Guideline (TG) 417—at a single dose of 10 mg/kg bw, only 3–4 % of the dose remained in the animals after 72 hours, indicating a low potential for bioaccumulation. Approximately 50 % and 35 % of the dose was excreted in the urine and faeces, respectively, within 72 hours (REACH).

The chemical, administered orally to Sprague Dawley (SD) rats at 4 or 6.45 mg/kg bw, was rapidly absorbed and excreted in the urine at 57–60 % and 74–81 %, respectively, and in the faeces at 19–23 % and 13–19 %, respectively (SCCP, 2006).

When the chemical at 2 % was mixed with hydrogen peroxide (hair dye formulation) and applied to the human scalp, the absorbed dose was calculated (using excretion rate in rats through urine and faeces) as only 0.54 % of the applied dose (SCCP, 2006).

When a commercial hair dye formulation containing 2.7 % of the chemical was applied to the scalp of humans and monkeys, the maximum penetration was calculated as 4.47 µg/cm². The extent of dermal absorption of the chemical was shown to decrease to 'almost negligible levels' when mixed with hydrogen peroxide (SCCP, 2006).

Acute Toxicity

Oral

The chemical is classified as hazardous with the risk phrase ‘Toxic if swallowed’ (T; R25) in HSIS (Safe Work Australia). The available data support this classification.

The median lethal dose (LD50) is 80–100 mg/kg bw in rats, 290 mg/kg bw in mice, 250 mg/kg bw in rabbits and 100 mg/kg bw in cats (SCCP, 2006). Reported sublethal signs of toxicity in animals include lacrimation (tearing), swelling of conjunctivae, unsteady gait, tremor and subdued behaviour (REACH; SCCP, 2006).

Dermal

The chemical is classified as hazardous with the risk phrase 'Toxic in contact with skin' (T; R24) in HSIS (Safe Work Australia). While the available data do not support this classification, in the absence of more comprehensive information, it is not recommended that this classification be amended.

The SCCP opinion in 2006 stated that no data were submitted on acute dermal toxicity of the chemical.

The National Institute for Occupational Safety and Health (NIOSH) report in 2011 indicated the LD50 in New Zealand White rabbits as >7940 mg/kg bw (study conducted prior to 1977 and details not available). However according to a REACH dossier on the chemical, this study was conducted using only one animal per dose and with a 40 % aqueous solution.

The lowest lethal dose (LDLo) in New Zealand White rabbits is 5000 mg/kg bw (details not available) (NIOSH, 2011).

Inhalation

The chemical is classified as hazardous with the risk phrase 'Toxic by inhalation' (T; R23) in HSIS (Safe Work Australia). The available data support this classification.

The median lethal concentration (LC50) in rats **(**exposed to the chemical as an aerosol) is 0.92 mg/L/four hours. Reported sublethal signs of toxicity include red nasal discharge, cyanosis, red ocular discharge, brown-stained fur around the eyes, diarrhoea, no righting reflex (reflex that corrects the orientation of the body) and tremors (REACH).

Corrosion / Irritation

Skin Irritation

The chemical may cause slight skin irritation. However, the limited information available is not sufficient to warrant a hazard classification.

The chemical is reported to be non-irritant or irritant to the skin depending on the animal species and the dose tested (NIOSH, 2011; REACH):

- in guinea pigs, topical application of 40 to 90 mg of the chemical to intact or abraded skin caused mild to moderate irritation; 0.05 mL of a 1 % solution (equivalent to 0.05 mg of chemical) or 25 % solution caused mild to strong erythema. Irritation scores are not available. However, other reports of the same study indicated negative responses after applying 0.05 mL of 25 or 10 % solutions, and concentrations of 2.5, 3 and 30 % of the chemical; and
- in rabbits, doses above 450 mg/kg produced erythema and oedema (irritation scores not available); another study in rabbits indicated that no irritation was observed with exposure to 500 mg/kg bw.

