Phenol: Human health tier II assessment

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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 and published separately, using information available at the time, and may be undertaken at different tiers.

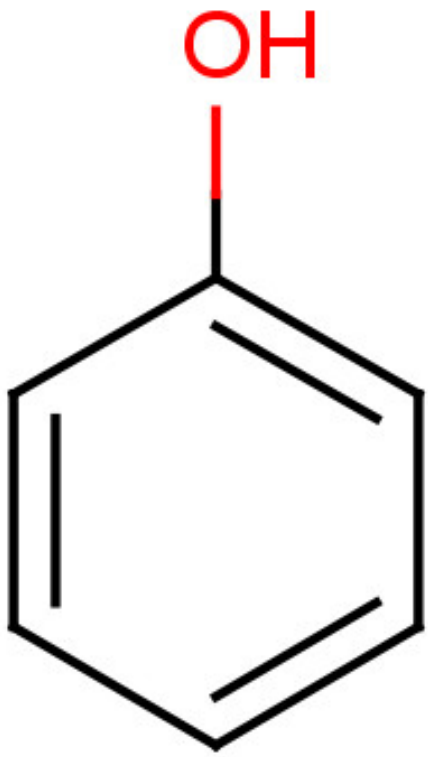
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	Benzenol Carbolic acid Phenic Acid Phenyl alcohol Monohydroxybenzene
Structural Formula	

Molecular Formula	C6H6O
Molecular Weight (g/mol)	94.11
Appearance and Odour (where available)	Pure phenol is colourless to light pink crystalline solid. Phenol has distinct aromatic and somewhat sickening sweet and acrid odour.
SMILES	c1(O)ccccc1

Import, Manufacture and Use

Australian

The following Australian industrial uses were reported under previous mandatory and/or voluntary calls for information.

The chemical has reported commercial use including in:

- adhesives (binding agents);
- plastics; and
- surface coatings.

The chemical has reported site-limited use including manufacturing other chemicals.

The chemical is listed on the 2006 High Volume Industrial Chemicals List (HVICL) with a total reported volume of 10000-99999 tonnes (NICNAS, 2006).

International

The following international uses have been identified through European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers; the European Chemicals Bureau (ECB) Risk Assessment Report; Galleria Chemica; Substances and Preparations in the 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 and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported site-limited use (major use) including:

- as an intermediate in organic synthesis of bisphenol A, phenol resins, alkylphenols, caprolactam, salicylic acid, nitrophenols, diphenyl ethers, halogen phenols and other chemicals.

The chemical has reported commercial use including:

- as a component of adhesive (binder), paint and varnish removers, lacquers, paints, rubber, ink, illuminating gases, tanning dyes, colouring agents, construction materials, corrosion inhibitors, lubricants, additives, solvents, impregnation materials, insulating materials, stabilisers, and surface-active agents;
- as a general disinfectant, cleaning agents, and a slimicide; and
- non-agricultural pesticides and preservatives.

The chemical has reported domestic use including:

- as a general disinfectant; and

- in adhesives, paints, laquers and varnishes;

The chemical has reported domestic use in the SPIN database. However, it should be noted that SPIN does not distinguish between direct use of the chemical or use of the material that are produced from chemical reactions with the chemical.

The chemical has reported cosmetic use with the following functions:

- antimicrobial;
- deodorant;
- denaturants;
- masking
- oral care; and
- preservative.

Whilst use in cosmetics is prohibited in some countries (see **Restrictions—International**), there is reported use of this chemical in cosmetics in the United States of America (Personal Care Products Council 2011, HHPD).

The chemical has reported non-industrial use including:

- in medical preparations including lotions, ointment, mouthwashes etc; and
- in pesticides

Restrictions

Australian

This chemical is listed in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) in Schedule 6 as follows:

PHENOL, including cresols and xylenols and any other homologue of phenol boiling below 220°C, **except**:

(a) when separately specified in these Schedules;

(b) when included in Schedule 5; or

(c) in preparations containing 3 per cent or less of such substances.

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.

The chemical is also listed in schedules 2, 4 and 5 for non-industrial uses. The Schedule 5 entry relates to use in animal feed.

International

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

- EU Cosmetic Directive 76/768/EEC Annex II—List of substances which must not form part of the composition of cosmetic products;
- New Zealand Cosmetic Products Group Standard—Schedule 4: Components cosmetic products must not contain;
- Health Canada List of Prohibited and Restricted Cosmetic Ingredients ("Hotlist").

