Phenylmercury compounds: Human health tier II assessment

03 July 2015

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Mercury, (acetato-O)phenyl-	62-38-4
Mercury, (benzoato-O)phenyl-	94-43-9

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

These chemicals are assessed together as they are structurally related, being carboxylates of the phenylmercury moiety. Available data for phenylmercuric acetate are assumed to be relevant to phenylmercuric benzoate. Phenylmercuric salts are rapidly metabolised to phenylmercuric ions and mercury (II) ions upon absorption, and can be metabolised further via oxidation-reduction, to elicit their toxic effects (ATSDR, 1999).

Import, Manufacture and Use

Australian

The following non-industrial use has been identified for phenylmercuric acetate:

- an approved active constituent in agricultural or veterinary chemical products (the Australian Pesticides and Veterinary Medicines Authority—APVMA) as at 19 February 2014.

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

International

The following international uses have been identified through Galleria Chemica: the Substances and Preparations in Nordic countries (SPIN) database; 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 US Environmental Protection Agency's (EPA) Aggregated Computer Toxicology Resource (ACToR); and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

Phenylmercuric acetate and phenylmercuric benzoate have reported cosmetic use as preservatives in eye products.

Phenylmercuric acetate has reported site-limited use as a catalyst.

Phenylmercuric acetate has reported non-industrial uses as:

- a water treating agent;
- an active ingredient in fungicide, herbicide, mildewcide or slimicide preparations for paper mills and paints;
- a pesticide active ingredient; and
- an ingredient in ophthalmic ointments and topical emulsions/creams.

Restrictions

Australian

Phenylmercuric acetate is listed in Schedule 7 of the *Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP):

'Phenylmercuric acetate **except** in preparations containing 0.01 per cent or less of mercury as a preservative' (SUSMP, 2015).

There is also a general entry for mercury in Schedule 7 of the SUSMP, and this applies to phenylmercuric benzoate:

'MERCURY **except**:

(a) when separately specified in this Schedule;

(b) when included in Schedule 2, 4 or 6;

(c) in preparations containing 0.01 per cent or less of mercury in organic form as a preservative;

(d) mercury (metallic) in scientific instruments;

(e) dental amalgams; or

(f) in a sealed device, for therapeutic use, which prevents access to the mercury' (SUSMP, 2015).

Schedule 7 chemicals are described as 'Substances with a high potential for causing harm at low exposure and which require special precautions during manufacture, handling or use. These poisons should be available only to specialised or authorised users who have the skills necessary to handle them safely.

Special regulations restricting their availability, possession, storage or use may apply' (SUSMP, 2015).

International

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

A. United Nations Minamata Convention on mercury 'to protect human health and the environment from anthropogenic emissions and releases of mercury and mercury compounds';

B. Rotterdam Convention Annex III—Chemicals subject to the prior informed consent procedure (under the entry 'Mercury compounds, including inorganic mercury compounds, alkyl mercury compounds and alkyloxyalkyl and aryl mercury compounds');

C. Council of Europe Resolution ResAP(2008)1 on requirements and criteria for the safety of tattoos and permanent make-up (PMU), Table 3: Maximum allowed concentrations of impurities in products for tattoos and PMU (limit of 0.2 ppm of mercury);

D. European Union (EU) Cosmetics Regulation 1223/2009 Annex V—List of preservatives allowed in cosmetic products (under the entry 'Phenylmercuric salts (including borates)' with the condition 'If mixed with other mercurial compounds authorised by this Regulation, the maximum concentration of Hg remains fixed at 0,007 %'); and

E. Annex XVII to the REACH Regulations

- Phenylmercuric acetate is not to be manufactured, placed on the market or used as a substance, or in mixtures, in articles or parts of articles if the concentration of mercury is equal to or greater than 0.01% by weight;
- Phenylmercuric benzoate is covered by the entry for organic compounds of mercury—Mercury compounds 'Shall not be placed on the market, or used, as substances or in mixtures where the substance or mixture is intended for use:

  (a) to prevent the fouling by micro-organisms, plants or animals of

  - the hulls of boats,
  - cages, floats, nets and any other appliances or equipment used for fish or shellfish farming,
  - any totally or partly submerged appliances or equipment;

  (b) in the preservation of wood;

  (c) in the impregnation of heavy-duty industrial textiles and yarn intended for their manufacture;

  (d) in the treatment of industrial waters, irrespective of their use'.

