1,4-Benzenediamine, N-phenyl and a salt: Human health tier II assessment

07 February 2014

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
1,4-Benzenediamine, N-phenyl-	101-54-2
1,4-Benzenediamine, N-phenyl-, monohydrochloride	2198-59-6

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

Grouping Rationale

The chemical, 1,4-Benzenediamine, N-phenyl-, monohydrochloride (CAS No. 2198-59-6) is a salt resulting from 1,4-Benzenediamine, N-phenyl- (CAS No. 101-54-2; referred to as the parent base in this report) reacting with one molecule of hydrochloric acid. Therefore, these two chemicals are considered together in this assessment report. The speciation of these chemicals in biological fluids will be dependent on pH but independent of the original form.

Import, Manufacture and Use

Australian

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

International

The following international uses have been identified through European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers; the Organisation for Economic Cooperation and Development Screening information data set International Assessment Report (OECD SIAR); 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; and 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 Chemicalland21.

These chemicals have reported cosmetic use including:

- in hair dye preparations, including to colour eyelashes (SCCS, 2012 a).

These chemicals are used at a maximum concentration of 0.4 % (0.2 % after mixing with hydrogen peroxide at 1:1 ratio) in oxidative hair dyes (SCCP, 2006).

The parent base (1,4-benzenediamine, N-phenyl-) has reported commercial use including in:

- lubricants and additives;
- rubber additives; and
- photographic chemicals.

The parent base has reported site-limited use including as an intermediate:

- in manufacturing rubber chemicals and hair dyes.

The following non-industrial uses have been reported for the parent base:

- in manufacturing pharmaceuticals and pesticides.

Restrictions

Australian

No known restrictions have been identified.

Although there is a group entry for 'Phenylenediamines and alkylated phenylenediamines' in Schedule 6 and Appendix C of the Poisons Standard (Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)), this group entry does not cover aryl N-substituted derivatives of phenylenediamines and their salts.

International

These chemicals are listed in the following (SCCP, 2006; Galleria Chemica; CosIng):

- EU Cosmetic Regulations 1223/2009 Annex III, part 1—List of substances which cosmetic products must not contain except subject to the restrictions and conditions laid down ('m- and p- phenylenediamines, their N-substituted derivatives and their salts; N-substituted derivatives of o-phenylenediamines, with the exception of those derivatives listed elsewhere in this Annex').

The following must be on the labels of products containing the chemical:

'a) for general use: Can cause an allergic reaction. Contains phenylenediamines.

Do not use to dye eyelashes or eyebrows.

b) for professional use: For professional use only. Contains phenylenediamines. Can cause an allergic reaction. Wear suitable gloves.'

- US Cosmetic Ingredient Review (CIR) Cosmetic ingredients found safe, with qualifications: up to 1.7 % as the free base.

Existing Worker Health and Safety Controls

Hazard Classification

These chemicals are 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

The CIR expert panel stated that the toxicological data available on the hydrochloride salt are limited, but the data available on the parent base are sufficient to evaluate the safety of the hydrochloride salt, as both these chemicals 'have essentially the same degree of biological activity' (CIR, 1994).

Where data are unavailable for 1,4-benzenediamine, N-phenyl-, monohydrochloride (CAS No. 2198-59-6), data available for 1,4-benzenediamine, N-phenyl- (CAS No. 101-54-2) are considered relevant for the risk assessment due to the structural similarity of the two chemicals. However, the hydrochloride salt may produce slightly different properties with respect to local effects, as it is expected to be closer to neutral pH.

Toxicokinetics

Animal studies showed that the parent base can be absorbed through oral and dermal routes and it can also bind to haemoglobin and proteins in the rat liver. The chemical and its metabolites are excreted through urine and faeces. The parent base has been detected in the urine of humans after a single dermal contact (quantity not reported) (OECD, 2004).

Acute Toxicity

Oral

Based on the available data, these chemicals are considered to be of moderate acute oral toxicity and warrant a hazard classification.