Eye Irritation

The chemical is classified as hazardous with the risk phrase 'Irritating to eyes' (Xi; R36) in HSIS (Safe Work Australia). The available data support this classification.

In an eye irritation study, 10 mg of the chemical was applied to the right eye of two male rabbits. Only one treated eye was washed after 20 seconds exposure and the other treated eye remained unwashed. The chemical was found to be moderately irritating with moderate iritis, conjunctivitis and slight corneal cloudiness observed at 1, 4, 24, 48, 72 hours (scores not available) and up to seven days after treatment. Washing reduced the severity of irritation. Effects were reversible within the 14-day observation period (REACH).

Sensitisation

Skin Sensitisation

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

In a mouse local lymph node assay (OECD TG 429), the mean stimulation indices were reported to be 2.6, 10.4 and 16.1 for the concentrations of 0.025, 0.25 and 1.25 % of the chemical, respectively. An estimated concentration to produce a stimulation index of three (EC3) was extrapolated to be 0.06 % (REACH; SCCP, 2006), indicating the chemical as a strong skin sensitiser.

Observation in humans

The chemical is a strong clinical contact allergen in humans and the sensitisation response varies with the vehicle, exposure condition and challenge concentration (SCCP, 2006).

The SCCP (2006) states, 'p-phenylenediamine (PPD) is a very strong potential skin sensitiser and included in the European Standard Series for diagnostic patch testing of eczema patients'; and 'Standard patch tests in more than 36000 eczema patients in Germany showed a sensitisation rate of PPD contact allergy of 4.8 % after standardisation for age and sex'.

Cases of severe blistering dermatitis were reported in patients who had used the chemical containing skin paints (in temporary tattoos). Patients found allergic to the chemical have reacted to concentrations as low as 1 % after only 15 minutes' exposure (SCCP, 2006).

Repeated Dose Toxicity

Oral

The chemical is not expected to cause serious damage to health from repeated oral exposure.

Several repeated dose toxicity studies are available:

- In a 13-week study (OECD TG 408), SD rats receiving the chemical at 2, 4, 8 or 16 mg/kg bw/d showed no significant toxic effects at the doses tested except for increased absolute and relative liver weights in males at 8 and 16 mg/kg bw/d, and minimal degeneration of the skeletal muscle in two animals at 16 mg/kg bw/d. A no observed adverse effect level (NOAEL) of 4 mg/kg bw/d was determined (SCCP, 2006).
- In a 13-week neurotoxicity study, Fischer 344 rats receiving the chemical at 4, 8 or 16 mg/kg bw/d had no mortalities or clinical signs associated with the chemical. A NOAEL of 16 mg/kg bw/d was established (SCCP, 2006).
- In a 12-week study, Fischer 344 rats (groups of 10–11 animals) receiving the chemical in their diet at 0.4 % (corresponding to 200 mg/kg bw/d) showed toxic effects marked by death (nine male rats and one female rat), a 50 % reduction in body weight and increased relative liver and kidney weights. The study authors reported 'no remarkable toxic changes' at the lower dietary doses of 0.2, 0.1 and 0.05% (100, 50 and 25 mg/kg bw/d, respectively) (Imaida et al., 1983; SCCP, 2006). The NOAEL is reported as 50 mg/kg bw/d (SCCP, 2006).
- In Fischer 344 rats receiving the chemical at 0.05 and 0.1% in their diet (approximately 25 and 50 mg/kg bw/d, respectively) for 80 weeks, except for a slightly decreased body weight in female rats at 0.1%, no toxic effects were reported (Imaida et al., 1983; SCCP, 2006).

Dermal

The repeated dose dermal toxicity studies in animals have tested only up to a 10 % concentration of the chemical. No serious health effects are reported in animals at the low concentrations tested.

