Ortho-toluenediamines: Human health tier II assessment

01 May 2019

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
1,2-Benzenediamine, 4-methyl-	496-72-0
1,2-Benzenediamine, 3-methyl-	2687-25-4
1,2-Benzenediamine, 3(or 4)-methyl-	26966-75-6

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 ortho-toluenediamines (o-TDA) category consists of 1,2-benzenediamine, 4-methyl- (3,4-TDA; CAS No. 496-72-0), its structural isomer 1,2-benzenediamine, 3-methyl- (2,3-TDA; CAS No. 2687-25-4), and a commercially supplied mixture composed of 2,3-TDA and 3,4-TDA in a 40/60 ratio (2,3/3,4-TDA (40/60); CAS No. 26966-75-6).

These chemicals are structural isomers having similar physical-chemical properties and most likely similar health effects. Much of the available data relate to the commercial mixture, further supporting the assessment of these chemicals as a group.

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 the Organisation for Economic Cooperation and Development Screening information data set International Assessment Report (OECD SIAR); the European Union (EU) Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) dossier; Galleria Chemica; the Substances and Preparations in Nordic countries (SPIN) database; European Commission Cosmetic Ingredients and Substances (CosIng) database; the United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary; the OECD High Production Volume chemical program (OECD HPV); the US Environmental Protection Agency's Aggregated Computer

Toxicology Resource (ACToR); the US National Library of Medicine's Hazardous Substances Data Bank (HSDB); and World Health Organisation (WHO) Environmental Health Criteria Document (INCHEM, 1987).

The chemical 3,4-TDA has reported cosmetic use as a hair colourant.

The chemicals have reported domestic use as spirit varnishes, wood stains and pigments.

The chemicals have reported commercial uses including:

- in manufacture of polyurethane products;
- as epoxy curing agents; and
- in photographic developing.

The chemicals have reported site-limited uses including:

- as intermediates in the manufacture of corrosion inhibitors and rubber antioxidants; and
- as intermediates in the synthesis of dyes used for textiles, furs, leathers and biological stains.

Restrictions

Australian

The chemicals are not 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 Schedule 10/Appendix C of the SUSMP (2015) that includes the chemicals in this group:

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 described as 'Substances with a moderate potential for causing harm, the extent of which can be reduced through the use of distinctive packaging with strong warnings and safety directions on the label'. Schedule 6 chemicals are labelled with 'Poison' (SUSMP, 2015).

Schedule 10/Appendix C:

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

Schedule 10/Appendix C chemicals are described as 'Substances, other than those included in Schedule 9, of such danger to health as to warrant prohibition of sale, supply and use' (SUSMP, 2015).

International

The chemical 3,4-TDA is listed on the EU Cosmetics Directive 76/768/EEC Annex II—List of substances which must not form part of the composition of cosmetic products (CosIng).

Existing Worker Health and Safety Controls

Hazard Classification

None of the chemicals in this group are listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

The chemical 2,3-TDA has an occupational exposure limit value (OELV) of 2 mg/m^3 for an 8-hr exposure in Latvia (Galleria Chemica).

Health Hazard Information

Where the available information for 3,4-TDA and 2,3-TDA is limited, data for the commercial TDA mixture (2,3/3,4-TDA (40/60)) (OECD, 2007; REACHb) are used in this assessment in accordance with the Organisation for Economic Co-operation and Development (OECD) Guidance on grouping of chemicals (OECD, 2014). Additionally, data for 1,2-benzenediamine (*O*-phenylenediamine; CAS No. 95-54-5) (NICNASd; REACHa) and other diaminotoluenes (NICNASa; NICNASb; NICNASc) are used in the toxicokinetics, skin sensitisation, and carcinogenicity sections, where relevant, due to their close structural similarity and taking into account the mechanism of action compared with the other chemicals in this category.

Toxicokinetics

Toxicokinetics data are not available for the chemicals in this group.

The analogue 2,4-TDA is completely absorbed from the gastrointestinal tract in rats, and well absorbed through the skin of monkeys and humans (NICNASa). Similarly, 2,6-TDA is absorbed readily in the gastrointestinal tract (NICNASb) and 2,5-TDA is absorbed readily through the skin (NICNASc). These chemicals are mainly hydroxylated to form aminophenols, which then undergo N-acetylation. The elimination of the metabolites of 2,4-TDA, 2,5-TDA and 2,6-TDA is mainly through the urine, and to a lesser extent through faeces (NICNASa; NICNASb; NICNASc).

