1,4-Benzenediamine, 2-methyl-: Human health tier II assessment

22 November 2013

CAS Number: 95-70-5

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

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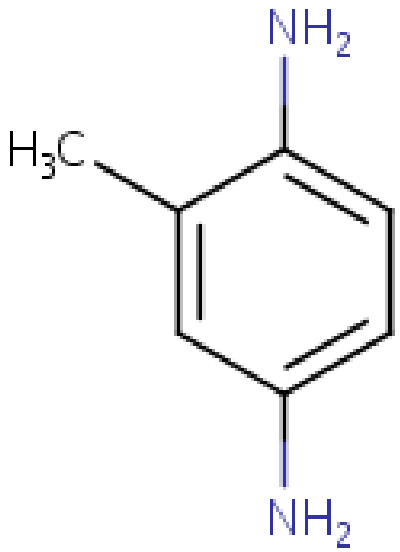
Acronyms & Abbreviations

Chemical Identity

Synonyms	toluene 2,5-diamine 1-methyl-2,5-diaminobenzene 2-methyl-p-phenylenediamine 4-amino-2-methylaniline 2-methyl-1,4-benzenediamine
Structural Formula	
Molecular Formula	C7H10N2
Molecular Weight (g/mol)	122.17
Appearance and Odour (where available)	Colourless, crystalline tablets
SMILES	c1(N)c(C)cc(N)cc1

Import, Manufacture and Use

Australian

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

The chemical has reported cosmetic use:

- in permanent hair dye preparations.

International

The following international uses have been identified through 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), and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported cosmetic use in:

- permanent hair dyes; and
- nail polish.

The chemical has reported site-limited use including:

- as an intermediate in the synthesis of dyes used for textile, paper, inks, biological stains and solvents.

Restrictions

Australian

This chemical is not listed in 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 include this chemical:

Schedule 6:

- 'TOLUENEDIAMINE not elsewhere specified in these Schedules:

(a) 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

(b) 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:

- 'TOLUENEDIAMINE 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):

- 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;
- EU Cosmetics Regulation 1223/2009 Annex III—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; R25 (acute toxicity)
- Xn; R20/21 (acute toxicity)

- R43 (sensitisation)

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

The chemical is reported to be used in the formulation of hair dyes in the form of its free base or its sulfate salt (2,5-TDS; CAS No. 615-50-9). Therefore, when data are lacking on the chemical, the available data on the sulfate salt of the chemical were used in this assessment. HSIS indicates similar hazard classifications for the chemical and its sulfate salt.

Toxicokinetics

Studies in rats, dogs and humans indicated that the chemical can be absorbed through the skin. The main route of excretion is via urine, as N,N-diacetyl-p-toluenediamine (N,N'-dpt) rather than as a free amine. Faecal excretion is also possible (HSDB).

The following are reported for 2,5-toluenediamine sulfate (2,5-TDS; CAS No. 615-50-9 (studies conducted according to OECD Test Guideline (TG) 417 or 427):

- The bioavailability in Kyoto rats was > 90% after oral administration and 2 % after dermal application. The main metabolite found in the urine and the faeces was N,N-diacetyl-toluene-2,5-diamine (SCCS a, 2012).
- The bioavailability in Sprague Dawley rats was 69 % after oral administration and 2 % after dermal application (SCCS a, 2012).

The free base form of the chemical may have higher dermal absorption, as 2,5-TDS is ionised and therefore likely to have lower dermal bioavailability than the neutral organic compound.

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.

Administration of the chemical as a single oral dose of 64, 100, 160 or 250 mg/kg bw in CFY rats established a median lethal dose (LD50) of 102 mg/kg bw. Reported sublethal effects include lethargy, piloerection (bristling of hairs), ataxia (lack of control over bodily movements) and increased salivation (SCCS a, 2012).

Dermal

The chemical is classified as hazardous with the risk phrase ‘Harmful in contact with skin’ (Xn; R21) in HSIS (Safe Work Australia). No data are available to support this classification. Although the calculated LD50 value provided below does not support classification of the chemical, this limited information alone is not sufficient to remove an existing classification.

