p-Methylaminophenol and its sulfate: Human health tier II assessment

13 February 2015

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Phenol, 4-(methylamino)-, sulfate (2:1) (salt)	55-55-0
Phenol, 4-(methylamino)-	150-75-4

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 parent chemical, *p*-methylaminophenol (CAS No. 150-75-4) and its sulfate (CAS No. 55-55-0) are assessed together in this assessment as both chemicals are expected to have similar toxicity profiles and uses.

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacturing information has been identified for the parent base, *p*-methylaminophenol.

The chemical, *p*-methylaminophenol sulfate is on the 'List of chemicals used as dyes in permanent and semi-permanent hair dyes in Australia' (NICNAS, 2007), indicating cosmetic use in permanent hair dye preparations.

International

The following international uses have been identified through European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers; the Organisation for Economic Co-operation and Development Screening information data set International Assessment Report (OECD SIAR); Galleria Chemica; the Substances and Preparations in the Nordic countries (SPIN); the 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).

The chemicals have reported cosmetic use in several oxidative permanent hair dye/colour products.

The concentrations of *p*-methylaminophenol sulfate used in the majority of these products are reported to be between ≤0.1–1 % (CIR, 1991).

The chemicals have reported commercial uses including:

- as a component of fur dyes;
- in photographic developing; and
- as a corrosion inhibitor in steel.

Restrictions

Australian

No known restrictions have been identified.

International

The chemicals are listed on the following (Galleria Chemica):

- ASEAN Cosmetic Directive Annex III—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—the chemical, ‘after mixing under oxidative conditions, the maximum applied to hair must not exceed 0.68 %’; and
- New Zealand Cosmetic Products Group Standard—Schedule 5—Table 1: Components cosmetic products must not contain except subject to the restrictions and conditions laid down—the maximum authorised concentration in the finished cosmetic product is 3.0 %.

Existing Worker Health and Safety Controls

Hazard Classification

The parent chemical, *p*-methylaminophenol, is not listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia). However, *p*-methylaminophenol sulfate is classified as hazardous, with the following risk phrases for human health in the HSIS (Safe Work Australia):

- Xn; R22 (acute toxicity);
- Xn; R43 (sensitisation); and
- Xn; R48/22 (repeat dose toxicity).

Exposure Standards

Australian

No specific exposure standards are available for either chemical.

International

No specific exposure standards are available for *p*-methylaminophenol.

The following exposure standards are identified for *p*-methylaminophenol sulfate (Galleria Chemica):

- Temporary emergency exposure limits (TEELs) of 10 mg/m^3 (TEL-0), 30 mg/m^3 (TEL-1), 50 mg/m^3 (TEL-2), 250 mg/m^3 (TEL-3) by the United States Department of Energy.

Health Hazard Information

Toxicokinetics

As these are N-substituted *p*-aminophenols, they are expected to display similar properties to *p*-aminophenol and, for certain end points, *m*-aminophenol (CIR, 1991). In vitro metabolism studies conducted with *p*-aminophenol using human, rat, and mouse hepatocytes have identified common metabolites of glucuronides and sulfates in all three species. Paracetamol (a widely used antipyretic and analgesic drug, with paediatric use) was identified as a metabolite only in human hepatocytes. Compared with human hepatocytes, mouse hepatocytes were deficient in sulfotransferase activity and showed a greater capacity to form reactive electrophilic metabolites (SCCP, 2005).

The chemical *p*-aminophenol was metabolised in the skin to paracetamol. The in vitro reconstructed human skin model, Episkin®, indicated that the epidermis transformed *p*-aminophenol into paracetamol via N-acetylation, allowing systemic exposure to paracetamol or its metabolites (SCCP, 2005). Compared with *p*-aminophenol, acetylation is not expected to occur with *p*-methylaminophenol sulfate due to the methylated amino group (CIR, 1991).

The reaction of *p*-methylaminophenol sulfate with haemoglobin has been studied in different animal species using in vivo and in vitro models. The chemical reacted with haemoglobin to form methaemoglobin at a much faster rate than *p*-aminophenol. The reaction of the chemical with haemoglobin was also found to be slightly faster in human and rabbit erythrocytes, compared with dog and ox erythrocytes (CIR, 1991).

