Phenol, 3-amino-: Human health tier II assessment

21 April 2016

CAS Number: 591-27-5

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.

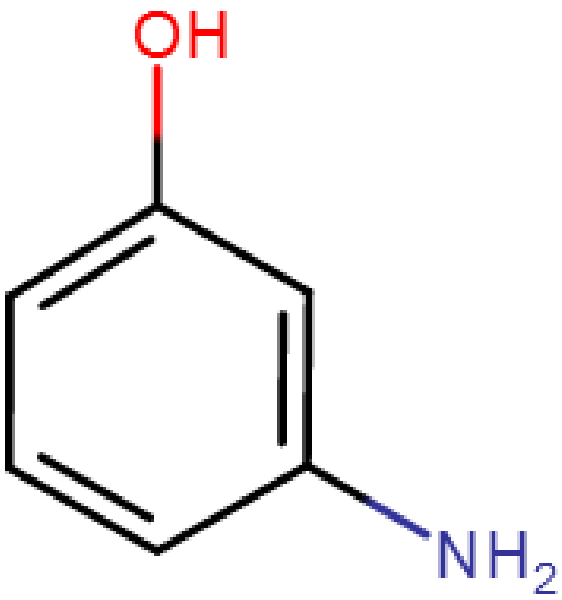
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	3-hydroxyaniline m-aminophenol
Structural Formula	
Molecular Formula	C6H7NO
Molecular Weight (g/mol)	109.13
Appearance and Odour (where available)	White crystals
SMILES	c1(O)cc(N)ccc1

Import, Manufacture and Use

Australian

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

The chemical has reported cosmetic 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 Substances and Preparations in Nordic countries (SPIN) database;
- the European Commission Cosmetic Ingredients and Substances (CosIng) database;
- United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary;
- the US Environmental Protection Agency (EPA) Aggregated Computer Toxicology Resource (ACToR);
- National Toxicology Program (NTP);
- US EPA Chemical and Product Categories (CPCat); and
- the US National Library of Medicine Hazardous Substances Data Bank (HSDB).

The chemical has reported cosmetic use internationally including in:

- hair dyes, colours (including aerosols), conditioners and tints;
- aftershave lotions; and
- nail basecoats and undercoats.

The chemical has reported domestic use including in:

- paints, lacquers and varnishes; and
- colouring agents.

The chemical has reported commercial use including in the manufacture of:

- adhesives and binding agents;
- anti-freezing agents;
- heat transferring agents;
- surface treatments;
- stabilisers;
- construction materials such as fillers; and

- leather and fur products (colouring agent).

The chemical has reported site-limited use including:

- as an intermediate in the synthesis of dyes; and
- in the manufacture of tobacco products.

The chemical has reported non-industrial use, including in the manufacture of non-agricultural pesticides and therapeutics.

Restrictions

Australian

No known restrictions have been identified.

International

The chemical is listed on the following (Galleria Chemica):

- Association of South East Asian Nations (ASEAN) Cosmetic Directive Annex III Part 1: List of substances which cosmetic products must not contain except subject to restrictions and conditions;
- EU Cosmetics Regulation 1223/2009 Annex III—List of substances which cosmetic products must not contain except subject to restrictions; and
- New Zealand Cosmetic Products Group Standard—Schedule 5, Table 1: Components cosmetic products must not contain except subject to restrictions and conditions.

Under the above regulations, the use of the chemical in hair dyes is restricted to a maximum concentration of 1.2 % applied to hair after mixing under oxidative conditions.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is classified as hazardous, with the following risk phrase for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

- Xn; R20/22 (acute toxicity)

Exposure Standards

Australian

No specific exposure standards are available.

International

The following exposure standards are identified (Galleria Chemica):

Temporary Emergency Exposure Limits (TEELs) defined by the US Department of Energy (DOE):

TEEL-1 = 0.056

TEEL-2 = 0.61

TEEL-3 = 51

Exposure limits of 1.8 mg/m^3 (1 ppm) time weighted average (TWA) and 2.25 mg/m^3 (1.25 ppm) short-term exposure limit (STEL) in Argentina.