Data are available only for the parent base. The chemical had moderate acute toxicity in animal tests using oral exposure. The median lethal dose (LD50) is 336-847 mg/kg bw in rats and 244 mg/kg bw in mice (IUCLID, 2000; ChemIDplus and REACH). Observed sub-lethal effects included piloerection (erection of hair on the skin), decrease activity, urine/faecal strains with reddish coloured urine, breathing abnormalities and dark material around the facial area (REACH).

Dermal

Based on the available data, these chemicals are considered to be of low acute dermal toxicity.

Data are available only for the parent base. The chemical had low acute toxicity in animal tests using dermal exposure. The LD50 in rabbits is greater than 5000 mg/kg bw (OECD, 2004).

In an acute dermal toxicity study (comparable to OECD test guideline (TG) 402), groups of New Zealand White rabbits (n=5/dose/sex) were treated with the chemical at 5000 mg/kg bw (occlusive patch for 24 hours). No mortality was observed by 14 days after patch removal. No significant signs of systemic toxicity were observed. However, occurrences of nasal and /or ocular discharge, red and/or swollen eyes and food consumption decrease were observed. The dermal LD50 is concluded to be greater than 5000 mg/kg bw (IUCLID, 2000; REACH).

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

Based on the available data for the parent base, both chemicals are not considered to be skin irritants.

In a skin irritation study (OECD TG 404), a group of New Zealand White rabbits (n=3) were treated with 0.5 g of the chemical on the shaved intact skin (semi-occlusive) for four hours. There were no signs of irritation at one, 24, 48, 72 hours and seven days and the irritation scores were zero at all time points (Draize scale) (OECD, 2004; REACH).

In another skin irritation study (non-guideline), 0.5 g of the chemical was applied to the shaved skin on the flank of three male albino rabbits (semi occlusive patch) for 4 hours. No skin irritation was observed at one, 24, 48 and 72 hours after patch removal or on day seven (SCCP, 2006).

Eye Irritation

Two rabbit studies indicated the parent base to be an eye irritant. However, the scores reported are not sufficient to warrant a hazard classification. There are no studies conducted using the hydrochloride salt.

The chemical was reported to be a slight irritant to the eyes of New Zealand White female rabbits (OECD TG 405). The chemical (100 mg) was instilled into the conjunctival sac of one eye of each rabbits (n=3). The treated eyes were washed with water after 24 hours. The average primary irritation score (for 24, 48 and 72 h) was 8.1 out of 110. All symptoms were reversible after 72 hours (IUCLID, 2000; CIR 1994).

In another eye irritation study (non-guideline), 0.1 mL of the chemical was instilled into the conjunctival sac of one eye of each New Zealand White rabbit (n=6). After 24 hours the eyes were washed. All six animals exhibited moderate to severe conjunctival irritation (redness, chemosis, discharge and/or necrosis), three exhibited corneal opacity and/or ulceration at one-hour following exposure, but not at later times. The mean (1, 24, 48 and 72 h) scores for conjunctival redness and chemosis in individual animals were all below 2.5. All ocular effects were reversible within seven to 14 days after instillation of the chemical (IUCLID, 2000; REACH).

Sensitisation

Skin Sensitisation

Based on the available data for the parent base, both chemicals are considered to be very strong skin sensitisers and warrant a hazard classification.

Data are available only for the parent base. Positive results were reported in a local lymph node assay (LLNA) in mice (OECD TG 404). The concentration of the chemical for tripling the response (EC3) was reported as 0.0175 % (SCCP, 2006), indicating that the chemical is a very strong skin sensitiser.

In a maximisation test, guinea pigs (n=10) were topically induced with 50 mg of 1 % of the chemical in petroleum jelly (occlusive patch), three times per week for two weeks. The animals were challenged after a resting period of 14 days with 0.1 % or 1 % of the chemical in petroleum jelly for 48 hours. Positive skin reactions were reported in 4/10 and 10/10 animals, respectively. The chemical was considered to be a skin sensitiser (OECD, 2004).