The following studies are available (REACH; SCCP, 2006; NIOSH, 2011):

- Percutaneous application of the chemical at a 5 or 10 % concentration (in acetone) twice a week (corresponding to 8.6 and 17.2 mg/kg bw/d respectively) for 135 weeks in Swiss mice and 85 weeks in rabbits did not induce any treatment-related effects (Stenback et al., 1977), establishing a NOAEL of 17.2 mg/kg bw/d in both animal species (NIOSH, 2011).
- Mice were administered the chemical at 1, 2, 3 or 4 % concentrations (mixed at 1:1 ratio with 6 % hydrogen peroxide), once a week for 21 to 23 months. There were no systemic toxic effects and a NOAEL of 4.3 mg/kg bw/d was determined (NIOSH, 2011).
- Topical application of a solution (0.05 mL or 5 mg) containing 1.5 % of the chemical equally mixed with 6 % hydrogen peroxide was applied to the shaved skin of mice once a week for 18 months (corresponding to 3.2 mg/kg bw/d) did not induce toxic effects (NIOSH, 2011).
- Dermal exposure of guinea pigs to 0.1 mL of the chemical at 3 % for 15 or 30 days increased the activity of some enzymes (acid and alkaline phosphatases, beta-glucuronidases), lipid peroxidation and histamine content in the skin (REACH).

No other adverse effects were reported.

Inhalation

No reliable data are available.

Guinea pigs exposed repeatedly to the chemical showed dyspnoea (shortness of breath) due to irritation of the respiratory system (REACH).

Genotoxicity

Based on the available data, the chemical is not expected to be genotoxic. Although some in vitro studies showed positive results for genotoxicity, all in vivo studies in rats and mice showed negative results up to the doses close to the median lethal dose range (75–100 mg/kg bw).

There are several in vitro genotoxicity studies and some of them indicate positive results:

- In a bacterial gene mutation test (OECD TG 471), testing the chemical at 1.6–5000 µg/plate in *Salmonella typhymurium* strains TA98, TA100, TA1535 and TA1537, positive results were observed with TA98 with metabolic activation only (SCCP, 2006).
- When the chemical was tested alone (purified substance) or in a mixture with resorcinol and hydrogen peroxide at doses from 0 to 2000 µg/plate in strain TA98 in an Ames test, the purified chemical did not induce mutagenicity whereas the mixture was found to be mutagenic (Crebelli et al., 1981). The same mixture was found to be non-mutagenic in another Ames test with doses 'relevant to practical hair dying procedures' (SCCP, 2006). Only the chemical combined with hydrogen peroxide was mutagenic in strain TA98, possibly due to the formation of Bandrowski's base, a p-phenylenediamine trimer (Bracher et al., 1990).
- In a gene mutation test with mouse lymphoma cells (OECD TG 476), the chemical tested at doses from 2.5 to 1000 µg/mL did not induce a significant increase in the mutation frequency of the hprt gene locus (SCCP, 2006). Similarly, when the chemical was tested at 'concentrations relevant to practical hair dying procedure' by mixing with hydrogen peroxide or resorcinol and hydrogen peroxide (SCCP, 2006) it showed negative results in the mammalian gene mutation test with mouse lymphoma cells (Bracher et al., 1990).
- In a chromosome aberration test using Chinese hamster ovary cells (CHO-K1), doses of 15 to 87 µg/mL of the chemical induced a dose-related increase of chromosome aberrations (Chung et al., 1996).
- The chemical, mixed with hydrogen peroxide 'at concentrations relevant to practical hair dying procedure', increased the number of cells with chromosomal aberrations in human lymphocytes. The same test with a combination of resorcinol and hydrogen peroxide gave negative results (Bracher et al., 1990).