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; R23/24/25 (Acute toxicity)

C; R34 (Corrosive)

Xn; R48/20/21/22 (Danger of serious damage to health by prolonged exposure)

Xn; R68 (Muta.Cat.3) (Possible risks of irreversible effects)

Exposure Standards

Australian

The chemical has an exposure standard of 4 mg/m^3 (1 ppm) time weighted average (TWA).

International

The following exposure standards are identified (Galleria Chemica):

- An exposure limit (TWA) of 4–19 mg/m^3 in countries such as Canada, Denmark, France, Germany, Ireland, Japan, Norway, Singapore, Spain, Sweden, Switzerland, United Kingdom, and the USA.
- An exposure limit (STEL) of 6–38 mg/m^3 in countries such as Canada, France, Ireland, South Africa, Sweden, Switzerland, United Kingdom, and the USA.

Health Hazard Information

Toxicokinetics

The chemical has been reported to be well absorbed in animals and humans following oral, dermal, and inhalation exposure (US EPA, 2002; ECB, 2006).

In animals (pigs, sheep and rats), 84–90 % of the orally administered dose had been absorbed after eight hours. Following dermal application in rats, 80 % of the applied dose of the chemical was absorbed. In humans, 60–88 % of the chemical was reported to be absorbed following inhalation, while vapours can readily penetrate the skin surface with an absorption efficiency equal to that of inhalation.

Once absorbed, the chemical is widely and rapidly distributed in body tissues; higher levels have been reported in the lung, liver and kidney. The chemical is metabolised to its sulfate and glucuronide conjugates after administration by all the routes at the portal of entry. Small amounts of the hydroxylation products, catechol and hydroquinone, are also produced. Metabolism predominantly occurs in the liver, gut and kidneys. The chemical is rapidly excreted in animals and humans. Urinary excretion is the main elimination pathway for all exposure routes, with only a minor contribution of elimination in the bile. By 72 hours after exposure, 75–95 % of the recovered dose was excreted in the urine.

Acute Toxicity

Oral

The chemical is classified as hazardous with the risk phrase ‘Toxic if swallowed’ (T; R25) in the HSIS (Safe Work Australia). The data available (median lethal dose (LD50) of 340–530 mg/kg bw in rats) support this classification. The values in rats were obtained for aqueous preparations containing 2, 5, 10 and 20 % of phenol. The lowest value of 340 mg/kg bw was obtained for a preparation containing 20 % phenol (ECB, 2006; REACH).

Reported clinical signs were fluctuating body temperature; irregular and weak pulse; respiration became slow, irregular and weak; and pupillary construction followed by dilation. Salivation, marked dyspnoea, tremor and convulsions, lethargy, and coma were also reported. All of the animals that died were found dead within 5 to 150 minutes after exposure.

Dermal

The chemical is classified as hazardous with the risk phrase ‘Toxic in contact with skin’ (T; R24) in the HSIS (Safe Work Australia). The animal test data available (median lethal dose (LD50) of 660–707 mg/kg bw for undiluted phenol) (ECB, 2006; REACH) do not support this classification. However, a dose of 100 % phenol has been shown to be less toxic than the same dose of phenol given as a diluted solution (ASTDR, 2008). Given the effects observed in humans (see **Observation in humans**), an amendment of this classification is not recommended.

Following dosing (between 5–10 minutes), animals developed severe muscle tremors causing marked twitching that developed into generalised convulsions with loss of consciousness and prostration. At varying times between 45–90 minutes, depending upon the dose administered, the animals developed severe haemoglobinuria. Severe skin lesions were noted in all animals with immediate onset of oedema followed within four hours by necrosis, discolouration and surrounding erythema at 24 hours (ECB, 2006).

Inhalation

The chemical is currently classified as hazardous with the risk phrase ‘Toxic by inhalation’ (T; R23) in HSIS (Safe Work Australia). The data (LC50 values) on acute inhalation toxicity tests with animals are not available (ECB, 2006).

However, it is noted that rats are reported to have tolerated phenol concentrations as high as 236 ppm (900 mg/m3) for eight hours, resulting in ocular and nasal irritation, loss of coordination, tremors, and prostration. All the treated animals survived the 14-day observation period (ECB, 2006; REACH).