Health Hazard Information

The chemical is one of the three isomers of aminophenol. Where data on the chemical are limited, information available from previous NICNAS assessments on the other two isomers, 2-aminophenol (CAS No. 95-55-6) (NICNASb) and 4-aminophenol (CAS No. 123-30-8) (NICNASc), were used in the assessment where appropriate. The structural isomers have varied electronic properties due to the differing structural arrangements of the hydroxyl and amino functional groups around the benzene ring. The differences in chemical reactivities and resulting metabolism will have significant effects on some endpoints, particularly systemic toxicity. However, read across from the structural isomers is considered appropriate for some data gaps, such as local irritant effects.

Toxicokinetics

Limited data are available on the toxicokinetics of the chemical.

The chemical has high water solubility and is expected to be readily absorbed by the oral and inhalation routes and rapidly distributed throughout the body via the blood. Dermal availability was found to be low when the chemical (63 mg/kg bw/day, either a single dose or ten doses) was dermally administered to rats. Less than 0.2 % of the total amount applied was absorbed through the skin. The highest concentration of the chemical in a 60 mL sample of oxidative hair dye formulation is estimated as 1.2 % (based on current EU restrictions). At this concentration, the chemical is expected to be poorly absorbed through the skin compared with the oral route (CIR, 1988; REACH).

The bioaccumulation potential of the chemical is expected to be low due to rapid metabolism and excretion in the urine. An oxidative metabolic pathway has been shown to occur with the structural isomers, 2-aminophenol and 4-aminophenol, via quinone imine intermediates. However, this is expected to occur to a lesser extent for 3-aminophenol because it cannot form a stable quinone imine and is therefore less susceptible to oxidation compared with the other isomers. The N-acetylated metabolites of 2- and 4-aminophenol have been found in urine (CIR, 1988), and this metabolic pathway is considered relevant for the chemical.

Acute Toxicity

Oral

The chemical is classified as hazardous with the risk phrase ‘Harmful if swallowed’ (Xn; R22) in the HSIS (Safe Work Australia). The available data support this classification.

The chemical was of moderate acute toxicity in animal tests following oral exposure. The median lethal doses (LD50) were reported to be in the range of 812–1000 mg/kg bw in rats (CIR, 1988; SCCP, 2006; REACH). Reported signs of toxicity include hypoactivity or sedation, piloerection and dyspnoea.

Dermal

No data are available for the chemical. Based on the data available for the structural isomer 4-aminophenol, the chemical may have low acute dermal toxicity.

A LD50 of >8000 mg/kg bw in New Zealand White (NZW) rabbits was reported for 4-aminophenol (50 % w/w in 1% aqueous gum tragacanth) in an occlusive patch test. There were no mortalities, changes in weight gain or gross abnormalities at doses of 2000, 4000 or 8000 mg/kg bw over a 2-week observation period (CIR, 1988).

Inhalation

The chemical is classified as hazardous with the risk phrase ‘Harmful by inhalation’ (Xn; R20) in the HSIS (Safe Work Australia). The limited data available for the chemical support this classification.

The chemical was of moderate acute toxicity in animal tests following inhalation exposure. A median lethal concentration (LC50) of 1162 mg/m^3 (1.162 mg/L) was obtained in rats. Reported signs of toxicity include spastic paralysis of the peripheral nerves, sensations and changes in behaviour (excitement). Further experimental details were not described (REACH; RTECS).

Corrosion / Irritation

Skin Irritation

The chemical is not considered to be irritating to the skin. No irritation effects were observed for the structural isomers, 2-aminophenol and 4-aminophenol (NICNASb; NICNASc; SCCP, 2006).

In a study performed in accordance with OECD Test Guideline (TG) 404, a single dose (0.5 mL) of 3-aminophenol (2 % in a suspension of 0.5 % methylcellulose in purified water) was applied under a semi-occlusive dressing for 4 hours in three male NZW rabbits. In 1/3 animals, very slight erythema was noted one hour after application. No skin reactions were observed from 24 hours onwards (SCCP, 2006).

