Phenol, 4-amino-, hydrochloride: Human health tier II assessment

30 June 2017

CAS Number: 51-78-5

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.

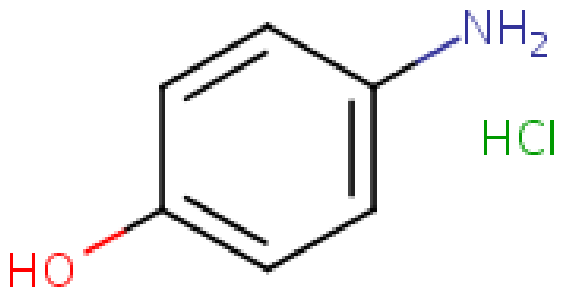
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	4-amino-1-hydroxybenzene, hydrochloride p-aminophenol, hydrochloride p-hydroxyaniline, hydrochloride 4-hydroxyanilinium chloride CI 76551
Structural Formula	
Molecular Formula	C6H7NO.ClH
Molecular Weight (g/mol)	145.59
Appearance and Odour (where available)	Crystalline powder
SMILES	c1(O)ccc(N{+}.Cl{-})cc1

Import, Manufacture and Use

Australian

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

The chemical is not listed on the 'List of chemicals used as hair dyes in permanent and semi-permanent hair dyes in Australia' (NICNAS, 2007). However, the free base parent chemical, p-aminophenol (CAS No. 123-30-8), is listed with use in permanent hair dye preparations.

International

The following international uses have been identified through the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers; Galleria Chemica; the Hazardous Substance Data Bank (HSDB); the European Commission Cosmetic Ingredients and Substances (CosIng) database.

The chemical has reported cosmetic use in permanent hair dyes.

The chemical has reported commercial use as a photographic developer.

Restrictions

Australian

The free base of the chemical, p-aminophenol (CAS No. 123-30-8), is listed in the *Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) in Schedule 6 (SUSMP, 2017). This covers all derivatives, including the hydrochloride salt.

Schedule 6:

'p-aminophenol except when used in hair dye and eyebrow/eyelash colouring products at a concentration of 1 per cent or less of p-aminophenol after mixing for use when the immediate container and primary pack are labelled with the following statements:

(a) KEEP OUT OF REACH OF CHILDREN; and

(b) WARNING - This product contains ingredients which may cause skin sensitisation to certain individuals. 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, 2017).

International

No known restrictions have been identified for the chemical.

The free base parent chemical, p-aminophenol (CAS No. 123-30-8), is subject to restrictions described in the European Union (EU) Regulation Annex III (EC No. 1197/2013). The maximum concentration of the free base chemical that can be applied to hair must not exceed 0.9 % after mixing under oxidative conditions (CosIng).

Existing Work Health and Safety Controls

Hazard Classification

The chemical is not listed on the Hazardous Chemical Information System (HCIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

No specific toxicity data are available for the chemical.

The chemical is the hydrochloride salt of the free base parent chemical, p-aminophenol (CAS No. 123-30-8). The health hazard information of the parent chemical is considered relevant to this assessment (NICNASa).

The parent chemical is considered hazardous for acute toxicity, sensitisation, genotoxicity and repeat dose toxicity. The available data supported most of the existing hazard classifications, including evidence of genotoxicity and acute oral toxicity. Further classifications (skin sensitisation) and regulatory controls were also recommended—such as the inclusion in any IMAP Tier III assessment that may be conducted regarding azo dyes in textiles. These data and recommendations are considered relevant to the hydrochloride salt of p-aminophenol (see **Recommendation** section).

The Tier II assessment for the parent chemical is available at: https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-assessment-details?assessment_id=1666. The report should be read in conjunction with this Tier II assessment.

Risk Characterisation

Critical Health Effects

Based on the information for the free base parent chemical, p-aminophenol (CAS No. 123-30-8), the critical health effects for the risk characterisation include:

- systemic long-term effects (mutagenicity);
- systemic acute effects (acute toxicity from oral and inhalation exposure); and
- local effects (skin sensitisation).

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

Public Risk Characterisation

The free base parent chemical is reported to be used in permanent hair dyes in Australia. The EU has restricted the use of the free base parent chemical in hair dyes (maximum concentration applied to hair should not exceed 0.9 % after mixing under oxidative conditions).

If the free base parent chemical or its derivatives (including salts) is included in cosmetic products containing N-nitrosating agents, carcinogenic N-nitrosamine compounds could be formed (SCCS, 2012).

The free base parent chemical, p-aminophenol (CAS No. 123-30-8), is scheduled to restrict its use in hair dyes and eyebrow/eyelash colouring products. It is listed in Schedule 6 (see **Restrictions** section). This entry covers all derivatives, including salts.

Internationally, the free base parent chemical is also used in textile dyes or as an intermediate to manufacture dyes used in textiles. The public could be exposed to the chemical as an impurity in, or through release of the chemical from dyes manufactured using the chemical, by:

- dermal contact with the chemical from prolonged exposure to articles of clothing and leather goods containing the dye; and
- oral exposure through young children sucking articles and textiles containing the dye.

The risk to the public from oral and dermal exposure to the free base parent chemical and its derivatives from use in textile dyes will be considered in subsequent IMAP assessments of dye and pigment chemicals.

Occupational Risk Characterisation

During product formulation, oral, dermal and inhalation 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 health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise exposure are implemented. The chemical 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.

The data available matches the hazard classification in the HCIS (Safe Work Australia) (see **Recommendation** section).

NICNAS Recommendation

Assessment of the chemical is considered to be sufficient, provided that the recommended amendment to the 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.

This chemical is also recommended to be included in any IMAP Tier III assessment of 'Azo dyes that cleave to aromatic amines of potential toxicological concern' (NICNASb).

Regulatory Control

Public Health

Products containing the chemical should be labelled in accordance with state and territory legislation (SUSMP, 2017).

For use in textile dyes, further regulatory controls for public health may be determined as part of a Tier III assessment for 'Azo dyes that cleave to aromatic amines of potential toxicological concern' (NICNASb).

Work Health and Safety

The chemical is recommended for classification and labelling aligned with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below. This does not consider classification of physical hazards and environmental hazards.

From 1 January 2017, under the model Work Health and Safety Regulations, chemicals are no longer to be classified under the Approved Criteria for Classifying Hazardous Substances system.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Not Applicable	Harmful if swallowed - Cat. 4 (H302) Harmful if inhaled - Cat. 4 (H332)
Sensitisation	Not Applicable	May cause an allergic skin reaction - Cat. 1 (H317)
Repeat Dose Toxicity	Not Applicable	May cause damage to organs through prolonged or repeated exposure through the oral route - Cat. 2 (H373)
Genotoxicity	Not Applicable	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 consumers

Products containing this chemical should be used in according to the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from oral, dermal 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 that could 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 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 chemical has not been undertaken as part of this assessment.

References

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