Dermal absorption of *p*-methylaminophenol sulfate was tested in an in vitro percutaneous absorption study (OECD Test Guideline (TG) 428) using dermatomed human skin samples from the breast and abdomen (SCCP, 2006). The chemical was tested under oxidative (with *m*-aminophenol as a coupler) and non-oxidative conditions with a final concentration of 0.68 %, which is typical in hair colouring formulation. The radiolabelled (^{14}C) chemical (20 mg/cm^2) was applied onto the skin surface for 30 minutes and the absorption was evaluated 24 hours after exposure. Based on the results, the dermal absorption at the concentration tested was estimated to be 1.35 ± 0.78 µg/cm^2 under oxidative conditions and 6.19 ± 2.24 µg/cm^2 under non-oxidative conditions (SCCP, 2006).

Acute Toxicity

Oral

The chemical, *p*-methylaminophenol sulfate is classified as hazardous with the risk phrase ‘Harmful if swallowed’ (Xn; R22) in the Hazardous Substance Information System (HSIS) (Safe Work Australia). No median lethal dose (LD50) value is available to support or amend the classification for this chemical. However, the available LD50 value for *p*-methylaminophenol supports this classification.

The oral LD50 for *p*-methylaminophenol was 380 mg/kg bw in male mice (European Commission, 2000).

In a preliminary acute toxicity study (OECD (TG) 420—fixed dose method), female Sprague Dawley (SD) rats (n = 1/dose) were exposed to *p*-methylaminophenol sulfate by oral gavage, at doses of 100, 200 or 500 mg/kg bw. The animals died at 200 and 500 mg/kg bw and the minimal lethal dose was reported to be 200 mg/kg bw. In the main experiment, four females SD rats were

administered *p*-methylaminophenol sulfate at 100 mg/kg bw. No mortalities were observed up to day 14. Following three hours of exposure, animals showed hypoactivity, piloerection and dyspnoea (SCCP, 2006). This study indicates an LD50 value of >100 mg/kg bw in rats for *p*-methylaminophenol sulfate.

Dermal

No data are available.

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

No data are available for *p*-methylaminophenol and only limited data are available for *p*-methylaminophenol sulfate. Based on the information available, both chemicals are expected to cause only slight skin irritation at up to a 3 % concentration.

No skin reactions were observed in New Zealand White rabbits (OECD TG 404) following exposure to *p*-methylaminophenol sulfate at a 3 % concentration under semi-occlusive conditions (SCCP, 2006).

Slight skin irritation (primary skin irritation index = 0.74/8 at 24 hours exposure and 48 hours after the application ceased) was observed in albino Bouscat rabbits (n = 3/sex) when a 2 % aqueous *p*-methylaminophenol sulfate solution was applied (0.5 mL, under occlusion) to intact and abraded skin for 24 hours (European Commission, 2000).

Eye Irritation

No data are available for *p*-methylaminophenol and only limited data are available for *p*-methylaminophenol sulfate. The chemicals are expected to cause slight eye irritation at a 3 % concentration based on the information available information for *p*-methylaminophenol sulfate.

Results from an OECD TG 405-compliant study indicated that *p*-methylaminophenol sulfate was slightly and transiently irritating to rabbit eyes. In this study, the New Zealand White rabbits were exposed to a 3 % solution of the chemical in 0.5 % aqueous carbomethylcellulose. The chemical was applied into the conjuctival sac of the left eye and changes associated with the treatment were monitored at one, 24, 48 and 72 hours following exposure. The results included a very slight swelling of the mucus membrane of the eyeball and eyelid lining (chemosis) and redness of the conjuctiva (left eye) observed as early as one hour after exposure (SCCP, 2006).

No eye irritation was observed in male albino rabbits (n = 6) during the seven-day observation period following administration of a 2 % aqueous solution of *p*-methylaminophenol sulfate into the conjunctival sac (0.1 mL/animal, without rinsing) (European Commission, 2000).

Sensitisation

Skin Sensitisation

The chemical, *p*-methylaminophenol sulfate is classified as hazardous with the risk phrase ‘May cause sensitisation by skin contact’ (R43) in the HSIS (Safe Work Australia). The data available support this classification. Although the guinea pig skin

sensitisation study with *p*-methylaminophenol gave negative results, based on the positive results observed for *p*-methylaminophenol sulfate in a more reliable assay, both chemicals are expected to be skin sensitisers.