Phenylmercuric acetate is also listed on the following (Galleria Chemica):

- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient ‘Hotlist’);
- EU Cosmetics Regulation 1223/2009 Annex II—List of substances prohibited in cosmetic products (under the entry 'Mercury and its compounds, except those special cases included in Annex V');
- Association of Southeast Asian Nations (ASEAN) Cosmetic Directive Annex II, Part 1: List of substances which must not form part of the composition of cosmetic products (under the entry 'Mercury and its compounds except those special cases included in Annex VI, Part 1');
- ASEAN Cosmetic Directive Annex VI, Part 1: List of preservatives allowed for use in cosmetic products (under the entry 'Phenylmercuric salts (including borates)', for eye make-up and eye make-up remover only, with the condition of 'If mixed with other mercurial compounds authorized by this Directive, the maximum concentration of Hg remains fixed at 0,007 %');
- New Zealand Cosmetic Products Group Standard—Schedule 4: Components cosmetic products must not contain (under the entry 'Mercury and its compounds, except those special cases included in Schedule 7');
- New Zealand Cosmetic Products Group Standard—Schedule 7: Preservatives cosmetic products may contain with restrictions, Table 1: List of preservatives allowed (under the entry 'Phenylmercuric salts (including borates)', for eye make-up and eye make-up remover only, with the condition of 'If mixed with other mercurial compounds authorized by this Directive, the maximum concentration of Hg remains fixed at 0,007 %'); and
- Council of Europe Resolution AP (92) 2 on control of aids to polymerisation for plastic materials and articles—Limits for finished articles (limit of 0.005 mg/kg mercury compounds (as Hg)).

Existing Worker Health and Safety Controls

Hazard Classification

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

- T; R25 (acute toxicity)
- T; R34 (corrosive)

- T; R48/24/25 (repeat dose toxicity)

Phenylmercuric benzoate is not specifically listed in the HSIS. The entries 'Mercury aryl compounds (as Hg) with the exception of those elsewhere specified' and 'Mercury, organic compounds with the exception of those specified elsewhere in HSIS' apply to phenylmercuric benzoate and have the following risk phrases for human health:

- T+ R26/27/28 (acute toxicity)
- R33 (cumulative effects)

Exposure Standards

Australian

The entry for 'Mercury, aryl compounds (as Hg)' applies to phenylmercuric acetate and phenylmercuric benzoate, with an exposure standard of 0.1 mg/m^3 time weighted average (TWA). This exposure standard is accompanied by a skin absorption (Sk) notation, stating that 'absorption through the skin may be a significant source of exposure' (HSIS, Safe Work Australia).

International

The following exposure standards are identified (Galleria Chemica).

Phenylmercuric acetate and phenylmercuric benzoate (mercury as aryl compounds) have:

- an exposure limit of 0.01–0.1 mg/m^3 TWA in different countries such as Canada (Alberta, British Columbia, Quebec, Saskatchewan), Malaysia, Mexico, Singapore, Spain and the USA (California); and
- a short-term exposure limit (STEL) of 0.3 mg/m^3 in Canada (Saskatchewan).

Health Hazard Information

When data for phenylmercuric benzoate are not available, data for phenylmercuric acetate are considered appropriate from which to read across since the chemicals are structurally related.

The IMAP reports on (elemental) mercury (NICNASa) and mercuric sulfate (NICNASb) complement this report.