Acute Toxicity

Oral

The chemicals have moderate acute toxicity based on results from animal tests following oral exposure, and therefore warrant hazard classification. The median lethal dose (LD50) in rats is 660-812 mg/kg bw.

In an animal study similar to OECD Test Guideline (TG) 401, ten Wistar rats per group were administered the 2,3/3,4-TDA commercial mixture by oral gavage as single administrations at doses of 0, 400, 600, 640, 720, 760 or 800 mg/kg bw. Observed clinical effects included decreased locomotor activity, ptosis, piloerection and death. The LD50 in rats was reported as 660 mg/kg bw (OECD, 2007; REACHb).

In another animal study, five rats (sex and strain not reported) were treated with single administrations of 2,3-TDA by oral gavage at 0, 500, 1000, or 2000 mg/kg bw. All animals in the 2000 mg/kg bw dose group and four animals in the 1000 mg/kg bw dose group died. Observed clinical effects included ruffled fur and sluggish behaviour, while gross necropsy showed congestion in the lungs and abdomen, mottled livers and other effects on the stomach and intestines. The LD50 was reported as 812 mg/kg bw (OECD, 2007; REACHb).

Dermal

The chemicals have low to moderate acute toxicity based on inconsistent results from animal tests following dermal exposure. The LD50 in rabbits is in the range of 1120 to >5750 mg/kg bw.

In a study conducted on groups of four male New Zealand White rabbits, 1.0, 3.0, 5.0 or 9.2 mL/kg doses of the 2,3/3,4-TDA commercial mixture (40/60) were applied for 24 hours. The test chemical was diluted in water in a 5:3 ratio by weight. Observations were made for 14 days post treatment. No treatment-related toxicity or mortality was seen in any of the treatment groups. The LD50 was >9.2 mL/kg (equivalent to >5750 mg/kg bw) (OECD, 2007; REACHb).

In another study, the 2,3/3,4-TDA commercial mixture (40/60) was applied occlusively to groups of four rabbits (strains and sex not reported) at doses of 0.5, 1.0 or 2.0 g/kg bw for 24 hours. One animal in the low dose group, one animal in the mid dose group, and all animals in the high dose group died. Necropsy examination showed congestion in the lungs and abdominal viscera, pale or/and mottled livers with prominent acini and pale or/and mottled kidneys. The LD50 was 1.12 g/kg bw (equivalent to 1120 mg/kg bw) (OECD, 2007; REACHb).

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

The chemicals are slightly irritating to the skin in animal studies. The effects are not sufficient to warrant hazard classification.

In a skin irritation study, 0.5 mL of undiluted 2,3/3,4-TDA mixture (40/60) was applied occlusively to the skin of six albino New Zealand White rabbits for 24 hours. Observations were made at 24 and 72 hours post treatment. Slight oedema seen at 24 hours and none to slight oedema was observed at 72 hours. The primary dermal irritation index was 1.25 (OECD, 2007; REACHb).

In a study conducted similarly to OECD TG 404 with some deviations, the 2,3/3,4-TDA mixture (40/60) was applied to the skin of ten Dunkin Hartley guinea pigs under occlusive conditions for 48 hours at 0.1, 0.2, 0.5, 1, 2, 5 or

10 % concentrations. Irritation reactions were seen in 3 animals at 10 % concentration while no irritation was observed in animals treated with 5 % or less of the chemical mixture (REACHb).

Eye Irritation

The chemicals are slightly irritating to the eye in animal studies using the diluted chemical. The effects were not sufficient to warrant a hazard classification.

In an eye irritation study, 0.1 mL of a 5 % aqueous solution of the 2,3/3,4-TDA mixture (40/60) was instilled in the eyes of six albino New Zealand White rabbits as a single application. The eyes were not rinsed post-treatment. Observations were made up to seven days post-instillation. Slight conjunctival redness was observed in all animals at 2, 24 and 48 hours, but was reversed at 72 hours. Slight reddening of the iris was seen in two animals at 24 hours, but was fully reversed at 72 hours (OECD, 2007; REACHb).

Sensitisation

Skin Sensitisation

Based on the available animal and human data, the chemicals are considered to be skin sensitisers, warranting hazard classification.

The 2,3/3,4-TDA mixture (40/60) was sensitising in a test in Dunkin Hartley guinea pigs (10 animals/dose) at 1 % (induction dose) and 0.1% or 1 % (challenge dose) via epicutaneous exposure. All 10 animals in the 1% challenge dose group had positive responses. Nine animals in the 0.1 % challenge dose group showed positive responses (REACHb).