In another skin sensitisation study (non-guideline), groups of male Pirbright-White guinea pigs (n=8) were topically treated daily with the chemical in petroleum jelly, five days per week at 1, 2, 5 and 10 % concentrations (induction phase). After 16 days, a challenge dose (0.5, 1, 2.5 and 5 %) was applied to an untreated skin site of the guinea pigs. Half of the animals were sensitised (details not reported) (CIR, 1994).

Observation in humans

There were reports of skin sensitisation in humans exposed to the chemicals. A number of patch tests using the chemical on a wide range of dermatology patients (individuals, hairdressers and hairdressers' clients) produced positive reactions to the chemical. Skin sensitisation reactions were observed in 32 of 302 dermatitis patients (hairdressers) and 11 of 261 dermatitis patients (hairdressers' clients) tested with the parent base at 0.25 % concentration (SCCP, 2006; CIR, 1994).

Repeated Dose Toxicity

Oral

Considering the no observed adverse effect level (NOAEL) available from a 90-day study in rats (100 mg/kg bw/d) for the parent base, both chemicals are not considered to cause serious damage to health from repeated oral exposure.

In a 90-day repeated dose toxicity study, male Wistar rats (n=12/dose) were administered the chemical in the diet at 0, 100, 250, 500 or 750 mg/kg bw/d. There was no information on mortalities or clinical signs related to treatment. Changes in haematological parameters (such as reduction of erythrocytes and haemoglobin counts with increased mean corpuscular volume) and marker enzymes in the serum were observed from 250 mg/kg bw/d. Reduced food intake and decreased body weight gains (11.7 % body weight gain compared to 36 % in the control group) were observed at 500 mg/kg bw/d. Hepatotoxicity (increased liver weights by 35 % at both 500 and 750 mg/kg bw/d) and decreased hyaluronidase (enzyme which degrades hyaluronic acid) in the testis were reported. Degeneration of seminiferous tubules in the testes was observed at 750 mg/kg bw/d. A NOAEL of 100 mg/kg bw/d was established (IUCLID, 2000; REACH).

There were two other seven-week studies in rats (Fischer 344) and mice (B6C3F1) indicating no adverse effects up to the doses 2200 mg/kg in the diet of the rats and 14700 mg/kg in the diet of the mice (IUCLID, 2000). The administered doses were reported to be in the range of 60 to 120 mg/kg bw/d in rats and mice (REACH).

Dermal

No data are available for the parent chemical. The hydrochloride salt (N-phenyl-p-phenylenediamine hydrochloride) used in a hair dye formulation at a low concentration (2 %), did not cause any clear signs of systemic toxicity in rabbits. Based on the limited data available, no conclusion can be made on the repeated dose dermal toxicity of these chemicals.

In a 13-week repeated dose study, a group of New Zealand White rabbits (n=12, 6/sex) received a topical dose of 0.1 mL/kg bw of an oxidative hair dye formulation containing four hair dyes including the chemical as a hydrochloride salt at 2 % concentration mixed with an equal volume of 6 % hydrogen peroxide. The dose was applied to the shaved and abraded skin of the rabbits. No statistically significant differences in clinical chemistry were seen between the treated and control groups. A statistically significant increase in the methaemoglobin (when oxyhaemoglobin in a ferrous (Fe^{2+}) state is transformed into a ferric (Fe^{3+}) state, which cannot transport oxygen) in the treated males compared with the control group was reported. This was not considered by the author to be of toxicological significance (SCCP, 2006).

Inhalation

No data are available.

Genotoxicity

Data are available only for the parent base. The chemical showed no genotoxicity in most of the in vitro assays and in all in vivo assays available. Therefore, both chemicals are not expected to be genotoxic.