Eye Irritation

The chemical is not considered to be irritating to the eyes. The structural isomers, 2-aminophenol and 4-aminophenol, are also considered non-irritating (NICNASb; NICNASc; SCCP, 2006).

The chemical was reported to slightly irritate the eyes when tested according to OECD TG 405. Instillation of a single dose (0.1 mL) of 3-aminophenol (2 % in a suspension of 0.5 % methylcellulose in purified water) into the conjunctival sac of three NZW rabbits resulted in very slight chemosis and very slight conjunctival redness in 2/3 animals on the day of dosing. The symptoms reversed rapidly. No ocular reactions were observed during the remainder of the study (SCCP, 2006; REACH).

Sensitisation

Skin Sensitisation

The available information support the classification of the chemical as hazardous with the risk phrase ‘May cause sensitisation by skin contact’ (R43) in the HSIS (Safe Work Australia) (see **Recommendation** section). The chemical is considered to be a moderate to strong skin sensitiser based on the positive results seen in animal tests (guinea pig maximisation test (GPMT) and local lymph node assay (LLNA)). The EC3 values (concentration required to provoke a 3-fold increase in lymph node cell proliferative activity compared with controls) in several LLNA studies were reported to be in the range of 0.24–3.2 %. This classification is supported by instances of sensitisation in humans (see **Observation in humans** section).

In an in vivo mouse LLNA conducted in accordance with OECD TG 429, 28 female CBA/J mice (4 animals/group) were administered concentrations of 0 %, 1 %, 2.5 %, 5 %, 10 % or 25 % (w/v) of the chemical in dimethylformamide (DMF). Stimulation indices (SI) of 0, 7.6, 12.6, 10.4, 7.2 and 6.0 were reported, respectively. In a second experiment, concentrations of 0 %, 0.05 %, 0.1 %, 0.5 %, 1.0 % and 2.5 % of the chemical in the same vehicle were administered to the animals. The SI of 1.0, 1.4, 5.9, 9.0 and 11.0 were reported, respectively. The EC3 value (0.24 %) indicated strong sensitisation potential for the chemical (SCCP, 2006; ICCVAM, 2011; REACH).

In another mouse LLNA study, CBA/Ca mice were administered concentrations of 0 %, 2.5 %, 5 % or 10 % (w/v) of the chemical in acetone/olive oil (ratio of 4:1). The SI of 0, 2.8, 3.5 and 5.7 were reported, respectively. The EC3 value was reported to be 3.2 % (ICCVAM, 2011).

In a non-guideline GMPT, guinea pigs were administered a 1.0 % (v/v) solution of the chemical in acetone/olive oil (ratio of 4:1) by intradermal injection, followed by topical induction with a 10 % solution of the chemical one week later. After two weeks, a topical challenge dose of 5 % resulted in positive reactions observed in all animals tested (Basketter et al., 1991).

Observation in humans

Sensitisation in humans exposed to the chemical has been observed both in a repeat insult patch test and during diagnostic patch testing.

In two semi-occlusive repeat insult patch tests, 0.1 mL doses of the chemical (3 % solution in Schultz vehicle II or similar) were applied to the backs of 98 and 99 test subjects over a 6 week period. There were ten consecutive induction patch applications at 48–72 hours, followed by 1 day of no application. Challenge patch application on previously unexposed skin on the back was conducted 48 hours following the rest period. In both studies, irritant effects (erythema) were observed in several subjects during the induction phase. In the first study (98 subjects), no reactions to the challenge patches were observed. In the second study (99 subjects), two subjects showed reactions following the challenge patches, as well as additional rechallenge patches on different parts of the body (CIR, 1988).

In an Australian case study, 164 hairdressers and hairdressing apprentices who presented with allergic contact dermatitis at a dermatology clinic were patch-tested against 36 chemicals used in hair salons. Four subjects, currently exposed to 3-aminophenol in the workplace, had positive reactions when patch tested with the chemical (Lyons et al., 2013).

Repeated Dose Toxicity

Oral

Based on the data available, the chemical is not considered to cause serious damage to health from repeated oral exposure at low doses.