Toxicokinetics

Mercury is a naturally occurring element and can exist in elemental, organic or inorganic forms, commonly as salts. Phenylmercuric acetate and phenylmercuric benzoate are structurally related, as they are both organic aryl mercury compounds. Organic mercury can be converted to inorganic divalent mercury (mercury (II) ions), but to a lesser extent than elemental mercury (ATSDR, 1999).

Organic mercury compounds are lipid-soluble and easily absorbed (90–100 %) via oral exposure. Absorption can involve binding to biological molecules (e.g. proteins) within the gastrointestinal tract, and this can also facilitate their mechanism of toxicity. In rodents, phenylmercuric salt administered in the diet was reported to be completely absorbed in mice and readily absorbed in rats (ATSDR, 1999).

Respiratory and dermal absorption data are limited. Some indirect evidence (radiolabelled dimethyl-mercury being excreted in two phases following inhalation exposure) suggests that organic mercury is readily absorbed via the lungs. Infants (n = 509) exposed to nappies contaminated with phenylmercuric acetate (used as a fungicide to disinfect the nappies) had a total urinary excretion of mercury that was 20 times higher than that of 166 matched controls. In rats exposed to phenylmercuric acetate (dose not available), there was 75 % absorption from the vaginal tract within eight hours of administration (IARC, 1993; ATSDR, 1999).

Organic mercury compounds are distributed throughout the body, including the brain and foetus (if relevant), but the organs with the greatest mercury accumulation are the kidneys and the liver. Uniform tissue distribution of the chemicals is due to their lipophilicity, and blood levels are a good representation of tissue concentrations (ATSDR, 1999).

Phenylmercury compound metabolism is rapid. The benzene ring is hydroxylated to an unstable metabolite that releases inorganic divalent mercury. This was confirmed in rats exposed to phenylmercuric acetate via intraperitoneal injection, where it was rapidly metabolised to inorganic divalent mercury. Organic mercury compounds are primarily excreted in the faeces (through bile) in humans, and mostly as the inorganic form. In animals, faecal excretion occurs initially, followed by excretion in the urine of the parent compound and then as inorganic mercury. In rats that were administered phenylmercuric acetate at 0.120 mg mercury/kg bw as a single oral or intravenous dose, 65 % of an oral dose and 30 % of an intravenous dose was excreted in the faeces within 48 hours of administration (IARC, 1993; ATSDR, 1999).

Acute Toxicity

Oral

Phenylmercuric acetate is classified as hazardous with the risk phrase 'Toxic if swallowed' (T; R25) in the HSIS (Safe Work Australia). Aryl and organic mercury compounds (which includes phenylmercuric benzoate) are classified as hazardous with the risk phrase 'Very toxic if swallowed' (T+; R28) in the HSIS (Safe Work Australia). The available data support the higher classification (T+; R28) for phenylmercuric acetate. Although there is an absence of data for phenylmercuric benzoate, considering the similar structure and metabolism of both chemicals, this classification is also supported for phenylmercuric benzoate (see **Recommendation** section).

The following oral median lethal dose (LD50) values were available for phenylmercuric acetate (HSDB; RTECS):

- 22 and 41 mg/kg bw in rats; and
- 13.25 mg/kg bw in mice.

Dermal

Aryl and organic mercury compounds (including phenylmercuric benzoate) are classified as hazardous with the risk phrase 'Very toxic in contact with skin' (T+; R27) in the HSIS (Safe Work Australia). No data are available to evaluate or to support a recommendation to amend this classification, apart from indications that they are readily absorbed from dermal exposure. Although there is an absence of data for both chemicals, considering their similar structure and metabolism, this classification is also supported for phenylmercuric acetate (see **Recommendation** section).