Based on the oral LD50 of 102 mg/kg bw/d and the oral and dermal bioavailability of the sulfate form of the chemical (see **Toxicokinetics** section), the dermal LD50 was calculated as approximately 3519 mg/kg bw for rats (REACH). However, this is likely to underestimate the dermal toxicity of the chemical as, following dermal absorption, a chemical passes directly into systemic circulation, without first pass metabolism.

Inhalation

The chemical is classified as hazardous with the risk phrase 'Harmful by inhalation' (Xn; R20) in HSIS (Safe Work Australia). No data are available to support this classification. However, the calculated LC50 values provided below support the classification of the chemical for its inhalation toxicity.

Based on the oral LD50 of 102 mg/kg bw, oral bioavailability of 69 % (see **Toxicokinetics** section) and intravenous bioavailability of 100%, the median lethal concentration (LC50) was calculated as 0.99 mg/L in rats. Similarly, the LC50 for the sulfate form (2,5-TDS; CAS No. 615-50-9) was extrapolated as 1.77 mg/L (REACH). As for dermal toxicity, this may underestimate the true inhalation toxicity.

Corrosion / Irritation

Skin Irritation

No data are available on the chemical at 100 % concentration. Based on the data available at more dilute concentrations (50.6 % and 2.5 %) of the chemical, it is considered to be a slight skin irritant. The limited information available is not sufficient to warrant a hazard classification.

The chemical (0.5 mL of 50.6 % aqueous solution) was applied (semi-occlusive) to the skin of New Zealand White rabbits (n=3 males) for four hours (OECD TG 404). No ulceration, oedema or necrosis was recorded. Due to the black colouration of the skin after the treatment, it was not possible to observe any erythematous response (REACH; SCCS a, 2012).

In another study (following the Code of Federal Regulation (CFR) 1500.41), 0.5 mL of an aqueous solution containing 2.5% w/v of the chemical was applied (occlusive patch) to either intact or abraded skin of three New Zealand White rabbits for 24 hours. Immediately after the removal of the patch, slight erythema and slight oedema were seen in one animal; no signs of irritation were recorded after 72 hours. The chemical was found to be slightly irritating to the skin based on a primary irritation index (PII) calculated as 0.3 (REACH; SCCS a, 2012).

Eye Irritation

No data are available on the chemical at 100 % concentration. Based on the data available (at 50.6 % concentration), the chemical is considered to be an eye irritant to warrant a hazard classification.

The chemical (0.1 mL of 50.6 % aqueous solution, pH = 9.71) was instilled to the conjunctival sac of the left eye of a rabbit (OECD TG 405). Within 72 hours, the chemical induced marked conjunctival irritation with chemosis (mean score 3.7) and redness (mean score 3.0), slight iridial irritation (mean score 1.0) and moderate to slight corneal opacity (mean score 1.3). Effects were reversible within eight days. The chemical was found irritating to rabbit in this study but the high pH rather than the chemical itself could be the cause of irritation (REACH; SCCS a, 2012).

In another study (following CFR 16, 1500.42), 0.1 mL of an aqueous solution containing 2.5% w/v of the chemical (pH = 7) was applied into one eye of each New Zealand White rabbit (n=3) and rinsed after 10 seconds. Two rabbits exhibited a mild conjunctival irritation after one and three days (score 1). The chemical was slightly irritating to the eyes of rabbits (REACH; SCCS a, 2012).

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). No data are available on the chemical. The positive results shown in a guinea pig maximisation test and a local lymph node assay for the salts of the chemical support this classification.

A local nymph node assay (LLNA) was conducted on CBA mice (OECD TG 429) to test 2,5-toluenediamine sulfate (2,5-TDS; CAS No. 615-50-9) at the following concentrations: 0.5, 1.5 and 2.8%. The mean stimulation indices (SI) of 4.0, 10.4 and 19.4 were recorded respectively, indicating a positive response from the lowest dose. An estimated concentration needed to produce a stimulation index of three (EC3) was extrapolated as 0.31% from the results, showing that the test substance is a strong sensitiser under the conditions of the test (REACH; SCCS a, 2012).

A maximisation test (similar to OECD TG 406) was conducted in Hartley female guinea pigs using 0.1% of *p*-toluenediamine dihydrochloride (PTD). Using intradermal induction and topical induction (1 %), the chemical exhibited extreme sensitising potential in the challenge phase (5/6 positive responses at 0.01 % and 6/6 positive responses at 0.1 %). The challenge concentration of 0.001 % did not induce a positive result (0/6) (SCCS a, 2012).