In a 90-day oral toxicity study conducted according to OECD TG 408, Sprague Dawley (SD) rats (10 animals/sex) were administered the chemical daily by oral gavage at doses of 0, 20, 70, 200 or 600 mg/kg bw/day for 13 weeks. No treatment-related mortalities were observed at any dose level. While no clinical changes in the 20 mg/kg bw/day group were observed, ptyalism (excessive production of saliva) was observed in some animals in the 70 mg/kg bw/day group, and in all animals at higher doses. At 70 mg/kg bw/day and above, dose-related thyroid hyperactivity and the presence of the chemical in the renal tubules were reported. Haemosiderosis (iron overload) was noted in the spleen and abnormal biochemical parameters in blood were observed at 200 mg/kg bw/day. At 600 mg/kg bw/day, lacrimation, and red or orange colour in the urine (all animals) and the tail (females only) were reported. Signs of clinical, haematological, biochemical and histopathological toxicity were also observed. The no observed adverse effect level (NOAEL) was 20 mg/kg bw/day and the lowest observed adverse effect level (LOAEL) was 70 mg/kg bw/day based on effects on thyroid activity and kidney effects (SCCP, 2006; REACH).

In a non-guideline study, newborn and young SD rats were administered the chemical for 18 days and 28 days, respectively. In the newborn rat study (starting at day four after birth), doses of 0, 24, 80 or 240 mg/kg bw/day were administered daily by oral gavage. No chemical-related changes were observed at 24 mg/kg bw/day. Increased liver weights in males and decreases in blood sugar in females without any histopathological changes were reported at 80 mg/kg bw/day. Tremors and decreases in body weight gain, increased relative kidney weights, and hypertrophy of thyroid follicular epithelial cells were reported at 240

mg/kg bw/day. The NOAEL was reported as 80 mg/kg bw/day in newborn SD rats. In the 28-day study (starting at 5 weeks of age) of rats, doses of 0, 80, 240, 720 mg/kg bw/day were administered daily by oral gavage. Tremors, anaemia, decreases in body weight gain were observed at 720 mg/kg bw/day. Liver, kidney and thyroid toxicity were also reported. Slight pigmentation of the renal proximal tubular epithelium was observed in females at 240 mg/kg bw/day. This effect was not considered to be an adverse effect because of the lack of changes in related toxicological parameters. The NOAEL for young rats was reported as 240 mg/kg bw/day (Koizumi et al, 2002; REACH).

Dermal

Limited data are available for the chemical and its structural isomers. Based on the available information and the poor dermal absorption of the chemical (see **Toxicokinetics** section), the chemical is not expected to cause serious damage upon repeated exposure via the dermal route.

In a non-guideline combined chronic toxicity and carcinogenity study (see **Carcinogenicity** section), the chemical was topically applied to two groups of Charles River rats (60/sex/group) for 24 months. Each test group was topically administered a dye formulation containing the chemical (either 0.02 % or 0.09 %) and hydrogen peroxide. The formulation (0.5 mL) was applied to the shaved skin of each rat twice a week for 24 months. Slight changes in body weight and food consumption were observed in the treated rat groups, although further details about these results were not described. Scattered non-neoplastic lesions were observed in various organs and tissues of rats from both the control and experimental groups (SCCP, 2006; REACH).

In a non-guideline combined dermal toxicity and carcinogenicity study (see **Carcinogenicity** section), two hair dye formulations containing 3-aminophenol (0.7 %) and hydrogen peroxide were applied to a 1 cm^2 area of skin of Swiss Webster mice (50/sex/dose) once a week for 21 months. No significant differences in absolute or relative liver or kidney weights were observed (SCCP, 2006).

Inhalation

No data are available on the chemical or its isomers.

Genotoxicity

Based on the weight of evidence from the available in vitro and in vivo genotoxicity studies, the chemical is not considered to be genotoxic. Due to metabolic differences, data for the structural isomers (2-aminophenol and 4-aminophenol) are not considered relevant for this endpoint.

Some in vitro genotoxicity tests (bacterial reverse mutation assay and chromosomal aberration test) indicated positive or weakly positive results, but all in vivo tests (dominant lethal test and mammalian micronucleus test) were negative.