Inhalation

Aryl and organic mercury compounds (including phenylmercuric benzoate) are classified as hazardous with the risk phrase 'Very toxic by inhalation' (T+; R26) in the HSIS (Safe Work Australia). No data are available to evaluate or to support a recommendation to amend this classification, apart from indications that they are readily absorbed from the lungs. Although there is an absence of data for both chemicals, considering their similar structure and metabolism, this classification is also supported for phenylmercuric acetate (see **Recommendation** section).

Corrosion / Irritation

Corrosivity

Phenylmercuric acetate is classified as hazardous with the risk phrase 'Causes burns' (C; R34) in the HSIS (Safe Work Australia). Only limited data are available to support this classification. In the absence of any data for phenylmercuric benzoate, but considering the similar structure and metabolism of both chemicals, this classification is also supported for phenylmercuric benzoate (see **Recommendation** section).

Mice (strain and number not specified) were injected subcutaneously with a 1 mg/ mL solution of phenylmercuric acetate. Extensive and severe necrosis of the skin was reported, and the experiment was terminated due to animal welfare concerns (ECHA, 2011).

Corrosive chemicals are also considered to cause irreversible effects on the eyes. The available eye irritation data for phenylmercuric acetate support this finding. In a Draize test in rabbits, ocular exposure to 50 µg of phenylmercuric acetate for 24 hours caused a severe reaction (RTECS). No further details were available.

Observation in humans

In a Draize test in humans, dermal exposure to 100 µg of phenylmercuric acetate for 24 hours caused a severe reaction (RTECS). No further details were available.

Sensitisation

Skin Sensitisation

No animal data are available.

Observation in humans

The data available on phenylmercuric acetate are insufficient to make a conclusion on the skin sensitisation potential of these chemicals.

The human data available are inconclusive (ECHA, 2011). A case study was reported in a 54-year-old female farmer with a 20-year history of eczema on both hands, a genetic predisposition to hypersensitivity reactions (atopic condition), and periodic mild facial swelling with or without rhinoconjunctivitis and asthma in the previous two years. She had prior exposure to phenylmercuric acetate in her workplace. In an open test on her back, a 0.01 % solution of phenylmercuric acetate was applied. Erythema was observed 30 minutes after application, urticaria (skin rash) 60 minutes after application and these effects were both associated with her previously reported symptoms of facial swelling, allergy and asthma. However, the results of an open test with phenylmercuric acetate were negative in three healthy control subjects (ATSDR, 1999; ECHA, 2011).

In an epidemiological study, patch test results from 49256 patients examined in muliple centres from Germany and Austria were assessed for reactions to phenylmercuric acetate exposure at 0.05 %. Patients were previously diagnosed with allergic periorbital contact dermatitis (APD), non-APD (NAPD) and other cases (OC) of dermatitis. The incidence of positive reactions was 9.2 % of the APD patients, 5 % of the NAPD patients and 6.7 % of the OC patients. It was reported that the incidence of positive reactions in APD patients was significantly higher than that in OC patients (ECHA, 2011).

In two separate patch tests, 1151 and 1927 patients with suspected exposure to allergens or with chronic eczema, respectively, were exposed to 0.05 % of phenylmercuric acetate. In the first study 14 % of patients had a positive response, and in the second study 3.1 % of patients had a positive response, indicating potential sensitisation to phenylmercuric acetate in those patients, prior to testing (ECHA, 2011).

A four-year-old male child was diagnosed with acrodynia (childhood allergic reaction to mercury) following exposure for approximately one month to phenylmercuric acetate (measured at 930–955 ppm mercury) as mercury vapours released from his newly painted home. The condition included pain and weakness in the extremities (arms and legs); rash, itching, peeling and redness of the hands, feet and nose; tachychardia and hypertension (ATSDR, 1999).

Repeated Dose Toxicity

Oral

Phenylmercuric acetate is classified as hazardous with the risk phrase 'Toxic: Danger of serious damage to health by prolonged exposure if swallowed' (T; R48/25) in the HSIS (Safe Work Australia). The available data support this classification. Although there is an absence of data for phenylmercuric benzoate, considering the similar structure and metabolism of both chemicals, this classification is also supported for phenylmercuric benzoate (see **Recommendation** section).