In a skin sensitisation test, albino Hartley guinea pigs (n = 10/sex) were treated topically (occlusive, behind the right shoulder blade) with 0.5 g of *p*-methylaminophenol, three times per week for three weeks and once at week four. The animals also received two intradermal injections of Freund's complete adjuvant on days one and 10. Twelve days after induction, the untreated left flank was challenged with 0.5 g of the chemical for 48 hours under occlusion. No skin reactions were observed (European Commission, 2000).

The skin sensitising potential of *p*-methylaminophenol sulfate was investigated in a local lymph node assay (LLNA) (OECD TG 429). A solution containing the chemical at 0.25, 0.5, 1, 2.5 or 5 % was applied (25 µL) to the dorsal surface of both ears of CBA/J mice, once daily for three days. The treated animals were monitored daily for mortality and clinical signs. The study reported a dose-related increase in the stimulation index (SI), with 2.5 % and 5 % concentrations, exceeding the value of three. The effective concentration needed to produce a three-fold increase in lymphocyte proliferation (EC3) was calculated to be 2.2 %, indicating the chemical as a moderate skin sensitiser (SCCP, 2006).

Repeated Dose Toxicity

Oral

The chemical, *p*-methylaminophenol sulfate, is classified as hazardous with the risk phrase 'Harmful: danger of serious damage to health by prolonged exposure if swallowed' (Xn; R48/22) in the HSIS (Safe Work Australia).

Results from a 13-week study showed pathological changes in the kidneys of rats within the hazard classification range for severe effects (at 30 mg/kg bw/day). Although the kidney effects were reversible within the recovery period, the classification is considered appropriate based on the severity of the effects. This classification is supported for both chemicals.

In another 13-week oral gavage study (OECD TG 408), SD rats were dosed with *p*-methylaminophenol sulfate (suspended in 0.5 % carboxymethylcellulose) at 0, 3, 10, or 30 mg/kg bw/day. There were no mortalities, treatment-related clinical signs or behavioural changes and no effects on haematological parameters, body weight or food consumption. A no observed adverse effect level (NOAEL) of 10 mg/kg bw/day was reported based on tubular epithelial degeneration/single cell necrosis in the kidneys of most males and in half of the female rats at 30 mg/kg bw/day. In addition, some males of this group had higher urinary volumes with lower specific gravity. However, these changes were reported as completely reversible within the four-week recovery period (SCCP, 2006).

In a short-term study, SD OFA rats (n = 10/sex/dose) were administered (via gavage) *p*-methylaminophenol sulfate (in water) at doses of 0, 10, 30 or 90 mg/kg bw/day for 30–31 days. The treatment-related effects identified in female rats at the highest dose included discolouration of the spleen (9/10) and anaemia. At doses of 30 and 90 mg/kg, females rats also displayed acute tubular necrosis with pigments and cells present in the urine. The NOAEL was reported as 10 mg/kg bw/day for *p*-methylaminophenol (European Commission, 2000). No details were available on methaemoglobin formation.

Dermal

Only limited data are available. The chemicals, up to a 1 % concentration, are not considered to cause serious damage to health from repeated dermal exposure.

In a 13-week dermal toxicity study, groups of 12 adult New Zealand White rabbits were treated with two hair dye formulations containing *p*-methylaminophenol sulfate at 0.05 % and 1.0 % mixed with an equal volume of hydrogen peroxide. The skin of three rabbits in each group was abraded at the beginning of each week and the formulations were applied twice weekly to clipped skin. While statistically significant differences were observed in some organ weights, clinical chemistry and haematological values, these effects were not deemed to be toxicologically significant (CIR, 1991).

In a two-year dermal toxicity study, groups of male and female Eppley Swiss Colony mice were treated (by applying 0.05 mL to clipped skin) with two hair dye formulations containing *p*-methylaminophenol sulfate at 0.05 % and 1.0 % mixed with an equal

volume of hydrogen peroxide for 23 and 21 weeks, respectively. No significant differences in survival rates and organ and body weights of the treated animals were observed, relative to controls (CIR, 1991).

Inhalation

No data are available.