The parent base produced negative results for genotoxicity in the following in vitro assays (SCCP, 2006; OECD, 2004):

- Ames tests in *Salmonella typhimurium* strains T98, TA100, TA1535 and TA 1537, both in the presence and absence of S9 metabolic activation and at up to 3333 µg/plate;
- a gene mutation assay in mammalian cells (Chinese hamster ovary (CHO) cells) up to 100 µg/mL concentration and with or without metabolic activation; and
- unscheduled DNA synthesis test in rat hepatocytes up to 1 mg/L concentration.

However, three in vitro tests showed positive results: sister chromatid exchange assay in CHO cells (with and without metabolic activation from concentrations 5 µg/mL and 1 µg/mL, respectively), Ames test with *S. typhimurium* strain TA98 (with metabolic activation from 15 µg/plate) and mouse lymphoma assay with L5178Y cells (from 0.16 µg/mL to 4 µg/mL). These tests were reported as inadequate for evaluation due to lack of details (only abstracts were available) (SCCP, 2006). However, the OECD (2004) concluded that 'Based on the weight-of-evidence, and taking into account structure-activity relationship information, an in vivo genotoxic activity of 4-ADPA cannot be excluded'.

The parent chemical produced negative results for genotoxicity in the following in vivo assays (SCCP, 2006; OECD, 2004):

- a bone marrow micronucleus test in Sprague Dawley (SD) rats up to 100 mg/kg bw;
- unscheduled DNA synthesis in rat hepatocytes with up to 250 mg/kg bw (sacrifice times 16 and 48 hours after dosing) and up to 750 mg/kg bw (sacrifice times 2-4 hours and 12-16 hours after dosing); and
- alkaline single cell gel electrophoresis (Comet) assay in ddY mice up to 300 mg/kg bw per single oral gavage dose.

Carcinogenicity

Based on the data available, no conclusion can be made on the carcinogenic potential of these chemicals.

The National Cancer Institute (NCI), reported the parent base as non-carcinogenic (NCI, 1978) based on studies conducted in rats and mice. In long-term studies, Fisher 344 rats were fed the chemical at up to 1200 ppm in the diet for 78 weeks and B6C3F1 mice were fed up to 5000 ppm in the diet for males or 10000 ppm in the diet for females, for 48 weeks. There were no carcinogenic effects and no significant differences in body weight gain, clinical signs or mortality in rats compared with the control groups. Reduced body weight gain (no details on statistical significance) and increased mortality rates (approximately 25 % in the low dose group and 40 % in the high dose group compared with 15 % in the control group) were reported in mice. Hepatocellular neoplasms (not statistically significant compared with control groups and not dose-dependent) were observed in male mice that received the chemical at 1250-2500 mg/kg in the diet (IUCLID, 2000; NCI, 1978; REACH).

The OECD SIAP (2004) reported 'Early feeding studies in rats and mice revealed no evidence of carcinogenicity but they were not adequate to judge the carcinogenic potential of 4-ADPA, mainly because of the shortened period of administration of the test substance, i.e. only 78 weeks in rats, and 41-48 weeks in mice, respectively'.

The Scientific Committee on Consumer Products (SCCP) stated that carcinogenic effects of the chemical 'have been tested in a 2-year study with rats and mice. The rat study was negative. The mice study was not adequate for evaluation'.

A hair dye formulation containing the hydrochloride salt of the chemical at 2 % was mixed with an equal volume of hydrogen peroxide (6 %) and applied topically on mice and rats produced no tumours, although known carcinogens were present in the hair dye formulation. The SCCP (2006) concluded: 'Thus, no conclusions with regards to carcinogenicity can be drawn from the skin painting studies'.

Reproductive and Developmental Toxicity

Based on the data available, these chemicals are not considered to have reproductive or developmental toxicity.