In a 2-year study, rats (strain not specified; n = 10–24/dose/sex) were administered phenylmercuric acetate in the diet at 0, 0.1, 0.5, 2.5, 10, 40 or 160 ppm (measured as mercury). The no observed adverse effect level (NOAEL) was 0.1 ppm mercury (equivalent to 0.0084 mg mercury/kg bw/day), based on kidney damage (hypertrophy of the proximal convoluted tubules and ultimately enlarged, fibrous kidneys) in female rats receiving 0.5 ppm mercury (equivalent to 0.042 mg/kg bw/day phenylmercuric acetate). Kidney damage was observed in all rats that received ≥2.5 ppm mercury. Other effects included growth retardation in male rats that received 10 ppm mercury and in all rats that received ≥40 ppm mercury (ATSDR, 1999; US EPA IRIS).

In a two-year study in Wistar rats (n = 20/dose, sex not specified), animals were administered phenylmercuric acetate at 0–4.2 mg mercury/kg bw/day (specific doses not provided) in drinking water. The lowest observed adverse effect level (LOAEL) was 0.4 mg/kg bw/day, based on degeneration of the kidney tubules (nephrosis). Lower doses were not tested, and so an NOAEL could not be derived. A 10 % decrease in body weight was reported for rats administered mercury at 0.4 mg/kg bw/day. Ulcers and necrosis of the large intestine (caecum) were observed in rats administered mercury at 4.2 mg/kg bw/day, and blood loss associated with these lesions caused anaemia (reduced haemoglobin, haematocrit and red blood cell counts) (ATSDR, 1999).

Based on the NOAEL reported above, the reference dose for chronic oral exposure (RfD) to phenylmercuric acetate in humans was derived as 0.08 µg/kg bw/day (US EPA IRIS).

Dermal

Phenylmercuric acetate is classified as hazardous with the risk phrase 'Toxic: Danger of serious damage to health by prolonged exposure in contact with skin' (T; R48/24) in the HSIS (Safe Work Australia).

No data are available to evaluate or to support a recommendation to amend this classification, apart from indications that the chemicals are readily absorbed through the dermal exposure. Some inorganic mercury compounds (NICNASb) are also classified for repeated dose dermal toxicity. Although there is an absence of data for phenylmercuric benzoate, considering the similar structure and metabolism of both chemicals, this classification is also supported for phenylmercuric benzoate (see **Recommendation** section).

Inhalation

No data are available.

Observation in humans

A 39-year-old male farmer who was exposed to phenylmercuric acetate (dose not reported) for 6–7 seasons (years) when treating grain seeds, showed severe neurotoxicity which resulted in death. He also had a swollen mouth, gum disease, cavities and an infected pharynx. Purulent bronchopneumonia was observed at autopsy, although it was unclear whether these respiratory effects were primarily due to the chemical exposure or secondary to severe neurotoxicity (ATSDR, 1999).

Five other farmers with similar exposure patterns were reported to have motor disabilities (HSDB) (see **Other Health Effects: Neurotoxicity** for classification).

Genotoxicity

Limited data are available for phenylmercuric acetate and no data are available for phenylmercuric benzoate. While the data are largely positive, confounding factors cannot be ruled out in some studies. Therefore the available data are insufficient to make a conclusion on the genotoxicity of these chemicals.

In a rec-assay using *Bacillus subtilis*, phenylmercuric acetate induced cell death at 200 µg/mL, but not at 12 µg/mL (IARC, 1993), indicating a potential for phenylmercuric acetate to damage DNA at high concentrations.