Genotoxicity

The available data are not sufficient to make a conclusion on the genotoxic potential of these two chemicals. Two oral studies in rats with *p*-methylaminophenol sulfate, including one micronucleus assay (conducted according to OECD TG 474), gave negative results for genotoxicity at doses up to 500 mg/kg bw. However, one micronucleus assay in mice showed positive results with single intraperitoneal (i.p.) doses of *p*-methylaminophenol sulfate at 50 mg/kg bw and above. The stability of the carcinogenic nitrenium ions (expected to form by metabolism of these chemicals) is important to predict the mutagenicity of these chemicals (see **Carcinogenicity** section).

Negative results were reported for *p*-methylaminophenol in the following in vitro and in vivo genotoxicity assays (European Commission, 2000):

- spot and plate tests in *Salmonella typhimurium*;
- forward mutation assay in yeast *Saccharomyces pombe* P1;
- chromosome aberration assay in Chinese hamster ovary (CHO) cells;
- micronucleus test in mice with two i.p. injections (24 hours apart), up to 100 mg/kg bw; and
- sex-linked recessive lethals test (SLRL) in *Drosophila melanogaster*.

Mixed results (positive or negative) were reported for *p*-methylaminophenol sulfate in several in vitro tests for gene mutation and clastogenicity (CIR, 1991; SCCP, 2006):

- in a bacterial gene mutation assay (OECD TG 471) that used *S. typhimurium* strains TA98, TA100, TA102, TA1535 and TA1537 with or without metabolic activation at up to 2000 µg/plate, positive results were seen in strain TA100 with or without metabolic activation, and in strains TA98 and TA1537 only with metabolic activation;
- in a chromosome aberration test (OECD TG 473) in cultured human lymphocytes at up to 27.49 µg/mL, increased frequency of chromosome aberrations was found, with or without metabolic activation;
- a gene mutation assay in mammalian cells (OECD TG 476) (L5178Y mouse lymphoma cells (TK+/-)) up to 38 µg/mL concentration and with metabolic activation showed positive results;
- negative results were seen in a gene mutation assay (OECD TG 476) in mammalian cells (L5178Y mouse lymphoma cells (hypoxanthine-guanine phosphoribosyltransferase)) up to 60 µg/mL concentration and with or without metabolic activation; and
- negative results in a chromosome aberration test in CHO cells at up to 1 mg/mL concentration.

In vivo assays in rats with *p*-methylaminophenol sulfate showed generally negative results for genotoxicity (CIR, 1991; SCCP, 2006):

- a micronucleus assay (OECD TG 474) in SD rats administered the chemical orally up to 400 mg/kg bw showed no increase in the incidence of micronuclei in bone marrow cells;
- in an unscheduled DNA synthesis test (draft OECD TG 486), no DNA damage in hepatocytes of male Wistar Han rats was observed with oral gavage doses up to 500 mg/kg bw; and
- an in vivo micronucleus test (test guideline not reported) in Swiss mice showed an increased incidence in the number of micronuclei in bone marrow cells following i.p. administration of the chemical at 50, 75 or 100 mg/kg bw.

A structurally-related chemical, *p*-aminophenol, was classified as a category 3 mutagen in the HSIS (Safe Work Australia). The chemical *p*-aminophenol induced clastogenic effects at high doses (SCCP, 2005).

Carcinogenicity

Only limited data are available. The chemicals are not expected to be carcinogenic via dermal exposure at 1 % concentration.

No carcinogenicity studies were available for the neat chemicals. Two long-term dermal studies in rodents were available that used up to a 1 % concentration of *p*-methylaminophenol sulfate. The first, a lifetime combined chronic toxicity and carcinogenicity study (non-guideline), SD rats (n = 60/sex/dose) were treated topically on clipped skin with 0.05 % or 1.0 % of *p*-methylaminophenol sulfate mixed with an equal volume of hydrogen peroxide (up to 0.5 mL), twice weekly. The treatment produced no local adverse effects and no compound-related variations on survival compared with control groups (SCCP, 2006). In the second study, Swiss Webster mice (n = 50/sex/dose) were treated topically (on clipped skin) with 1 % or 0.05 % of *p*-methylaminophenol sulfate (with hydrogen peroxide) for 23 and 21 weeks, respectively. The results showed no statistically significant differences in tumour distribution among treated and control groups. The chemical 2,4-diaminoanisole, which is considered a likely human carcinogen, was also tested in the same experiments with negative results, indicating low sensitivity of the tests (CIR, 1991; SCCP, 2006).