Observation in humans

The chemical is a confirmed contact sensitiser in humans from both occupational and consumer exposure (SCCS, 2012).

The available data from diagnostic patch tests in patients with dermatitis indicate that the chemical is a strong contact allergen. The patients who are hairdressers showed the highest rate of allergy (16.8%), followed by patients exposed to cosmetics (9.5%) (SCCS, 2012 a). These results support the classification of the chemical as skin sensitiser.

Repeated Dose Toxicity

Oral

No data are available for the chemical. Based on the data available for 2,5-toluenediamine sulfate (2,5-TDS, CAS No. 615-50-9), the chemical is considered to cause serious damage to health from repeated oral exposure. Considering the low doses that produced severe adverse effects in rats, a hazard classification is warranted for the chemical.

The following studies are available for the analogue chemical 2,5-TDS (SCCS a, 2012):

- In a 90-day study (OECD TG 408) conducted in 1997, Sprague-Dawley (SD) rats (n=15/dose), received the test substance in deionised water at oral gavage doses of 0, 2.5, 5, 10 or 20 mg/kg bw/d. Increased aspartate aminotransferase (AST) levels from 5 mg/kg bw/d in females and increased incidence of abnormal-shaped pituitary glands at the highest dose were reported. A NOAEL of 2.5 mg/kg bw/d (or 1.4 mg/kg bw/d for free base) is reported. Further evaluation of the results of this study derived a NOAEL of 10 mg/kg bw/d, based on elevated AST levels and other pathological findings such as muscle degeneration in multiple organs (not indicated) at 20 mg/kg bw/d.
- Another 90-day study identical to the above study was performed (in 2010) in SD rats with a 28-day recovery period (n=5/sex/dose). There were no treatment-related changes in mortality, clinical signs, functional observational battery findings, haematology and urinalysis parameters. Increased AST levels at 20 mg/kg bw/d correlated with microscopic changes in the skeletal muscle (thigh, diaphragm, tongue and periocular muscle of the eye), but became comparable to controls at the end of the recovery period. A NOAEL of 10 mg/kg bw/d was established.
- In a 14-day study, SD rats (n=10/sex/dose) received oral gavage doses of 2,5-TDS (in deionised water) at 0, 7.5, 15, 30 or 60 mg/kg bw/d. There were no changes in the haematological parameters, but altered biochemistry parameters (AST, creatine phosphokinase (CPK), lactate dehydrogenase (LDH), alanine aminotransferase (ALT; only at the highest dose)) were observed in treated rats at and above 30 mg/kg bw/d. Increased liver weights (absolute and relative) were observed in males at 30 mg/kg bw/d and in both sexes at 60 mg/kg bw/d. Myocyte (a type of cell found in muscle tissues) degeneration was observed in the heart, skeletal muscle, tongue and diaphragm in all treated animals (SCCS a, 2012). Further reviews confirmed treatment-related myofiber necrosis, degeneration, and/or inflammatory changes in skeletal muscle, tongue, and diaphragm of both males and females at 30 or 60 mg/kg bw/d. A NOAEL of 15 mg/kg bw/d was suggested based on muscle degenerative changes.

The release of AST is reported to be closely related to myotoxicity. Therefore, the increased AST level in plasma in treated rats indicates the test substance as an inducer of myodegenerative changes (SCCS a, 2012).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on the limited data available for the chemical and data available for 2,5-TDS (CAS No. 615-50-9), the chemical is not considered to be genotoxic.

There are several in vitro and in vivo studies available for 2,5-TDS (listed below). It induced gene mutations in bacteria but not in mammalian cells in vitro. 2,5-TDS was negative in two in vivo mouse bone marrow micronucleus tests (with oral and i.p. administration), in an in vivo unscheduled DNA synthesis (UDS) test and in two dominant lethal assays. 2,5-TDS is considered to have no in vivo genotoxic potential (SCCS a, 2012).