The International Programme on Chemical Safety (IPCS) indicated that dermal contact with diaminotoluenes caused possible skin sensitisation (INCHEM, 1987). No other details were provided.

The analogue chemicals, *o*-phenylenediamine, 2,4-TDA, 2,5-TDA, and 2,6-TDA are classified as hazardous with the risk phrase 'May cause sensitisation by skin contact' (R43) in HSIS (Safe Work Australia). Hazard classification for skin sensitisation is considered appropriate for the chemicals in this group, based on both read across and the available human and animal data.

Observation in humans

The positive skin sensitisation data from animal studies are supported by the human cohort study in 51 workers from a pharmaceutical company. The 2,3/3,4-TDA mixture (40/60) was positive for skin sensitisation in 29 patients with dermatitis (REACHb).

Repeated Dose Toxicity

Oral

Based on the available data, histopathological changes in the liver are seen at high doses. The effects are not sufficient to warrant hazard classification.

In a repeated dose oral toxicity study conducted according to OECD TG 407, Wistar rats (five animals/sex/dose) were administered the mixed chemicals (2,3/3,4-TDA (40/60) at doses of 0, 10, 50 or 250 mg/kg bw/day for 28 days by gavage. No mortalities were reported. Clinical signs observed during the treatment were half-closed eyelids in all animals of the 250 mg/kg bw/day dose group. Two males and three females showed piloerection after treatment between days 7 and 26 at 250 mg/kg bw/day. Salivation was seen on all animals of the high dose group on several treatment days and in four females in the 50 mg/kg bw/day dose group between days 20 and 28. No changes in the food consumption were seen in any dose groups. Significant decrease in the body weights and significant increases in the relative liver weights of the high dose males (250 mg/kg bw/day) were observed. Statistically significant decreases in relative thymus weights without any correlating histopathology were observed in all the animals at the 250 mg/kg bw/day dose group. The NOAEL was 50 mg/kg bw/day (REACHb).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on the available data, the chemicals in this group are mutagenic, warranting hazard classification. Both in vitro and in vivo assays gave positive results.

In vitro studies

In a bacterial gene mutation test, 3,4-TDA was tested in *Salmonella typhimurium* strains TA 97, TA 98, TA 100, TA 1535, TA 1537, and TA 1538, with and without metabolic activation up to 10,000 µg/plate. The chemical gave positive results for all strains tested with and without metabolic activation. The chemical was negative for genotoxicity in a bacterial gene mutation test in *S. typhimurium* strains TA98, TA100, TA1535 and TA1537 at a dose of 3 µmol/plate (approximately 400 µg/plate), with and without metabolic activation (OECD, 2007; HSDB).

In a mammalian cell gene mutation test, mouse lymphoma L5178Y cells were treated with 3,4-TDA at up to 150 µg/mL in Aroclor 1254-induced rat liver S9 cultures and with 0.239-37.5 µg/mL of 3,4-TDA without metabolic activation. Significantly greater frequencies of mutations were observed in the treated groups compared to controls both with and without activation (OECD, 2007; HSDB).

In a gene mutation assay in Chinese hamster ovary (CHO) cells with and without Aroclor-induced rat liver metabolic activation, 3,4-TDA was tested at concentrations up to 500 µg/mL in non-activated cultures, and up to

1000 µg/mL in the activated cultures. Significantly greater frequencies of mutations were observed in the treated groups compared to the negative controls both with and without activation (OECD, 2007; HSDB).

The chemical 3,4-TDA was reported to be weakly active in three different cell transformation assays in hamster embryo cells (OECD, 2007, HSDB).

In vivo studies

In a micronucleus test conducted according to OECD TG 474 in groups of five male NMRI mice, the 2,3/3,4-TDA commercial mixture (40/60) was administered to the mice at 0, 75, 150 or 300 mg/kg bw twice (split dose), 24 hours apart, by intraperitoneal (i.p.) injections. Analyses of 2000 polychromatic erythrocytes from bone marrow of each animal were conducted. Treatment-related adverse effects seen in the treated males included apathy, roughened fur, loss of weight, sternal recumbency, spasm, difficulty in breathing, slitted eyes and closed eyes. No mortality was reported. No alterations in the ratio of polychromatic to normochromatic erythrocytes were seen in any dose groups. The clastogenic effect of the chemical mixture was seen at 300 mg/kg, when biologically important and statistically significant variation was noted in the incidence of micronucleated polychromatic erythrocytes (PCEs) (OECD, 2007).