Experimental genotoxicity data from animal studies (see **Genotoxicity** section) did not clearly indicate whether *p*-methylaminophenol and *p*-methylaminophenol sulfate are genotoxic. Repeated dose toxicity results did not indicate methaemoglobin formation, which is related to the N-hydroxylation reaction, and which is also relevant to carcinogenicity of aromatic amines.

For *p*-methylaminophenol, QSAR modelling using OASIS–TIMES gave positive predictions for in vitro genotoxicity and negative results for in vivo genotoxicity. However, the chemical structure of *p*-methylaminophenol was out of the applicability domain of the QSAR models, indicating greater uncertainty about the reliability of the models for the chemical. The QSAR results are consistent with experimental genotoxicity data and do not indicate a high concern for carcinogenicity, particularly given that results in *S. typhimurium* were not consistently positive, as seen in many carcinogenic aromatic amines.

Reproductive and Developmental Toxicity

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

In a reproductive and developmental toxicity study (OECD TG 414), four groups of 24 pregnant female rats [SD Crl CD (SD) IGS BR] were orally dosed with *p*-methylaminophenol sulfate at 0, 5, 25 or 125 mg/kg bw/day on gestation days (GD) 6–19. No mortalities occurred during the study. The maternal body weight gain was slightly reduced in the 25 and 125 mg/kg bw/day dose groups. Neither embryotoxic nor teratogenic effects were observed at any dose level and the NOAEL was reported to be 125 mg/kg bw/day for developmental toxicity. A NOAEL of 5 mg/kg bw/day was established for maternal toxicity based on decreased maternal weight gain observed at 25 mg/kg bw/day (SCCP, 2006).

Pregnant rats administered *p*-methylaminophenol sulphate in sterile water on GD 6–15 at 0, 10, 30, 70 or 150 mg/kg bw/day showed no embryotoxic or teratogenic activity up to 70 mg/kg bw/day. Adverse clinical signs (details not available) and dam mortality were reported at the highest dose (European Commission, 2000).

No teratogenic effects were reported in rats treated dermally with formulations containing *p*-methylaminophenol sulphate at 0.05 % or 0.1 % in water (European Commission, 2000). Details of the study are not available.

A formulation containing *p*-methylaminophenol at 1 % in water did not cause reproductive effects in rats (European Commission, 2000). Details of the study are not available.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include:

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

Public Risk Characterisation

Considering the use of these chemicals in permanent hair dyes in Australia, the main route of public exposure is expected to be through the skin.

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

Several countries such as New Zealand and in the European Union have restricted the use of these chemicals in cosmetics. However, there are no restrictions in Australia on using these chemicals in cosmetics or hair dyes.

In the absence of any regulatory controls, the characterised critical health effects (skin sensitisation) have the potential to pose an unreasonable risk for the uses identified.

Occupational Risk Characterisation

Given the critical health effects (skin sensitisation and acute/repeated dose oral toxicity), the chemicals may pose an unreasonable risk to workers unless adequate control measures to minimise exposure to the chemicals are implemented. Based on the available data, the hazard classification in HSIS is considered appropriate for *p*-methylaminophenol sulfate. The parent chemical, *p*-methylaminophenol should also be included in the HSIS entry for *p*-methylaminophenol sulfate, to indicate the same hazard classification for both chemicals.

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 chemicals in hair dye products be managed through changes to the Poisons Standard (*Standard for the Uniform Scheduling of Medicines and Poisons*), and risks for workplace health and safety be managed through 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

Given the risk characterisation, it is recommended that these chemicals be included in Schedules 5 or 6 of the Poisons Standard with an appropriate concentration cut-off (exemption) for hair dye use.

Consideration should be given to the following:

- the chemicals are expected to be moderate skin sensitisers;
- limited data available on eye and skin irritation (3 % concentration was slightly irritating to the eyes of rabbits);
- no acute dermal toxicity data and limited data on repeated dose dermal toxicity (up to 1 % concentration was tested); and

- the maximum concentrations allowed in the European Union in hair dyes is 0.68 %.

Work Health and Safety

The chemicals are recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical hazards and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22)	Harmful if swallowed - Cat. 4 (H302)
Sensitisation	May cause sensitisation by skin contact (Xi; R43)	May cause an allergic skin reaction - Cat. 1 (H317)
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 chemicals should be used according to the instruction on the label.