In a developmental toxicity study, groups of SD female rats (n=12/dose) were orally administered the parent base at 0, 50, 100 or 200 mg/kg bw/d in propylene glycol on gestation days (GD) 6 to 15. The chemical did not induce significant differences in mean foetal weights or foetal skeletal abnormalities. A significant reduction in maternal weight gain was observed at 200 mg/kg bw/d and the NOAEL for maternal toxicity was established as 100 mg/kg bw/d (SCCP, 2006).

In a similar study, groups of SD female rats (n=24/dose) were orally dosed with the parent base at 0, 10, 50 or 100 mg/kg bw/d in corn oil on GD 6 -15. Maternal and foetal toxicity were only observed at 100 mg/kg bw. The maternal effects at this dose were: significantly reduced food consumption; and weight gain, salivation and staining of the skin in the ano-genital area. The foetal effects at 100 mg/kg bw dose were: significantly reduced weight; and low incidences of visceral and external malformations (not significant compared with control groups). Skeletal malformations were significantly increased compared with the control group but the author attributed this incidence to maternal toxicity. The NOAEL for maternal toxicity was reported as 50 mg/kg bw/d (IUCLID, 2000; CIR, 1994).

In another study, 2 mL/kg of a permanent dye formulation containing 2 % of the hydrochloride salt was applied to the shaved skin of a group of female rats (Charles River CD) on GD 1 to 19. No significant changes in soft-tissue anomalies and skeletal variations compared to the control groups were observed. No significant differences in the mean number of corpora lutea, live foetuses or resorptions were reported. The same hair dye formulation was applied to the skin of groups of rats in a 2-generation reproductive toxicity study. There were no significant differences in fertility, gestation, survival, live births, or body weight gains compared to the control groups (CIR, 1994).

Other Health Effects

Neurotoxicity

The parent base at very high doses produced signs indicative of central nervous system (CNS) damage. Groups of female mice (n=50) were administered the chemical orally at 0, 5000 or 10000 ppm in diet for 91 weeks. Significantly reduced mean body weight gains and significantly increased mortalities compared to the control group were reported at both dose levels. Approximately 25 % of the low dose group and 40 % of the high dose group died with signs of CNS damage (details not reported) (CIR, 1994; NCI, 1978).

Risk Characterisation

Critical Health Effects

The critical health effect for risk characterisation include:

- local effect—skin sensitisation.

These chemicals may cause slight eye irritation. The potential for carcinogenicity is inconclusive.

Public Risk Characterisation

Although use in cosmetic products in Australia is not known, these chemicals are reported to be used in cosmetic products overseas. These chemicals are not on the 'List of chemicals used in permanent and semi-permanent hair dyes in Australia' (NICNAS, 2007).

The European Union has imposed restrictions and conditions for the use of these chemicals in cosmetics (hair dye preparations). The Cosmetic Ingredient Review (CIR) Expert Panel concluded that these chemicals are safe for use in hair dyes

at concentrations up to 1.7 % (as the free base) (CIR, 1994).

If these chemicals are included in cosmetic products containing N-nitrosating agents, carcinogenic N-nitrosamine compounds could be formed (SCCS, 2012 b).

Currently, there are no restrictions on using these chemicals in Australia. Although there is a group entry for 'Phenylenediamines and alkylated phenylenediamines' in Schedule 6 and Appendix C of the SUSMP, this group entry does not cover aryl N-substituted derivatives of phenylenediamines and their salts. In the absence of any regulatory controls, the characterised critical health effects (skin sensitisation) have the potential to pose an unreasonable risk for the uses identified.

Occupational Risk Characterisation

Given the critical health effects (skin sensitisation and acute toxicity), these chemicals may pose an unreasonable risk to workers unless adequate control measures to minimise exposure to the chemical are implemented. The chemicals should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine appropriate controls.

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 these chemicals in cosmetics and/or domestic products be managed through changes to poisons scheduling, and risks for workplace health and safety be managed through changes to classification and labelling.

Assessment of these chemicals is considered to be sufficient, provided that the recommended classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Public Health

It is recommended that the entries in Schedule 6 and Appendix C of the SUSMP for 'Phenylenediamines' be amended to include aryl N-substituted derivatives of phenylenediamines.