The available data do not support this classification. However, in the absence of more comprehensive information, and given that human toxicity from inhalation has been reported, there is insufficient evidence to support a recommendation to amend this classification.

Observation in humans

Phenol has been reported to cause poisoning in humans from ingestion, skin absorption, and by inhalation. Signs and symptoms of acute toxicity of phenol in laboratory animals and humans are similar regardless of the route of administration.

Oral toxicity of phenol in humans leading to the death of the victim is reported for doses as low as 140–290 mg/kg bw (ECB, 2006).

Death following dermal application of phenol has been reported. Following skin contact, absorption is very rapid and the symptoms develop rapidly (within 15–20 minutes). Death can occur within 30 minutes to several hours (ECB, 2006).

Corrosion / Irritation

Corrosivity

The chemical is classified as hazardous with the risk phrase 'Causes burns' (C; R34) in the HSIS (Safe Work Australia). The available data support this classification.

Although appropriate skin irritation data are not available due to the chemical's corrosive properties (ECB, 2006), some information is available (REACH). In these studies, the chemical (0.5 g) produced necrosis of unabraded rabbit skin following application for 24 hours and was determined to have corrosive properties. The chemical was also determined to have corrosive properties in an in vitro skin corrosion test (OECD TG 431).

Respiratory Irritation

Signs of respiratory irritation have been observed in a number of animal studies following acute and repeat inhalation exposure to the chemical.

Eye Irritation

Corrosive chemicals are also considered to cause irreversible effects on the eyes; the available eye irritation data for the chemical support this finding.

In an eye irritation study in rabbits, the chemical produced conjunctivitis, iritis, and corneal opacities occluding most of the iris, and corneal ulcerations extending over the entire corneal surface 24 hours after exposure. There was no improvement in the condition of the eyes during the observation period, and by the 14th day, all exposed eyes exhibited keratoconus and pannus formation. In another study in rabbits, eye irritation caused by a 5 % aqueous solution of the chemical was irreversible after an observation period of seven days (ECB, 2006; REACH).

Observation in humans

There have been frequent reports of human experience with occupational exposure to phenol (since 1871). Based on these experiences, the chemical has been reported to cause burns in humans (ECB, 2006).

While a 10 % solution of the chemical has been reported to produce corrosion in humans, occasionally skin necrosis has also been seen with solutions as dilute as 1 % (ECB, 2006). It has been noted that, due to the local anaesthetic properties of the chemical, no pain is experienced at initial contact with skin and a white wrinkled discolouration is formed.

Sensitisation

Skin Sensitisation

The chemical is reported to be not sensitising to guinea pig skin.

In a study using the modified Buehler Test for sensitisation, 10 female Hartley albino guinea pigs were induced with an application of the chemical (10 %) to the skin for 48 hours. This procedure was repeated three times a week for two weeks. The animals were challenged for 48 hours with 0.1 % and 1 % concentration of the chemical, after a two-week rest period following induction. None of the animals showed a positive response. The data indicate that the chemical is not a skin sensitiser (ECB, 2006; REACH).

Observation in humans

The chemical has not been reported to be a skin sensitiser in humans.

There was no evidence of allergic contact dermatitis in 45 students exposed to the chemical before and after a four-week exposure during an anatomy dissection course (ECB, 2006; REACH). In another study (maximisation test), there was also no evidence of skin sensitisation to the chemical, where 24 human volunteers were induced (2 % phenol) and then later challenged (1 % phenol) at 48 hours (ECB, 2006; REACH).

Repeated Dose Toxicity

Oral

Repeated dose studies showed toxic effects on target tissues such as the kidney, liver, lung, the haematopoietic system and nervous system, although effects were not consistent between studies (US EPA, 2002; ECB, 2006; ASTDR, 2008). Based on the available data it appears that the toxicity of phenol is related to peak blood levels rather than total dose delivered.

Toxicity of phenol is higher when administered by gavage compared with administration in drinking water. Although histopathological changes in the kidney and liver have been observed following administration of the chemical by gavage, no histopathological changes in the kidney and liver were noted in studies where the chemical was administered in drinking water.

