1,3-Benzenediamine, 4-methyl-, sulfate (1:1): Human health tier II assessment

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CAS Number: 65321-67-7

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Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted



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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

NICNAS has made every effort to assure the quality of information available in this report. However, before relying on it for a specific purpose, users should obtain advice relevant to their particular circumstances. This report has been prepared by NICNAS using a range of sources, including information from databases maintained by third parties, which include data supplied by industry. NICNAS has not verified and cannot guarantee the correctness of all information obtained from those databases. Reproduction or further distribution of this information may be subject to copyright protection. Use of this information without obtaining the permission from the owner(s) of the respective information might violate the rights of the owner. NICNAS does not take any responsibility whatsoever for any copyright or other infringements that may be caused by using this information.

Acronyms & Abbreviations

Chemical Identity

Synonyms	toluene-2,4-diammonium sulfate 4-methyl-m-phenylenediamine sulfate 2,4-diaminotoluene sulfate 4-methylbenzene-1,3-diaminium sulfate	
Structural Formula	$+H_3N$ NH_3^+ O	
Molecular Formula	C7H10N2.H2O4S	
Molecular Weight (g/mol)	220.25	
Appearance and Odour (where available)	Not available.	
SMILES	c1(C)c(N{+}.O{-}S(=O)(=O)O{-})cc(N{+})cc1	

Import, Manufacture and Use

Australian

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

International

The following international use has been identified through the Chemical Abstracts Service database of the American Chemical Society (Scifinder).

The chemical has reported cosmetic use in hair dye formulations.

Restrictions

Australian

The 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 includes 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 dangerous enough 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 II Part 1: List of substances which must not form part of the composition of cosmetic products;
- European Union (EU) Cosmetics Regulation 1223/2009 Annex II—List of substances prohibited in cosmetic products;
- New Zealand Cosmetic Products Group Standard—Schedule 4: Components cosmetic products must not contain—Table 1 (4-Methyl-m-phenylenediamine and its salts);
- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient 'Hotlist') (4-Methyl-mphenylenediamine (toluene-2.4-diamine) and its salts); and
- Thailand Cosmetic Act—Prohibited Substances (4-Methyl-m-phenylenediamine and its salts).

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; R21 (acute toxicity)
- Xi; R36 (irritation)
- Xi; R43 (sensitisation)
- Carc. Cat. 2; R45 (carcinogenicity)

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are identified.

Health Hazard Information

Limited data are available for the health hazard assessment for this chemical. The chemical, 1,3-Benzenediamine, 4-methyl-, sulfate (1:1) (salt) is formed by treatment of 1,3-benzenediamine, 4-methyl- (CAS No. 95-80-7) with one molecule of sulfuric acid. In solution, this salt dissociates to form protonated 1,3-benzenediamine, 4 methyl-, which is expected to have similar systemic toxicity to the parent base (CAS No. 95-80-7). Therefore, in the absence of toxicological data for this chemical (salt), the relevant data from the parent chemical are used according to read-across principles (OECD, 2007) to assess the potential risk of exposure to the chemical.

The parent base, 1,3-benzenediamine, 4-methyl- (CAS No. 95-80-7) has been assessed as an Inventory Multi-tiered Assessment and Prioritisation (IMAP) Tier II assessment and health hazards identified. These include acute toxicity,

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sensitisation, repeated dose toxicity, genotoxicity, carcinogenicity and reproductive toxicity. Details can be found in the IMAP assessment of the parent base (NICNAS b).

In addition to health hazards identified for the parent chemical, 1,3-benzenediamine, 4-methyl-, sulfate (1:1) is currently classified as an eye irritant. In the absence of data to evaluate this classification, an amendment to the classification is not proposed.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include:

- systemic long-term effects—carcinogenicity, genotoxicity and reproductive toxicity;
- systemic acute effects—acute toxicity from oral and dermal exposure; and
- Iocal effects—skin sensitisation and eye irritation.

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

Public Risk Characterisation

Although use of the chemical in Australia is not known, it is reported to be used in hair dye formulations overseas (Scifinder). The chemical is not on the 'List of chemicals used in permanent and semi-permanent hair dyes in Australia' (NICNAS a).

Many countries such as Canada, New Zealand, Thailand and ASEAN countries have prohibited the use of this chemical in cosmetics. In Australia, a chemical group (toluenediamines), which includes this chemical, is listed on Schedule 6 and Appendix C of the SUSMP, with restriction/prohibition of its use in specific cosmetics 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.

While there is no identified use of this chemical in Australia based on voluntary surveys, should the chemical be used for hair dying and eyelash and eyebrow tinting, it will cause unreasonable risks to consumers based on the identified hazards of the chemical. NICNAS has recommended changes to the SUSMP entry for the parent base, and these changes should also apply to this salt.

Occupational Risk Characterisation

Given the critical health effects (systemic long-term effects, systemic acute effects and local effects), 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 dye and eyebrow/eyelash tinting products be managed through changes to poisons scheduling, and risks for workplace health and safety be managed through 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 toluenediamines in Schedule 6 of the SUSMP for use in hair dye preparations and in eyelash and eyebrow tinting products under specified conditions. Considering the severe health effects possible from exposure to this chemical (i.e. carcinogenicity, genotoxicity, fertility effects and skin sensitisation) and considering that this chemical is the salt of the parent chemical (1,3-benzenediamine, 4-methyl- (CAS No. 95-80-7)) it is recommended that this chemical be controlled, together with the parent chemical (refer NICNAS b).

For the parent chemical, it was recommended that it be excluded from the toluenediamine group entry in Schedule 6 of the SUSMP, and a separate Appendix C entry was recommended to prohibit the use of this chemical in hair dye preparations and in eyelash and eyebrow tinting products.

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)*	Toxic if swallowed - Cat. 3 (H301) Harmful in contact with skin - Cat. 4 (H312)
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)
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 - Cat. 2 (H373)
Genotoxicity	Muta. Cat 3 - Possible risk of irreversible effects (Xn; R68)	Suspected of causing genetic defects - Cat. 2 (H341)
Carcinogenicity	Carc. Cat 2 - May cause cancer (T; R45)*	May cause cancer - Cat. 1B (H350)
Reproductive and Developmental Toxicity	Repro. Cat 3 - Possible risk of impaired fertility (Xn; R62)	Suspected of damaging fertility - Cat. 2 (H361f)

^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, dermal and ocular exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures which 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.

References

Approved Criteria for Classifying Hazardous Substances [NOHSC: 1008(2004)] Third edition. Accessed October 2013 at http://www.safeworkaustralia.gov.au/sites/swa/about/publications/pages/ns2004criteriaforclassifyinghazardous

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