Work Health and Safety

The chemicals are 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	Harmful if swallowed (Xn; R22)	Harmful if swallowed - Cat. 4 (H302)
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 chemicals should be used according to label instructions.

Advice for industry

Control measures

Control measures to minimise the risk from oral, dermal and ocular exposure to the chemicals 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:

- 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 chemicals.

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 chemicals has not been undertaken as part of this assessment.

References

The Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)) 2013. Accessed January 2014 at **http://www.comlaw.gov.au/Details/F2013L01607/Download**

Chemicalland21.com Accessed January 2014 at **http://www.chemicalland21.com/specialtychem/finechem/4-AMINODIPHENYLAMINE.htm**

ChemIDPlus Advanced. Accessed January 2014 at **http://chem.sis.nlm.nih.gov/chemidplus/**

Cosmetic Ingredient Review (CIR) 1994. Final report on the safety assessment of N-phenyl-p-phenylenediamine, N-phenyl-p-phenylenediamine hydrochloride, and N-phenyl-p-phenylenediamine sulfate. Journal of the American College of Toxicology 13(5) pp. 374 - 394.

Cosmetics Directive (CosIng). N-phenyl-p-phenylenediamine (101-54-2). Accessed January 2014 at **http://ec.europa.eu/consumers/cosmetics/cosing/**

European Commission. IUCLID Dataset 2000 on N-(4-aminophenyl)aniline (101-54-2). Accessed January 2014 at **http://esis.jrc.ec.europa.eu/doc/IUCLID/data_sheets/101542.pdf**

Galleria Chemica. Accessed January 2014 at **http://jr.chemwatch.net/galleria/**

Hazardous Substances Data Bank (HSDB). National Library of Medicine. Accessed January 2014 at **http://toxnet.nlm.nih.gov**

National Cancer Institute (NCI) 1978. Bioassay of N-phenyl-p-phenylenediamine for possible carcinogenicity. Carcinogenesis Technical Report Series No.82 (NCI-CG-TR-82). U.S. Department of Health, Education, and Welfare.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) 2007. List of Chemicals used as Dyes in Permanent and Semi-Permanent Hair Dyes in Australia

OECD 2004. SIDS Initial Assessment Profile (SIAP) on 4-Aminodiphenylamine (101-54-2). Accessed January 2014 at **http://webnet.oecd.org/hpv/ui/handler.axd?id=ff9f4e92-614c-498a-b43e-d48566e264f2**

Personal Care Product Council (INCI Dictionary). Accessed January 2014 at **http://www.ctfagov.org/jsp/gov/GovHomePage.jsp**

REACH Dossier. N-phenyl-p-phenylenediamine (101-54-2). Accessed January 2014 at **http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances**

Safe Work Australia (SWA). Hazardous Substances Information System (HSIS). Accessed December 2013 at **http://hsis.safeworkaustralia.gov.au/HazardousSubstance**

Scientific Committee on Consumer Products (SCCP) December 2006. Opinion on N-phenyl-p-phenylenediamine (101-54-2). SCCP/0991/06. Accessed January 2014 at **http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_089.pd**

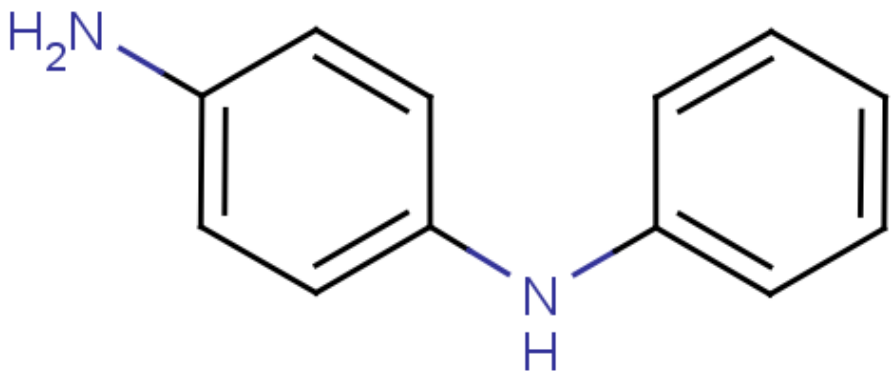
Scientific Committee on Consumer Safety (SCCS a) Opinion on oxidative hair dye substances and hydrogen peroxide used in products to colour eyelashes, 2012. Adopted on 12 October 2012. Accessed January 2014 at **http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_111.pdf**