Immunotoxicity and haematotoxicity were observed in a 28-day repeated dose study in CD-1 mice. The chemical was administered in drinking water at doses of 1.8, 6.2, and 33.6 mg/kg bw/day. The lowest observed adverse effect level (LOAEL) was established as 1.8 mg/kg-day, based on decreased antibody response, and decreases in haematocrit and red blood cells. However, similar effects were not observed in a 10-week study in which rats were dosed for 10 weeks with up to 301 mg/kg bw/day. No histopathological changes in the bone marrow, spleen, or lymph nodes were observed in longer-term studies in rats and mice (up to 103 weeks). Haematology parameters were not examined in these studies.

Reduced bodyweight gain, associated with decreased water consumption, has been observed in a number of drinking water studies. Decreased maternal weight was also observed in a developmental toxicity study in rats administered 120 mg/kg bw/day in a divided dosing protocol. The no observed adverse effect level (NOAEL) for this study was 60 mg/kg bw/day. This study has been identified internationally as the critical study to establish safety limits (US EPA, 2002; ASTDR, 2008; EFSA, 2013).

Dermal

In a dermal toxicity study in rabbits, the chemical was applied to the abdomen at concentrations of 1.18, 2.37, 3.56, 4.75, 5.93, and 7.12 % in aqueous solutions for five hours/day and five days/week for 18 days. Repeated dermal applications of the chemical at concentrations of ³ 2.37 % produced tremors, epidermal hyperkeratosis and ulceration in rabbits at concentrations > 3.56 %. Based on the limited information available, the NOAEL for systemic toxic effects was established as 1.18% (130 mg/kg bw/day), and for local effects on the skin as 2.37 % (260 mg/kg bw/day) (US EPA, 2002; ECB, 2006; ASTDR, 2008).

Considering tremors as a critical systemic effect that occurred at concentrations of 2.37 % (260 mg/kg bw/day) and above, the data (260 mg/kg bw/day) from a repeat-dose dermal study in rabbits was also below the stated guidance dose for R48 (300 mg/kg bw/day for subacute toxicity studies) (Approved Criteria) (ECB, 2006).

Inhalation

The majority of information on repeated dose effects following inhalation exposure is outdated and has limited value for risk assessment. Based on these studies, the heart, respiratory tract, liver, kidney and nervous system may be targets for phenol toxicity following inhalation exposure (US EPA, 2002; ECB, 2006; ASTDR, 2008).

In an inhalation study specifically designed to examine effects on the respiratory tract using the methodology similar to OECD TG 412, F344 rats were exposed to the chemical by 10 nose-only exposures (five days/week, six hours/day) at target concentrations up to 25 ppm (96 mg/m3). At concentrations up to 25 ppm, no adverse effects were seen in the respiratory tract or in any other organs. A local and systemic no observed adverse effect concentration (NOAEC) of 96 mg/m3 was determined in this study.

Observation in humans

Repeated oral, inhalation, and dermal exposure of humans has been reported to result in mucosal irritation, diarrhoea, dark urine, weakness, muscle pain, loss of appetite and body weight, and liver toxicity (ECB, 2006; ASTDR, 2008). There is also limited evidence of effects on the cardiovascular, haematopoetic and immunological systems, although exposure of workers to other chemicals was a possible confounding factor.

Overall

The chemical is classified as hazardous with the risk phrase 'Danger of serious damage to health by prolonged exposure' (Xn; R48/20/21/22) in the HSIS (Safe Work Australia). The available data support this classification (US EPA, 2002; ECB, 2006; ASTDR, 2008).

Genotoxicity

The chemical is classified as hazardous as a Category 3 mutagenic substance with the risk phrase 'Possible risk of irreversible effect' (R68) in the HSIS (Safe Work Australia). The available data support this classification (US EPA, 2002; ECB, 2006).

The chemical tested positive in mammalian cell gene mutation assays, gene mutation in mouse lymphoma assays, for chromosome aberrations in mammalian cell cultures, and positive results were also obtained from in vitro micronucleus tests with different mammalian cells. The chemical has also tested positive in several indicator tests such as a sister chromatid exchange (SCE) assay, an induction of unscheduled DNA synthesis (UDS) assay, an induction of DNA strand breaks, and formation of DNA adducts. Positive results were observed both in the presence and absence of metabolic activation.

The chemical tested negative in a rodent bone marrow chromosomal aberration test (in vivo), DNA strand breaks in testes (in vivo), and also in sex-linked recessive lethal tests with *Drosophila canton-s*.