The available in vivo studies indicated negative results for mutagenicity (SCCP, 2006):

- In a bone marrow micronucleus test (OECD TG 474), Wistar rats, orally administered the chemical at doses of 25, 50 or 100 mg/kg bw and examined for 24 hours following exposure, did not show biologically relevant increases of micronuclei.
- A bone marrow micronucleus test in mice treated with the chemical at 25, 50 or 100 mg/kg bw showed no increase of micronuclei.
- Negative results were reported in rats for the induction of micronuclei, when administered the chemical orally at 300 mg/kg bw.
- In an unscheduled DNA synthesis (UDS) assay, Wistar rats (OECD TG 486) received the chemical orally at 50 or 100 mg/kg bw showed no significant increase of the mean net nuclear grain count, indicating no mutagenic activity.
- In a single cell electrophoresis assay (Comet assay), rats orally dosed with the chemical at 75 mg/kg bw showed negative results for the induction of DNA damage in the organs examined (stomach, colon, liver, kidney, urinary bladder, lung, brain and bone marrow).

Carcinogenicity

The data available are insufficient to draw a conclusion on the carcinogenicity of the chemical. However, the two-year studies (NCI, 1979) with the hydrochloride salt of the chemical did not show a significantly increased incidence of tumours in rats and mice, indicating that the chemical is not carcinogenic up to dietary doses of 1250 ppm.

The SCCP (2006) concluded that 'p-phenylenediamine alone has not been demonstrated to be carcinogenic in experimental studies with rats or mice' and 'p-phenylenediamine together with hydrogen peroxide may be carcinogenic in experimental studies with rats'. The SCCP (2006) also stated, 'IARC has classified PPD as a category 3 carcinogen based on no data in human studies and inadequate data in animal studies' in 1978.

The International Agency for Research on Cancer (IARC) (1978) stated that the chemical 'has been inadequately tested in mice by skin application and in rats by oral and subcutaneous administration. Studies in mice in which para-phenylenediamine as a constituent of hair-dye preparations was tested by skin application cannot be evaluated. No evaluation of the carcinogenicity of this compound can be made'.

The hydrochloride salt of p-phenylenediamine (CAS No. 624-18-0) was tested in a two-year feeding study in Fischer 344 rats (n = 50/sex/dose) and B6C3F1 mice (n = 50/sex/dose). The test substance, administered at 625 ppm to 1250 ppm in the diet for 103 weeks, did not significantly increase the tumour incidence in either species (NCI, 1979).

In a long-term topical study, female mice and female rabbits were treated twice a week with a 5 or 10 % concentration of the chemical in acetone, until spontaneous death occurred. Various tumours including lymphomas, lung adenomas, liver haemangiomas, ovarian neoplasms and dermal fibromas were found in mice but were not statistically significantly increased compared with the controls. In rabbits, no neoplasms were found after 85 weeks of treatment (Stenback et al., 1977; SCCP, 2006).

In another long-term dermal study, Swiss Webster mice were treated once a week with four hair dye formulations containing the chemical at 1, 2, 3 or 4 % concentration, equally mixed with 6 % hydrogen peroxide, for 21 to 23 months. No statistical difference was found between the distribution of tumours among treated and untreated animals (SCCP, 2006).

Three other dermal studies on rats and mice, using hair dye formulations containing the chemical mixed with hydrogen peroxide, have been reported. The negative results reported in these studies for carcinogenicity may be due to the low sensitivity of the testing methods used, as some hair dye formulations tested contained known carcinogens (SCCP, 2006).

In a 18-month study on Wistar rats the chemical, mixed with hydrogen peroxide, was administered either topically or by subcutaneous injection at 2.5 % concentration, once a week. Results showed that both topical applications and subcutaneous injections induced a significant increase of tumour incidence—40 % of males and 60 % of females after dermal application; and 14 % of males and 85 % of females after injection (SCCP, 2006). Similar results (soft tissue tumours in both sexes and malignant mammary gland tumours in females) were obtained in another 18-month topical study in Wistar rats, which used the chemical at 5.93 % equally mixed with hydrogen peroxide (SCCP, 2006).