International reports have discussed the formation of potentially genotoxic aminophenol metabolites upon exposure of biological systems to the chemical and its isomers (CIR, 1988; CIR, 2008). It was the opinion of the CIR Expert Panel that there were sufficient endogenous stores of glutathione in mammalian systems to inactivate the metabolites of the chemical as they are formed, thereby reducing its genotoxic potential at low doses.

In vitro

In a bacterial reverse mutation assay carried out according to OECD TG 471, the chemical was tested for point mutations in *Salmonella typhimurium* (TA 98, TA 100, TA 102, TA 1535 and TA 1537), with and without metabolic activation (S9 mix). Negative findings were reported in most of the tested strains. A reproducible, dose-dependent increase in the number of revertants was found for TA 98 in the presence of S9 metabolic activation only, and the chemical was concluded to be weakly genotoxic (SCCP, 2006; REACH). In another bacterial reverse mutation assay (the WP2 Mutoxitest), the chemical was found to show no evidence of oxidative mutagenicity in *Escherichia coli* IC203 and IC188 at a dose of 750 µg/plate without metabolic activation (REACH).

In a study conducted according to OECD TG 476, the chemical was assayed for gene mutations at the *hprt* locus in L5178Y mouse lymphoma cells, with and without S9. Cells were treated with the chemical (25–1090 µg/mL) for 3 h, followed by an

expression period of 7 days to fix the DNA damage into a stable *hprt* mutation. No statistically significant increase in the mutant frequency at the *hprt* locus in mouse lymphoma cells was observed at any dose, with or without metabolic activation (SCCP, 2006; REACH).

The chemical did not induce chromosome aberrations in a study carried out according to OECD TG 473 with Chinese hamster lung cells in the presence of S9. Cells without S9 showed dose-dependent chromosomal aberrations with continuous treatment for 24 hours. The chemical was found to be clastogenic at 0.034 mg/mL without metabolic activation (REACH). In a similar study using human lymphocytes, the chemical at doses of 0, 0.63, 1.25, 2.5, 5.0, 7.5 or 10 mM (equivalent to 0, 69, 136, 273, 545, 818 or 1090 µg/mL), with and without S9, was found to increase the number of chromosomal aberrations in human lymphocytes. The chemical was concluded to be clastogenic (SCCP, 2006; REACH).

In a gene mutation study carried out according to OECD TG 487, human blood lymphocytes were treated with the chemical at doses ranging from 31 µg/mL to 1100 µg/mL, with and without metabolic activation. Induction of micronuclei was observed in the initial experiment; however, the results were not dose-related and not reproducible (SCCP, 2006; REACH).

In vivo

In a bone marrow micronucleus test carried out according to OECD TG 474, CD (SD) BR rats (5 rats/sex) were dosed with 0, 375, 750 and 1500 mg/kg bw of the chemical by oral gavage. The highest dose was above the reported rat LD50 values. No significant increases in the number of micronuclei in the bone marrow cells were found (SCCP, 2006).

A dominant lethal study was conducted in SD rats fed diets containing 0, 0.1 %, 0.25 % and 1 % (equivalent to 0, 10, 25 and 100 mg/kg bw/day) of the chemical for 19 weeks. Following the treatment period, 20 male rats from each dose group were removed from the test diet, placed on a basal diet and mated each week with two untreated females for 2 weeks. The body weights of the high dose males were significantly decreased by the end of the study; however, no significant differences in any other test parameters including reproductive effects were reported. It was concluded that the chemical did not produce a dominant lethal effect in rats following treatment for more than two cycles of spermatogenesis at doses sufficient to cause a reduction in body weight (CIR, 1988; REACH).

Observation in humans

No significant increases in chromosomal aberrations or sister chromatid exchanges were observed in human subjects dermally exposed to hair dye formulations containing the chemical. The hair was dyed for a total of 12 times at 3–6 week intervals. The concentrations of the chemical in each formulation were not reported (CIR, 1988).