In micronucleus assays in mice (in vivo), the chemical showed negative and weakly positive results. The positive effects in these tests were limited to high doses that induced toxic effects and may be due to an indirect mode-of-action from hypothermia and metabolic overload (ECB, 2006). The route of administration of the chemical has also been stated to be important in the induction of micronuclei (US EPA, 2002). While generally positive results have been obtained with the intraperitoneal route, negative or equivocal results have been obtained with the oral route. This route-related difference is likely to be due to the potential for first-pass detoxification of the chemical when it is administered by the oral route, but not when administered intraperitoneally (US EPA, 2002).

The genotoxic potential of the chemical appears to depend on the competing processes of activation to a genotoxic form and metabolic inactivation (e.g., by conjugation). A minor oxidation pathway for the chemical leads to quinone-related reactive intermediates that bind covalently to protein and are detoxified by conjugation with glutathione.

Carcinogenicity

The chemical was not carcinogenic in rats and mice up to and including the highest dose tested (450 and 375 mg/kg bw/d). Based on the extensive use of the chemical over the years, there are no epidemiological data that reveals an association of exposure to the chemical with increased tumour rates in humans (ECB, 2006).

The International Agency for Research on Cancer (IARC) has evaluated the chemical as not classifiable for carcinogenicity to humans (Group 3) (IARC, 1999).

Reproductive and Developmental Toxicity

There is no evidence of reproductive toxicity. Developmental effects were only observed secondary to maternal toxicity, so the chemical does not show specific developmental toxicity.

In a two-generation (drinking water) reproductive performance and fertility toxicity study in Sprague Dawley (SD) rats (OECD TG 416), the chemical was administered continuously in drinking water at concentrations of 0, 200, 1,000 and 5,000 ppm (calculated to a mean daily uptake of 14.7/20.0, 70.9/93.0 and 301.0/320.5 mg/kg bw/day in males/females, respectively) (ECB, 2006). A NOAEL of 1,000 ppm (70/93 mg/kg bw/day in males/females) can be derived for maternal toxicity, based on reduced water intake, and body weight and organ weight impairment in the P0 and F1 animals at 5,000 ppm. There was no impaired reproductive capability and fertility in either sex up to the highest dose, and no chemical related specific developmental toxicity was noted. However, litter survival and offspring body weights were reduced during the period of lactation and pre-weaning in the 5,000 ppm groups across both generations, with the effects on litter survival more pronounced in the F2 generation. Further signs of impaired offspring development were observed during the study in P0 progeny and in F1 progeny. A NOAEL of 1,000 ppm (70/93 mg/kg bw/day in males/females) can also be derived for developmental toxicity, based on observed impaired development noted at the highest dose.

The chemical was further evaluated for maternal and developmental toxicity in rats and mice exposed through oral gavage. In a developmental toxicity study, the chemical was administered (gavage) at 60, 120 and 360 mg/kg bw/day during days 6–15 of gestation to SD rats (ECB, 2006). A maternal NOAEL of 60 mg/kg bw/day was derived from the study, based on reduced maternal weight gain during the treatment period at the next higher dose (120 mg/kg bw/day). A developmental NOAEL of 120 mg/kg body weight/day was also derived, based on indications of foetal growth retardation and slight ossification delay at the next higher dose (360 mg/kg bw/day).

In another developmental toxicity study, the chemical was administered (by gavage) to CD-1 mice at doses of 0, 70, 140, and 280 mg/kg bw/day during gestational days of 6–15. A maternal NOAEL of 140 mg/kg bw/day was derived from this study, based on significantly reduced mean gravid uterine weight at the next dose (280 mg/kg bw/day). A developmental NOAEL of 140 mg/kg bw/day was also derived from this study, based on significantly reduced average foetal body weight per litter and increase in cleft palate at the next higher dose.

Based on the above, a maternal NOAEL of 60 mg/kg bw/day and a developmental NOAEL of 93 mg/kg bw/day can be chosen for the chemical.

Other Health Effects

Neurotoxicity

In a neurotoxicity study, the chemical was administered to SD rats in drinking water for 13 weeks at concentrations of 200, 1000 or 5000 ppm (18/25, 83/107, and 308/360 mg/kg bw/day for males/females) (ECB, 2006). The motor activity test indicated a significant reduction in total group mean activity counts at weeks four and eight for the 5000 ppm females and also for females in the 1000 and 5000 ppm groups at week 17 during recovery. At week 13, total mean activity counts were significantly higher in 1000 and 5000 ppm females. The NOAEL for neurotoxicity was determined to be 200 ppm (18/25 mg/kg bw/d in males/females) in rats.