Scientific Committee on Consumer Safety (SCCS b) Opinion on Nitrosamines and Secondary Amines in Cosmetic Products, 2012. Adopted at its 14th plenary meeting of 27 March 2012. Accessed December 2013 at **http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_090.pdf**

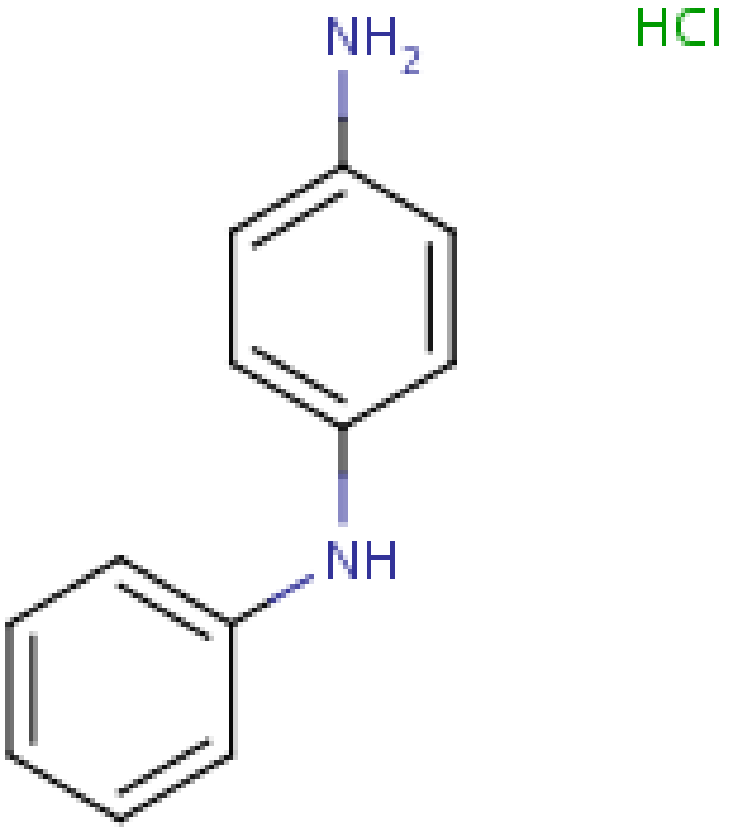
Last Update 07 February 2014

Chemical Identities

Chemical Name in the Inventory and Synonyms	**1,4-Benzenediamine, N-phenyl-** 4-aminodiphenylamine (4-ADPA) N-phenyl-p-phenylenediamine N-phenyl-1,4-phenylenediamine

	p-aminodiphenylamine N-(4-aminophenyl)aniline
CAS Number	101-54-2
Structural Formula	
Molecular Formula	C12H12N2
Molecular Weight	184.24

Chemical Name in the Inventory and Synonyms	**1,4-Benzenediamine, N-phenyl-, monohydrochloride** 4-aminodiphenylamine hydrochloride p-aminodiphenylamine hydrochloride N-phenyl-1,4-benzenediamine hydrochloride 1,4-benzenediamine, N-phenyl, hydrochloride CI76086
CAS Number	2198-59-6
Structural Formula	

	
Molecular Formula	C12H12N2.ClH
Molecular Weight	220.70

Share this page