The following in vitro studies are available for the chemical and its sulfate salt:

- bacterial gene mutation test (equivalent to OECD TG 471): the chemical at doses from 20 to 5000 µg/plate on *Salmonella typhimurium* strains TA1535, TA1537, TA 1538, TA98 and TA100, with or without metabolic activation induced positive responses from 400 µg/plate in all strains only with metabolic activation (REACH); when tested in TA1538 at a maximum dose of 100 µg/plate, the chemical also induced positive response with metabolic activation, and a 40-fold increase of its mutagenic activity was observed if mixed with hydrogen peroxide (Ames et al., 1975);
- bacterial gene mutation test (OECD TG 471) on 2,5-TDS: when tested at 3, 10, 33, 100, 333, 1000, 2500 or 5000 µg/plate on *S. typhimurium* strains TA1535, TA1537, TA98, TA100 and TA102 with or without metabolic activation, positive responses were rcorded for strains TA1535, TA1537, TA98 and TA100 only with metabolic activation (REACH; SCCS a, 2012);
- unscheduled DNA synthesis (UDS) test (conducted prior to OECD TG 486) on the chemical: primary hepatocytes from SD rats and Syrian golden hamsters exposed to 10^{-4}, 10^{-5}, 10^{-6} and 2 x 10^{-7} molar (M) concentrations induced a weak positive response (SCCS, 2012 a);
- mammalian cell gene mutation test (OECD TG 476) on 2,5-TDS: mouse lymphoma cells L5178Y exposed at 1-15 µg/mL without metabolic activation or 10-100 µg/mL with metabolic activation did not show any increase of mutant colonies (REACH; SCCS a, 2012); and
- chromosome aberration test (OECD TG 473) on 2,5-TDS: when tested on Chinese hamster lung fibroblasts (V79) at 2.5, 5 or 10 µg/mL without metabolic activation or at 200, 300 or 400 µg/mL with metabolic activation, 2,5-TDS increased the number of cells with chromosome aberrations

with or without metabolic activation (REACH; SCCS a, 2012).

The following in vivo studies are available for the chemical and its sulfate salt (SCCS a, 2012):

- mouse spot test (prior to OECD TG 484): the chemical administered intraperitoneally (i.p.) at 30 mg/kg bw to pregnant female mice on days 10 to 14 of gestation did not induce any significant increase of recessive spots in the offspring. The study did not report whether the applied dose induced toxic effects in the treated females to indicate compliance with the requirements of the currently valid TG.
- dominant lethal assay (non-guideline): the chemical was administered i.p. at 20 mg/kg bw to male Charles River rats (three times a week for eight weeks) which were then mated with female rats. The examination of live and dead foetuses, implantation and resorption sites did not show any differences from the controls. The chemical did not induce any dominant lethal mutations or chromosomal aberrations in germ cells.
- micronucleus tests (OECD TG 474) on 2,5-TDS: mice treated by i.p. (at 25, 50 or 90 mg/kg bw) or orally (at 15, 50 or 150 mg/kg bw) did not show any increase of micronuclei in bone marrow cells (REACH; SCCS a, 2012).

The SCCS (2012) only considered the first two in vivo studies as supporting information, as these were conducted prior to the implementaion of OECD TG and the test material used was unspecified in both studies (SCCS a, 2012).

Carcinogenicity

The limited data available are not sufficient to make a conclusion on the carcinogenic potential of the chemical. However, the chemical is not genotoxic compared to some other members of the toluenediamine group which are carcinogenic (e.g. 2,4-TDA).

The International Agency for Research on Cancer (IARC) has classified the chemical as ‘Not classifiable as to its carcinogenicity to humans’ (Group 3), based on inadequate evidence for carcinogenicity in humans and animal testing (IARC, 1978).

Hair dye formulations containing the chemical mixed with hydrogen peroxide have been tested topically in mice and rats (see details below). The negative results reported in these studies may have been due to the low sensitivity of the studies (SCCS a, 2012).

The chemical at 3 % concentration mixed with an equal amount of hydrogen peroxide was applied to the skin of Swiss Webster mice once a week (n=28/sex/dose) for two years (prior but similar to OECD TG 451). Both benign and malignant neoplasms developed in treated animals, but the incidence of these was not statistically significant (SCCS a, 2012).

In another two-year study (prior but similar to OECD TG 451), two formulations containing either 3 or 4 % of the chemical were equally mixed with hydrogen peroxide then applied to the shaved skin of SD rats (n=50/sex/dose) twice a week. The incidence of tumours was not significantly increased compared to controls (SCCS a, 2012).