Although not reported in the above study, dysfunctions of the nervous system including tremor, convulsions, loss of coordination, paralysis, reduced motor and spontaneous activity, and reduced body temperature associated with the chemical have been reported in other studies (ECB, 2006).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation are systemic acute and repeated dose effects (by all routes of exposure), and local effects (skin corrosion, respiratory irritation and the possibility of causing serious damage to eyes).

Local exposure to the chemical may diminish the sensation of pain, possibly leading to less awareness and thus higher degrees of local damage.

Based on the available data, the chemical may be genotoxic in vivo under certain conditions, especially high doses, although genotoxicity is not anticipated at likely exposure levels.

Public Risk Characterisation

Although use in cosmetic and domestic products in Australia is not known, the chemical has reported cosmetic and domestic uses overseas, where the general public may be exposed to the chemical through dermal and/or inhalation routes.

In Australia, for industrial uses, the chemical is currently listed in Schedule 6 of the SUSMP for preparations containing greater than 3 %. At concentrations greater than 3 %, a number of first aid instructions and safety directions relating to skin and eye contact apply. The current schedule entry covers phenol and a number of substituted phenols.

Given that necrosis has been seen in humans following exposure to solutions as diluted as 1 %, the chemical may pose an unreasonable risk to public health, particularly in cosmetic products where the chemical is purposely applied to the skin. The risks could be mitigated by reducing the concentration limit permitted in products without the need for safety directions. Typically, the risk of systemic effects would also be reduced for products containing lower concentrations of the chemical.

Furthermore, as vapours can readily penetrate the skin surface, safety directions relating to the use of the chemical in the presence of adequate ventilation may also minimise risk associated with the use of products with higher phenol concentrations that come under Schedule 6.

The chemical is used in phenolic resins manufacturing that are used in consumer products. However, it is expected that only residual traces of the chemical would be present. Therefore, the risk to the public from exposure to the chemical from articles manufactured from phenolic resins is not considered to be unreasonable.

Occupational Risk Characterisation

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

Given the critical systemic long-term, acute and local health effects, the chemical may pose an unreasonable risk to workers unless adequate control measures to minimise dermal, ocular and inhalation exposure to the chemical 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 appropriate controls.

Based on the available data, the hazard classification in HSIS is considered appropriate.

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 cosmetics and/or domestic products be managed through changes to poisons scheduling.

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

It is recommended that an amendment to the current entry for the chemical in the SUSMP be considered. Given the risk characterisation, it is recommended that the chemical remain in Schedule 6, but the allowable concentration of the chemical in cosmetics/personal care products and domestic products be further restricted. The safety directions and warning statements should also be reviewed.

Consideration should be given to the following:

- although use in cosmetic and domestic products in Australia is not known, the chemical has reported cosmetic and domestic uses overseas;
- the chemical has been reported to cause poisoning in humans by ingestion, skin absorption, and by inhalation;
- necrosis of human skin has been reported at concentrations as low as 1 %;
- local exposure to the chemical may diminish the sensation of pain, possibly leading to less awareness and thus higher degrees of local damage; and
- Canada, New Zealand and the European Union have prohibited the use of this chemical in cosmetics.

Work Health and Safety

The chemical is recommended for classification and labelling under the current Approved Criteria for Classifying Hazardous Substances (Approved Criteria) and adopted Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below. This assessment does not consider classification of physical hazards and environmental hazards.

It is noted that the higher concentrations used in the studies leading to the higher classification for acute toxicity and local effects may not occur under current use scenarios.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Toxic if swallowed (T; R25)* Toxic in contact with skin (T; R24)* Toxic by inhalation (T; R23)*	Toxic if swallowed - Cat. 3 (H301) Toxic in contact with skin - Cat. 3 (H311) Toxic if inhaled - Cat. 3 (H331)
Irritation / Corrosivity	Causes burns (C; R34)*	Causes severe skin burns and eye damage - Cat. 1 (H314)
Repeat Dose Toxicity	Danger of serious damage to health by prolonged exposure (Xn; R48)*	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)

[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 chemical should be used according to label instructions.

Advice for industry

Control measures

Control measures to minimise the risk from dermal, ocular, 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 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.

References

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