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 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;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- 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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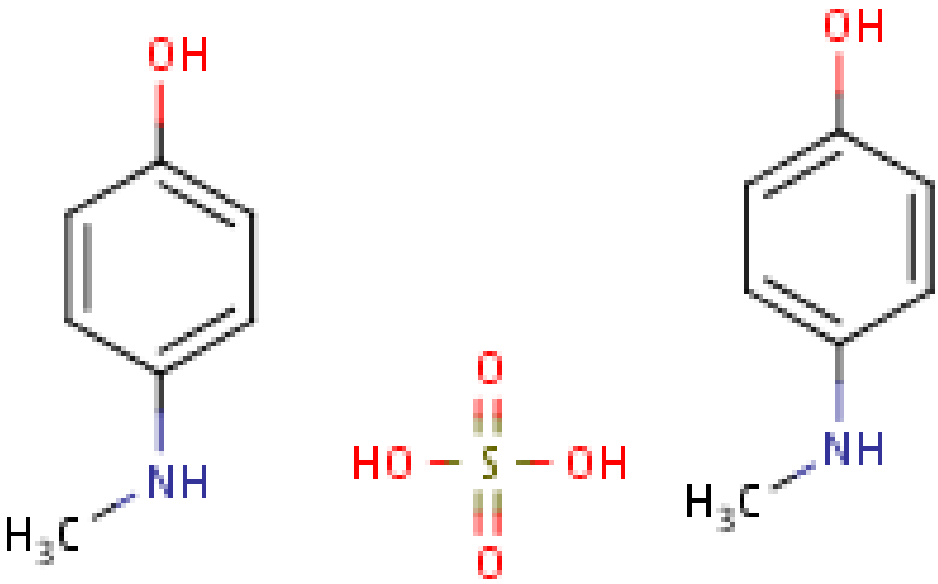
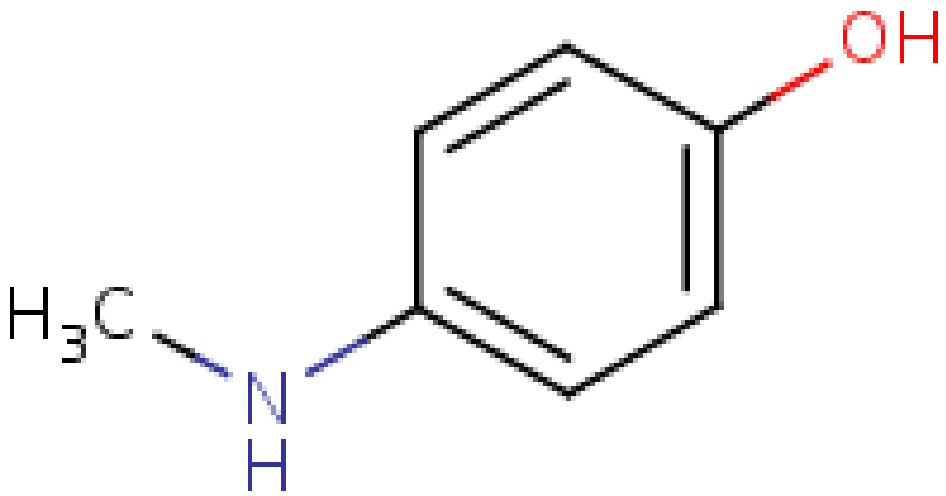
Last Update 13 February 2015

Chemical Identities

Chemical Name in the Inventory and Synonyms	**Phenol, 4-(methylamino)-, sulfate (2:1) (salt)** 4-(methylamino)phenol sulfate p-methylaminophenol sulfate 1-hydroxy-4-methylamino-benzene hemisulfate bis(4-hydroxy-N-methylanilinium)sulfate
CAS Number	55-55-0
Structural Formula	
Molecular Formula	C7H9NO.1/2H2O4S
Molecular Weight	344.39

Chemical Name in the Inventory and Synonyms	**Phenol, 4-(methylamino)-** methyl-p-aminophenol p-methylaminophenol 4-(methylamino)phenol N-methyl-4-aminophenol metol
CAS Number	150-75-4
Structural Formula	
Molecular Formula	C7H9NO
Molecular Weight	123.54

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