In another micronucleus test in NMRI mice, 3,4-TDA was tested at concentrations 122, 244 or 366 mg/kg bw by i.p. injections given as two equal doses separated by a 24 hour interval. Bone marrow cells were isolated six hours after the second dose and 1000 polychromatic erythrocytes from each animal were analysed. Significant increases in the incidences of micronucleated PCEs were reported at doses of 244 mg/kg bw and above (OECD, 2007).

In two different unscheduled DNA synthesis studies, male Charles River C57B1/6 X C3H mice were given 3,4-TDA at 500 mg/kg i.p as a single dose for the first study or 200, 229, 262 or 300 mg/kg bw i.p. as a single dose for the second study. The chemical was positive for genotoxicity in both the studies (OECD, 2007, HSDB).

Carcinogenicity

The International Agency for Research on Cancer (IARC, 1987) has classified mixed diaminotoluenes as ‘Probably carcinogenic to humans’ (Group 2B), based on inadequate evidence for carcinogenicity in humans, but sufficient evidence for carcinogenicity in animal testing for 2,4-diaminotoluene isomer (NICNASa). Mixed diaminotoluene (DAT), as identified by the US EPA in 1988,

was included in the Proposition 65 of California's Environmental Protection Agency's Office of Environmental Health Hazard Assessment (OEHHA) with a current classification for the group of mixed diaminotoluenes of probable human carcinogen - Group B2– based on the evidence on carcinogenic properties of the 2,4-diaminotoluene only. No data for other DAT isomers were included (OEHHA, 2015).

The chemicals in this group do not contain 2,4-TDA.

No carcinogenicity data are available for the chemicals in this group. Data for 3,4-TDA and the commercial 2,3/3,4-TDA mixture (40/60) indicate that the chemicals are genotoxic. The known carcinogen 2,4-TDA (NICNASa) induces its own activation through binding to the cytosolic aromatic hydrocarbon receptor (AhR) involved in gene transcription mechanisms to induce CYP1A1 (NICNASb). Among the chemicals in this group, only 2,3-TDA has a similar CYP1A1 induction mechanism to 2,4-TDA (OECD, 2007). In contrast to 2,4-TDA, 2,6-TDA is genotoxic but does not bind to DNA to form adducts, in contrast to 2,4-TDA (NICNASa; NICNASb).

Based on the available data from the close structural similarities of the chemicals in this group to 2,4-TDA and 2,6-TDA, and CYP1A1 induction mechanism, the chemicals may have carcinogenic potential. However, in the absence of sufficient data for these chemicals, hazard classification is not warranted.

Reproductive and Developmental Toxicity

The chemicals do not show specific reproductive or developmental toxicity. Any reproductive and developmental effects were only observed secondary to maternal toxicity.

In a reproductive toxicity study conducted according to OECD TG 421, 3,4-TDA was administered to Wistar rats (10 animals/sex/dose) in drinking water at 0, 10, 50 or 250 mg/kg bw/day once daily. The treatment duration was two weeks in the premating and mating period in both males and females and one week post mating in males. Females were treated throughout the gestation period and continued up to lactation day 4. No mortalities were reported in the parental animals. Reduced activity, salivation, piloerection and half-closed eyelids were clinical signs observed in all males of the 250 mg/kg bw/day and one male in the 50 mg/kg bw/day dose group. Five females in the

250 mg/kg bw/day dose group had half-closed eyelids and salivation in the premating phase and reduced activity and discoloured faeces were seen in four females during the gestation phase. All females of the 50 mg/kg bw/day showed salivation during premating, gestation and lactation phases. Males and females in the 10 mg/kg bw/day dose group showed no treatment-related effects. Significant increases in the mean absolute testes weight were seen in males of all treated groups. Males in the 10 and 250 mg/kg bw/day showed an significant increase in the mean relative testes and epididymis weight, but no significant increase was seen in the animals of the

50 mg/kg bw/day group. Males in the 250 mg/kg bw/day dose group showed significant decrease in the total spermatids. Sperm motility was significantly reduced in the 50 mg/kg bw/day and 250 mg/kg bw/day dose groups. Histopathological examination did not show any corelated effect with the changes in the testes and epididymis weights. A significant increase in the post implantation loss and significant decrease in the number of delivered pups were observed at 250 mg/kg bw/day. A NOAEL of 50 mg/kg bw/day and a LOAEL of 250 mg/kg bw/day were reported for both parental and developmental toxicity (REACHb).