Carcinogenicity

Limited animal studies are available for the chemical. Based on the available data and the lack of genotoxicity, the chemical is not expected to be carcinogenic. Due to metabolic differences, data on the structural isomers (2-aminophenol and 4-aminophenol) are not considered relevant for this endpoint.

In combined dermal toxicity and carcinogenicity studies in rats and mice, topical application of hair dye formulations containing the chemical (see **Repeat Dose Toxicity - Dermal** section) did not cause clinically-significant carcinogenic effects (CIR, 1988; SCCP, 2006; REACH).

Reproductive and Developmental Toxicity

Based on the available data, the chemical is not expected to have specific reproductive or developmental toxicity. Any effects observed were secondary to maternal toxicity.

In a prenatal developmental toxicity study (similarly to OECD TG 414), a total of 96 female SD rats (24/group) were dosed with the chemical at 0, 30, 100 and 300 mg/kg bw/day, from day 6 to day 19 post coitum. At 100 and 300 mg/kg bw/day, coloured urine in the dams and decreased weight gain were reported. At the highest dose (300 mg/kg bw/day), food consumption was also decreased. Foetal body weight and sex ratios at all doses were not affected, and no treatment-related incidences in external and visceral anomalies were observed. At 300 mg/kg bw/day, increases in post-implantation losses and early resorptions in pregnant animals were observed, and 15.7 % of foetuses in this group exhibited a short supernumerary 14th rib.

The NOAEL for maternal toxicity was determined to be 30 mg/kg bw/day, and the NOAEL for developmental toxicity was 100 mg/kg bw/day based on post-implantation losses and early resorptions (REACH; SCCP, 2006).

In a non-guideline 90 day oral study followed by a teratology study, 100 female SD rats (25 animals/group) were fed daily with the chemical at doses of 0, 10, 25 and 100 mg/kg bw/day prior to mating, then from gestation days (GD) 0–20. The NOAEL was determined to be 10 mg/kg bw/day based on effects on body weight and food consumption. No other significant differences were noted in any reproductive parameter except for a decrease in the mean number of corpora lutea in the highest dose group (100 mg/kg bw/day). No abnormal gross effects (visceral or skeletal) were noted in the foetuses (CIR, 1988; REACH).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include the local effects from skin sensitisation. It is also harmful by the oral and inhalation routes.

Public Risk Characterisation

New Zealand, ASEAN countries and the European Union have restricted the use of the chemical in cosmetics; however, currently there are no restrictions in Australia on this chemical for use in cosmetics or domestic products.

Considering the use of this chemical in permanent hair dyes in Australia and other potential domestic uses (based on overseas information), the main routes of public exposure are expected to be through the skin, and inhalation from products applied as aerosols.

In the absence of regulatory controls, the characterised critical health effects (acute toxicity and skin sensitisation) have the potential to pose an unreasonable risk under the identified uses. The risk could be mitigated by implementing restrictions for the use of the chemical in hair dyes and other cosmetic products.

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 support an amendment to the hazard classification in the (HSIS) (Safe Work Australia) (refer to **Recommendation** section).

NICNAS Recommendation

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

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

territory.

Regulatory Control

Public Health

Given the risk characterisation, it is recommended that the chemical be included in the Poisons Standard (*Standard for the Uniform Scheduling of Medicines and Poisons*—SUSMP) for use in hair dyes, to ensure appropriate labelling.

Consideration should be given to the following:

- the chemical is a skin sensitiser in humans;
- it is a strong skin sensitiser in animals; and
- there are overseas restrictions for use of this chemical in hair dyes (see **International Restrictions**).

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 and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22)* Harmful by inhalation (Xn; R20)*	Harmful if swallowed - Cat. 4 (H302) Harmful if inhaled - Cat. 4 (H332)
Sensitisation	May cause sensitisation by skin contact (Xi; R43)	May cause an allergic skin reaction - Cat. 1 (H317)

[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 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;

- 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 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

Basketter DA, Scholes EW, Kimber I, Botham PA, Hilton J, Miller K, Robbins MC, Harrison PTC and Waite SJ (1991). Interlaboratory Evaluation of the Local Lymph Node Assay with 25 Chemicals and Comparison with Guinea Pig Test Data. Toxicology Methods, 1: 30-43.