Reproductive and Developmental Toxicity

Based on the available data, the chemical is not expected to cause reproductive or developmental toxicity.

In a developmental toxicity study (OECD TG 414) conducted on SD rats, the chemical was orally administered to pregnant female rats at 5, 10 or 20 mg/kg bw/d from gestation day (GD) 6 to 19. A NOAEL of 5 mg/kg bw/d was determined for maternal toxicity based on a transiently lower mean body weight gain at 10 and 20 mg/kg bw/d. For developmental toxicity, a NOAEL of 10 mg/kg bw/d was determined based on slightly retarded ossification (supraoccipital, sternebrae, thoracic vertebrae and metacarpals) and reduced mean foetal weight (not statistically significant) at 20 mg/kg bw/d (REACH; SCCP, 2006).

These results were supported by another study (OECD TG 414) that administered the chemical at 5, 10, 15, 20 or 30 mg/kg bw/d in pregnant SD rats from GD 6 to 15. A NOAEL of 10 mg/kg bw/d was established for maternal toxicity, based on decreased body weight gain and food consumption at 20 and 30 mg/kg bw/d (REACH; SCCP, 2006). There were no teratogenic or embryotoxic effects (Re et al., 1981).

Dermal studies in rats that used hair dye formulations containing the chemical (mixed with hydrogen peroxide), showed no reproductive or developmental effects at 1–4 % concentrations (SCCP, 2006).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include:

- systemic acute effects (oral, dermal and inhalation); and
- local effects (skin sensitisation and eye irritation).

The potential for carcinogenicity is inconclusive. Although the chemical alone may not be carcinogenic, the chemical mixed with hydrogen peroxide may be carcinogenic when administered systemically.

Public Risk Characterisation

The chemical is reported to be used in permanent hair dye preparations in Australia.

Many countries, including Canada, New Zealand and the European Union, have imposed restrictions and conditions for the use of this chemical in cosmetics.

The chemical is a strong skin sensitiser. Mixing it with hydrogen peroxide may have some potential for carcinogenicity (inconclusive). However, this is not likely to be relevant under conditions of use due to its low bioavailability through dermal absorption under the use concentrations. If this chemical is included in cosmetic products containing N-nitrosating agents, carcinogenic N-nitrosamine compounds could be formed (SCCS, 2012).

In Australia, a chemical group (phenylenediamines), including this chemical, is listed on Schedule 6 and Appendix C of the SUSMP, with restriction and prohibition on its use in specific cosmetic products and other domestic uses such as photographic purposes and water testing in pools. The Schedule 6 entry in the SUSMP allows phenylenediamines to be included in hair dye preparations and in eyelash and eyebrow tinting products with specific labelling requirements.

Considering the identified health risks, the existing control measures imposed through the SUSMP are considered adequate to protect the public from use of this chemical in hair dye preparations.

Occupational Risk Characterisation

Given the critical health effects (skin sensitisation, eye irritation and acute toxicity), the chemical may pose an unreasonable risk to workers unless adequate control measures to minimise exposure to the chemical are implemented. Based on the available data, the hazard classification in HSIS is considered appropriate.

NICNAS Recommendation

Current risk management measures are considered adequate to protect public and workers' health and safety, provided that all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Public Health

The chemical falls within the scope of the listing of 'Phenylenediamines' in Schedule 6 of the SUSMP for use in hair dye preparations under specified conditions.

Work Health and Safety

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

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Toxic if swallowed (T; R25)* Toxic in contact with skin (T; R24)* Toxic by inhalation (T; R23)*	Toxic if swallowed - Cat. 3 (H301) Toxic in contact with skin - Cat. 3 (H311) Toxic if inhaled - Cat. 3 (H331)
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 oral, dermal, ocular and inhalation exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures which may minimise the risk include, but are not limited to:

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

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

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

Obligations under workplace health and safety legislation

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

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((m)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (m)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of the chemical has not been undertaken as part of this assessment.

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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