In a developmental toxicity study, groups of 20 female Sprague Dawley rats were treated with 2,3/3,4-TDA (40/60) in corn oil by oral gavage at doses of 0, 10, 30, 100 or 300 mg/kg bw/day on days six to 15 of gestation. All animals were sacrificed on day 20 of gestation. Significantly reduced maternal body weights and body weight gain were seen in the dams of the high dose group at 300 mg/kg bw/day. At 300 mg/kg bw/day, foetal body weights were also significantly reduced with a significant increase in the number of incompletely ossified vertebrae at 100 and 300 mg/kg bw/day. Increased incidence of missing sternebrae and incomplete skull closure was also noted in foetuses at 300 mg/kg bw/day. Treatment at 10, 30 and 300 mg/kg bw/day increased the occurrence of haemorrhagic abdomens. It was concluded that the foetal effects could be secondary to maternal toxicity. The NOAEL for maternal toxicity was reported to be 100 mg/kg bw/day and the NOAEL for developmental toxicity was 30 mg/kg bw/day (OECD, 2007; REACHb).

In another developmental toxicity study, Dutch-belted rabbits (groups of 15 females) were administered 2,3/3,4-TDA (40/60) at doses of 0, 3, 10, 30 or 100 mg/kg bw/day by gavage on gestation days 6 to 18. Clinical signs observed at 100 mg/kg bw/day were swollen, red or pink eyelids and significantly reduced body weights and body weight gains in maternal animals. Significant decreases in the percentage of dams with resorbed litters, reduced foetal weights and foetal survival were observed at 100

mg/kg bw/day. A NOAEL of 100 mg/kg bw/day for maternal toxicity and a NOAEL of 30 mg/kg bw/day for developmental toxicity were reported (OECD, 2007; REACHb).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects (mutagenicity), systemic acute effects including acute toxicity from oral exposure and local effects (sensitisation). Available data are insufficient to determine the carcinogenic potential of these chemicals.

Public Risk Characterisation

Although use in cosmetic products in Australia is not known, these chemicals are reported to be used in hair dye products overseas.

The European Union has restricted the use of these chemicals in cosmetics. In Australia, a chemical group (toluenediamines) including these chemicals is listed on Schedule 6 and Schedule 10/Appendix C of the SUSMP, with restriction/prohibition of their use in 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 requirements. The SUSMP controls are appropriate for sensitising hair dye ingredients and were recently reconfirmed for 2,6-TDA.

Occupational Risk Characterisation

During product formulation, exposure may occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical systemic long-term and systemic acute health effects, the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise exposure are implemented. These 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 the appropriate controls.

NICNAS Recommendation

Further risk management is required. Sufficient information is available to recommend that risks for workplace health and safety be managed through changes to classification and labelling.

Assessment of the chemicals 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 chemicals fall within the scope of the listing for toluenediamines in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) for use in hair dye preparations, in eyelash and eyebrow tinting products under specified conditions. Considering the serious health effects possible from exposure to these chemicals (i.e. skin sensitisation,

genotoxicity and reproductive toxicity), it is recommended that the chemicals be excluded from this group entry in Schedule 6 of the SUSMP. A separate Schedule 10/Appendix C entry is recommended to prohibit their use in hair dye preparations and in eyelash and eyebrow tinting products.

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 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)
Genotoxicity	Muta. Cat 3 - Possible risk of irreversible effects (Xn; R68)	Suspected of causing genetic defects - Cat. 2 (H341)

[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 industry

Control measures

Control measures to minimise the risk from oral and dermal 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 chemicals are used. Examples of control measures which could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- health monitoring for any worker who is at risk of exposure to the chemicals, if valid techniques are available to monitor the effect on the worker's health;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