Cosmetic Ingredient Review (CIR) 1988. Final report on the safety assessment of p-aminophenol, m-aminophenol, and o-aminophenol. Journal of the American College of Toxicology, 7(3): 279–333.

Cosmetic Ingredient Review (CIR) 2008. Annual Review of Cosmetic Ingredient Safety Assessments - 2005/2006. International Journal of Toxicology, 27(S1): 77–142.

European Commission Cosmetic Ingredients and Substances (CosIng) Database. Accessed December 2015 at http://ec.europa.eu/consumers/cosmetics/cosing/

Galleria Chemica. Accessed December 2015 at http://jr.chemwatch.net/galleria/

Hazardous Substances Data Bank (HSDB). National Library of Medicine. Accessed December 2015 at http://toxnet.nlm.nih.gov

Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) 2011. ICCVAM Test Method Evaluation Report: Usefulness and Limitations of the Murine Local Lymph Node Assay for Potency Categorization of Chemicals Causing Allergic Contact Dermatitis in Humans. NIH Publication No. 11-7709. Research Triangle Park, NC: National Institute of Environmental Health Sciences. Accessed December 2015 at http://iccvam.niehs.nih.gov/methods/immunotox/LLNA-pot/TMER.htm

Koizumi M, Nishimura N, Enami T, Sunaga M, Horikawa H, Kamata E and Hasegawa R (2002). Comparative Toxicity Study of 3-Aminophenol in Newborn and Young Rats. Journal of Toxicological Sciences, 27(5): 411–421.

Lyons G, Roberts H, Palmer A, Matheson M and Nixon R (2013). Hairdressers presenting to an occupational dermatology clinic in Melbourne, Australia. Contact Dermatitis, 68: 300–306.

National Industrial Chemicals Notification and Assessment Scheme (NICNASa) 2007. List of Chemicals used as Dyes in Permanent and Semi-Permanent Hair Dyes in Australia.

National Industrial Chemicals Notification and Assessment Scheme (NICNASb). Human Health Tier II assessment for 2-aminophenol (CAS No. 95-55-6). Australian Government Department of Health and Ageing. Accessed November 2015 at http://www.nicnas.gov.au

National Industrial Chemicals Notification and Assessment Scheme (NICNASc). Human Health Tier II assessment for 4-aminophenol (CAS No. 123-30-8). Australian Government Department of Health and Ageing. Accessed November 2015 at http://www.nicnas.gov.au

National Toxicology Program (NTP). Testing Status for 3-Aminophenol (CAS No. 591-27-5). Accessed December 2015 at http://ntp.niehs.nih.gov/testing/status/agents/ts-11461-s.html

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Dossier. 3-Aminophenol (CAS No. 591-27-5). Accessed December 2015 at http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

Registry of Toxic Effects of Chemical Substances (RTECS). Accessed February 2016 at http://ccinfoweb.ccohs.ca/rtecs/search.html

Safe Work Australia (SWA). Hazardous Substances Information system (HSIS). Accessed November 2015 at http://hsis.safeworkaustralia.gov.au/HazardousSubstance

Scientific Committee on Consumer Products (SCCP) 2006. Opinion on m-Aminophenol, COLIPA No. A15 (SCCP/0978/06). Adopted by the SCCP during the 10th plenary meeting of 19 September 2006. Accessed at http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_088.pdf

SPIN (Substances in Preparations in Nordic Countries) Database. Accessed December 2015 at http://195.215.202.233/DotNetNuke/default.aspx

United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) dictionary. Accessed December 2015 at http://gov.personalcarecouncil.org/jsp/gov/GovHomePage.jsp

US Environmental Protection Agency Aggregated Computational Toxicology Resource (ACToR). Accessed January 2016 at http://actor.epa.gov/actor/faces/ACToRHome.jsp

US Environmental Protection Agency Chemical and Product Categories (CPCat). Accessed December 2015 at http://actor.epa.gov/cpcat/faces/search.xhtml

Last update 21 April 2016

Share this page