The available data on 2,5-TDS (CAS No. 615-50-9) show inconclusive results in rats and mice following oral administration (NCI, 1978).

Reproductive and Developmental Toxicity

No data are available for the chemical. Based on the data available for 2,5-TDS (CAS No. 615-50-9), the chemical is not expected to have reproductive or developmental toxicity.

Reproductive toxicity of 2,5-TDS was investigated in a two-generation study in SD rats (OECD TG 416) with oral doses of 0, 5, 15 or 45 mg/kg bw/d (n=24/sex/dose). Examination of reproductive organs in parental generation (mammary gland, vulva, vagina, cervix, ovaries for females; and penis, testes, epididymes, prostate gland, and vesicular gland for males) did not show any effects related to treatment. Similarly, no treatment-related effect was noted for reproductive parameters such as the duration of gestation, gestation index and number of live/dead pups per litter in either P or F1 generation. No adverse effects were reported in pups of P and F1 generations. The NOAEL for reproductive toxicity was 45 mg/kg bw/d (SCCS a, 2012; REACH).

In a teratogenicity study (OECD TG 414), SD rats (n=23 mated females/dose) were orally administered 2,5-TDS at 0, 10, 50 or 80 mg/kg bw/d from day 6 to 15 of gestation. A reduction of body weight gain was noted at 50 and 80 mg/kg bw/d but was significant only at the highest dose. An increased post-implantation loss was recorded at 80 mg/kg bw/d. No significant effects on development of pups was recorded. NOAELs of 50 mg/kg bw/d for maternal toxicity and embryotoxicity and 80 mg/kg bw/d for teratogenicity were established (SCCS a, 2012; REACH).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include:

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

The chemical may also cause harmful health effects following repeated oral exposure.

Public Risk Characterisation

The chemical is reported to be used in permanent hair dye preparations in Australia. Apart from the use in hair dyes, use in nail polish is also indicated overseas.

Canada, New Zealand and the European Union have restricted the use of this chemical in cosmetics. In Australia, a chemical group (toluenediamine) including this chemical is listed on Schedule 6 and Appendix C of the SUSMP, with restrictions/prohibitions of its use in specific cosmetic products. The Schedule 6 entry in the SUSMP allows toluenediamines to be included in hair dye preparations and in eyelash and eyebrow tinting products with specific packaging and labelling requirements.

If this chemical is included in cosmetic products containing N-nitrosating agents, there is possibility to form carcinogenic N-nitrosamine compounds (SCCS b, 2012).

Considering the hazard properties of this chemical, it will cause unreasonable risks to consumers if used in hair dyes, eyelash and eyebrow tinting products and nail polish.

Occupational Risk Characterisation

Given the critical health effects (skin sensitisation, eye irritation, acute and repeat dose toxicity), the chemical may pose an unreasonable risk to workers unless adequate control measures to minimise exposure to the chemical are implemented. The data available support an amendment to the hazard classification in HSIS (refer to **Recommendation section**).

NICNAS Recommendation

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

Assessment of the chemical is considered to be sufficient provided that risk management recommendations are implemented and all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Public Health

At present, the chemical falls within the scope of the listing of ‘toluenediamine’ in Schedule 6 of the SUSMP for use in hair dye preparations and eyelash and eyebrow tinting products under specified conditions.

Only low systemic bioavailability of the chemical is expected through dermal exposure (2 %; refer to **Toxicokinetics section**). Therefore, potential consumer exposure to the chemical at low concentrations in hair dyes and nail polish may not cause unreasonable risk, when used under specified conditions. As hair dye preparations are already included in the 'toluenediamine' group entry in Schedule 6 of the SUSMP, it is proposed to also include nail polish use, with specified use 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)* Harmful in contact with skin (Xn; R21)* Harmful by inhalation (Xn; R20)*	Toxic if swallowed - Cat. 3 (H301) Harmful in contact with skin - Cat. 4 (H312) Harmful if inhaled - Cat. 4 (H332)
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)

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Repeat Dose Toxicity	Harmful: Danger of serious damage to health by prolonged exposure if swallowed (Xn; R48/22)	May cause damage to organs through prolonged or repeated exposure through the oral route - Cat. 2 (H373)

[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 instruction 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;
- 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.

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