In vivo genotoxicity tests with phenylmercuric acetate were mostly positive:

- aneuploidy was induced in *Drosophila melanogaster* exposed at 0.32 mg/kg bw (IARC, 1993);

- sex-linked recessive lethal mutations (but not dominant lethal mutations) were induced in *D. melanogaster* exposed to the fungicide Ceresan (reported to contain 1 % mercury as phenylmercuric acetate) at 200 mg/kg bw in the diet (IARC, 1993); and
- Swiss mice that received the chemical once at 2, 5 or 10 mg/kg bw showed high clastogenicity (chromosome damage) in bone marrow cells 24 hours after exposure (no details provided). In male germ cells, asynapsis/desynapsis and reciprocal translocations were reported in primary spermatocytes four weeks after exposure, and at eight weeks after exposure there were high percentages of abnormal sperm (HSDB).

In humans (n = 8), increased incidence of aneuploidy was reported in lymphocytes exposed to phenylmercury compounds (not specified). Chromosomal aberrations (increased incidence of hyperploidy) were observed in lymphocytes of 16 workers exposed to phenylmercuric acetate, compared with controls. However, details on the exposure to other agents were lacking in both reports, confounding the validity of these outcomes (IARC, 1993).

Increased sister chromatid exchange (SCE) rates were reported in lymphocytes of 38 children (aged one month to five years) exposed to nappies contaminated with phenylmercuric acetate (used as a disinfectant), compared with 19 unexposed children. The increased SCE rate was not measurable nine months after the exposure ended (IARC, 1993).

Carcinogenicity

Limited data are available for phenylmercuric acetate and no data are available for phenylmercuric benzoate. The available data are insufficient to make a conclusion on the carcinogenicity of these chemicals.

The International Agency for Research on Cancer (IARC) has reported that 'there is inadequate evidence in humans for the carcinogenicity of mercury and mercury compounds' (IARC, 1993).

In a two-year study, male Wistar rats that were exposed to mercury at 0–4.2 mg/kg bw/day as phenylmercuric acetate in drinking water had a significant increase in renal cell adenomas at the highest dose. No tumours were reported in another two-year study in rats exposed to mercury at 0–66 mg/kg bw/day as phenylmercuric acetate in the diet. Both studies were not designed to assess carcinogenicity as they used inadequate numbers of animals in the dose groups. Survival rates were not available and histopathological data were limited (ATSDR, 1999).

Reproductive and Developmental Toxicity

Limited data are available for phenylmercuric acetate and no data are available for phenylmercuric benzoate. The available data are insufficient to make a conclusion on the reproductive or developmental toxicity of these chemicals.

In rats, administration of phenylmercuric acetate (0.1 mg) via a vaginal tablet on gestation day (GD) seven resulted in tail and neural tube abnormalities in offspring (HSDB).

In golden hamsters, rats and rabbits, phenylmercuric acetate administered at doses ranging from one-sixth to half of the oral LD50 (actual doses not available) via a stomach tube on GD 5–12 resulted in embryotoxicity (resorption, death and developmental delays) and teratogenicity (decreased skull ossification, swollen body, haematomas and open eyes) (HSDB).

In hamsters, a single intravenous injection of phenylmercuric acetate at 5–10 mg/kg bw on GD 8 resulted in increased rates of resorption and teratogenic effects such as cleft palate and exencephaly (foetal brain outside the skull) (ATSDR, 1999).

Children born to 889 women who had previously used phenylmercuric acetate as a spermicide did not have increased rates of developmental defects compared with children whose mothers had not been exposed to phenylmercuric acetate spermicide (HSDB).

Other Health Effects

Neurotoxicity

Aryl and organic mercury compounds (which includes phenylmercuric benzoate) are classified as hazardous with the risk phrase ‘Danger of cumulative effects' (R33) in the HSIS (Safe Work Australia). Only limited data are available for phenylmercuric acetate to support this classification. In the absence of more comprehensive information for both chemicals, but considering their similar structure and metabolism, this classification is supported for both chemicals (see **Recommendation** section).