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

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective

equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

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

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

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

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

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

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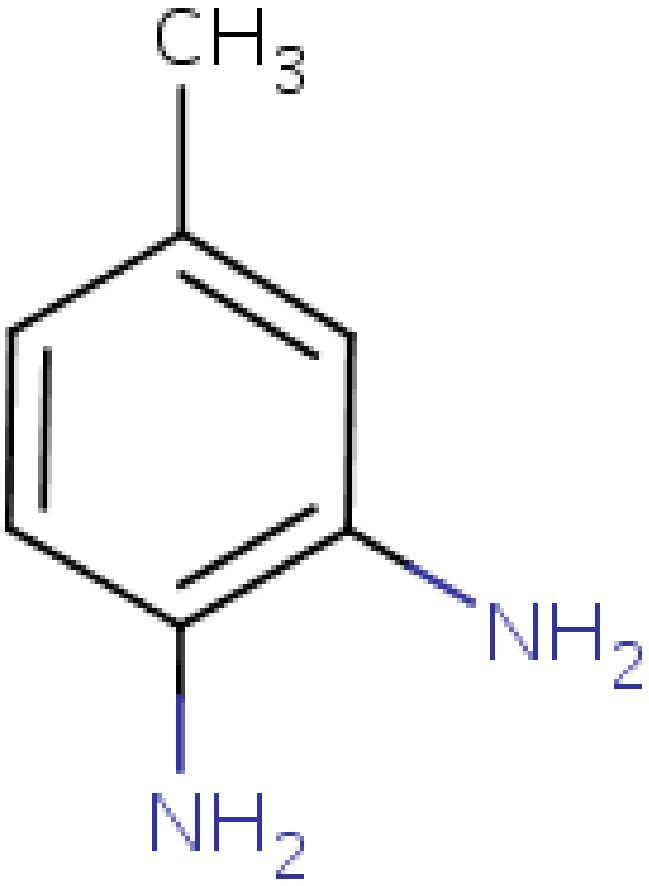
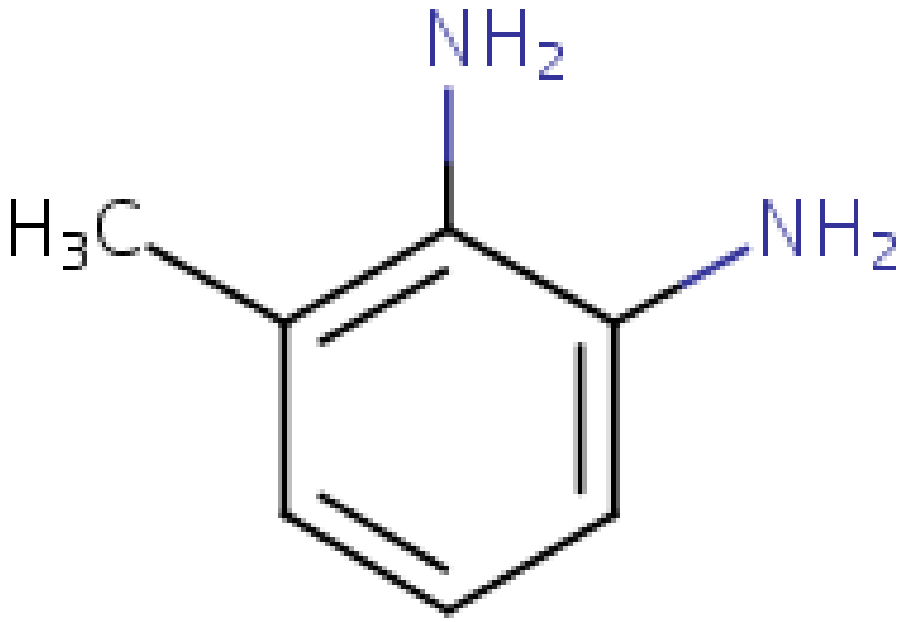
Last Update 01 May 2019

Chemical Identities

Chemical Name in the Inventory and Synonyms	**1,2-Benzenediamine, 4-methyl-** 1,2-diamino-4-methylbenzene toluene-3,4-diamine 4-methyl-1,2-phenylenediamine 3,4-TDA
CAS Number	496-72-0
Structural Formula	

	
Molecular Formula	C7H10N2
Molecular Weight	122.1

Chemical Name in the Inventory and Synonyms	**1,2-Benzenediamine, 3-methyl-** toluene-2,3-diamine 3-methyl-o-phenylenediamine 2,3-TDA
CAS Number	2687-25-4
Structural Formula	

	
Molecular Formula	C7H10N2
Molecular Weight	122.1

Chemical Name in the Inventory and Synonyms	**1,2-Benzenediamine, 3(or 4)-methyl-**
CAS Number	26966-75-6
Structural Formula	**No Structural Diagram Available**

Molecular Formula	C7H10N2
Molecular Weight	NA

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