Organic aryl mercury compounds, such as phenylmercuric acetate and phenylmercuric benzoate, are lipophilic and can therefore cross the blood-brain barrier. Mercury is retained in the brain more than other organs, with mercury ions becoming oxidised and trapped. This can result in severe neurotoxicity with prolonged or repeated exposure, as the level of mercury accumulates over time, damaging the brain (ATSDR, 1999).

Progressive neurotoxicity resembling amyotrophic lateral sclerosis (also known as Lou Gehrig’s disease and characterised by muscle weakness, paralysis and respiratory failure) was reported in a 39-year-old male farmer who died following exposure to phenylmercuric acetate (dose not available) for 6–7 seasons (years) when treating grain seeds with the chemical. Motor disabilities were reported in five other farmers with similar exposure (ATSDR, 1999; HSDB).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include acute toxicity from all routes of exposure as well as renal and cumulative neurotoxic effects following repeated exposure from any route. The chemicals can also cause corrosivity.

No conclusive data are available on genotoxicity, carcinogenicity or reproductive and developmental toxicity.

Public Risk Characterisation

Although use in cosmetic products in Australia is not known, the chemicals are reported to be used in cosmetic products overseas at concentrations up to 0.007 %.

Phenylmercuric acetate is currently listed on Schedule 7 of the SUSMP, except for use in preparations to 0.01 % or less of mercury as a preservative. There is also a general entry for mercury in Schedule 7 covering organic mercury compounds, with some exceptions (e.g. 'in preparations containing 0.01 % or less of mercury in organic form as a preservative') (SUSMP, 2015).

The current controls are considered adequate to minimise the risk to public health posed by any cosmetic use of these chemicals as preservatives. Therefore, the chemicals are not considered to pose an unreasonable risk to public health.

Occupational Risk Characterisation

Given the critical health effects, the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise oral, dermal and inhalation exposure are implemented. The chemicals 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) to extend the classification of phenylmercuric acetate to phenylmercuric benzoate, and to incorporate the generic classification for aryl and organic mercury compounds to both chemicals in this group (see **Recommendation** section).

NICNAS Recommendation

Assessment of these chemicals is considered to be sufficient, provided that the recommended amendment to the classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Public Health

Products containing the chemicals should be labelled in accordance with state and territory legislation (SUSMP, 2015).

Work Health and Safety

Both chemicals are recommended for classification and labelling under the current approved criteria and adopted GHS as below. Phenylmercuric benzoate should be listed separately from the general aryl or organic mercury compound entries, to specify the extra classifications relevant to this chemical based on the structural similarity to phenylmercuric acetate.

This assessment does not consider classification of physical and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Very toxic if swallowed (T+; R28) Very toxic in contact with skin (T+; R27) Very toxic by inhalation (T+; R26)	Fatal if swallowed - Cat. 2 (H300) Fatal in contact with skin - Cat. 1 (H310) Fatal if inhaled - Cat. 1 (H330)
Irritation / Corrosivity	Causes burns (C; R34)	Causes severe skin burns and eye damage - Cat. 1C (H314)
Repeat Dose Toxicity	Toxic: Danger of serious damage to health by prolonged exposure in contact with skin (T; R48/24) Toxic: Danger of serious damage to health by prolonged exposure if swallowed (T; R48/25)	Causes damage to organs through prolonged or repeated exposure through the dermal route - Cat. 1 (H372) Causes damage to organs through prolonged or repeated exposure if swallowed - Cat. 1 (H372)

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Other Health Effects	Danger of cumulative effects (R33)	Causes damage to organs through prolonged or repeated exposure - Cat. 1 (H372)

[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 instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from oral, dermal and inhalation 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 chemicals are used. Examples of control measures which could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemicals from entering the breathing zone of any worker;
- 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 chemicals.

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 chemicals 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 these chemicals has not been undertaken as part of this assessment.

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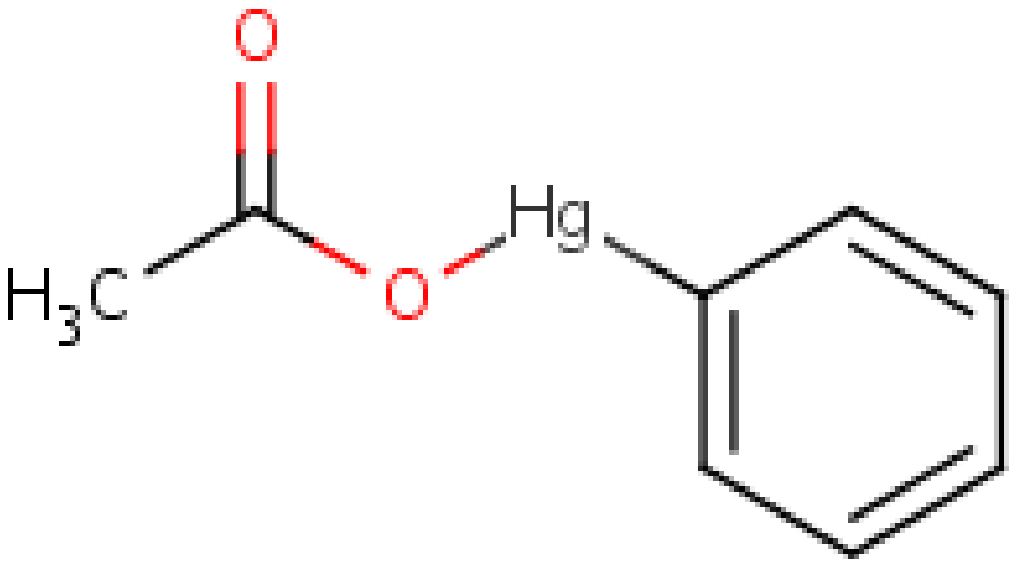
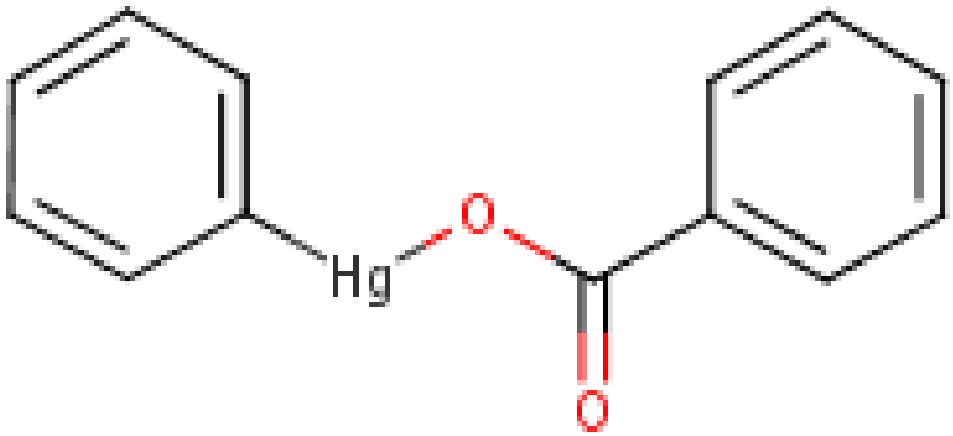
Last Update 03 July 2015

Chemical Identities

Chemical Name in the Inventory and Synonyms	**Mercury, (acetato-O)phenyl-** phenylmercuric acetate (acetato)phenylmercury acetic acid, phenylmercury (II) salt acetoxyphenylmercury
CAS Number	62-38-4
Structural Formula	

	
Molecular Formula	C8H8HgO2
Molecular Weight	336.74

Chemical Name in the Inventory and Synonyms	**Mercury, (benzoato-O)phenyl-** phenylmercuric benzoate phenylmercury benzoate
CAS Number	94-43-9
Structural Formula	

	
Molecular Formula	C13H10HgO2
Molecular Weight	398.91

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