Mercury: 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	elemental mercury metallic mercury colloidal mercury hydrargyrum quicksilver
Structural Formula	
Molecular Formula	Hg
Molecular Weight (g/mol)	200.59
Appearance and Odour (where available)	Silver-white, heavy, mobile, liquid metal with no odour
SMILES	[Hg]

Import, Manufacture and Use

Australian

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

The chemical has reported commercial use in batteries for hearing aids, calculators and watches.

The total volume introduced into Australia, reported under previous mandatory and/or voluntary calls for information, was <100 tonnes.

The National Pollutant Inventory (NPI) holds data for all sources of the chemical in Australia and has listed the following uses.

The chemical has reported commercial uses (generally in articles) including in:

- batteries;
- thermometers and barometers;
- thermostats; and

- floodlights, streetlights or other powerful outdoor lights.

The chemical has reported site-limited uses including:

- as a catalyst in chemical manufacturing; and
- to extract gold and silver ores in mining.

The chemical has reported non-industrial use in dental amalgams.

International

The following international uses have been identified through the European Union (EU) Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) dossiers; Galleria Chemica; the Substances and Preparations in Nordic countries (SPIN) database; the United States (US) Environmental Protection Agency's (EPA) Aggregated Computer Toxicology Resource (ACToR); and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemical has reported cosmetic uses in kohl and henna products.

The chemical has reported domestic and/or commercial uses including in:

- tile adhesives;
- coloured quick-setting concrete;
- thermometers and thermostats;
- fluorescent light tubes;
- electric switches;
- religious rituals;
- batteries;
- pyrotechnic initiators;
- construction materials; and
- dyestuffs and pigments.

The chemical has reported site-limited uses including:

- in manufacturing metal products (e.g. machinery);
- in manufacturing precision medical and optical instruments;
- in waste recovery;
- producing other chemicals (e.g. phenylmercury carboxylates, dental amalgam);
- as a cathode in chloroalkali electrolysis; and
- as a neutron absorber in nuclear power plants.

The chemical has reported non-industrial uses in:

- dental amalgams;
- pharmaceuticals;
- pesticides; and
- anti-fouling agents.

There is difficulty in establishing actual uses for the chemical as some of the reported uses (e.g. in cosmetics or adhesives) relate to mercury compounds rather than to elemental mercury.

Restrictions

Australian

This chemical is listed in the *Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) in Schedules 2, 4 and 7 (SUSMP, 2015).

Schedule 2:

'MERCURY for external use in preparations containing 0.5 per cent or less of mercury.'

Schedule 4:

'MERCURY for cosmetic or therapeutic use **except**:

(a) when separately specified in these Schedules; or

(b) in a sealed device which prevents access to the mercury.'

Schedule 7:

'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.'

The Schedule 6 entry above refers to specific mercury compounds and does not relate to elemental mercury.

Schedule 2 chemicals are described as 'Substances, the safe use of which may require advice from a pharmacist and which should be available from a pharmacy or, where a pharmacy service is not available, from a licensed person' (SUSMP, 2015).

Schedule 4 chemicals are described as 'Substances, the use or supply of which should be by or on the order of persons permitted by State or Territory legislation to prescribe and should be available from a pharmacist on prescription' (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

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

- United Nations Minamata Convention on mercury 'to protect human health and the environment from anthropogenic emissions and releases of mercury and mercury compounds';
- 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');
- 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;
- 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 mercury);
- EU Cosmetics Regulation 1223/2009 Annex II—List of substances prohibited in cosmetic products;
- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient ‘Hotlist’);
- New Zealand Cosmetic Products Group Standard—Schedule 4: Components cosmetic products must not contain;
- Canada Consumer Product Safety Act, Toys Regulations—Toxicological Hazards— Specific substances in surface coatings ('The surface coating material that is applied to a toy must not contain any of the following substances: a compound of mercury introduced as such'); and

- Europe Directive 2009/48/EC of the European Parliament and of the Council on the safety of toys—Maximum Migration Limits (limit of 7.5, 1.9 or 94 mg/kg mercury in dry, liquid or scraped-off toy material, respectively).

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+; R26 (acute toxicity)
- T; R48/23 (repeated dose toxicity)
- R61 Repr. Cat 2 (reproductive toxicity)

Exposure Standards

Australian

The chemical mercury (elemental vapour, as Hg) has an exposure standard of 0.025 mg/m^3 (0.003 ppm) time weighted average (TWA).

International

The following exposure standards are identified (Galleria Chemica):

- a TWA of 0.02–0.05 mg/m^3 in different countries such as Bulgaria, Canada (British Columbia, Quebec, Saskatchewan), China, Germany, Japan, Philippines, Singapore, South Africa, Sweden, Taiwan and the USA (California); and
- a short-term exposure limit (STEL) of 0.04–0.075 mg/m^3 in Canada and China.

Health Hazard Information

The IMAP reports on (organic) phenylmercury compounds (NICNASa) and mercuric sulfate (NICNASb) complement this report.

Toxicokinetics

Inhalation is the primary route of exposure for elemental mercury and approximately 80 % is rapidly absorbed through the alveolar membrane of the lungs by diffusion. Exposure to elemental mercury vapour ultimately results in approximately 97 % absorption via inhalation and approximately 3 % absorption via the skin. There is minimal absorption of liquid elemental mercury following oral exposure, most likely due to its conversion to divalent mercury and binding with sulfhydryl groups on proteins, or sloughing of the gastrointestinal tract lining containing bound mercury. In human case studies, single ingestions of approximately 15 mL (204 g) or 220 mL (3000 g) of liquid mercury did not cause any long-term toxicity, indicating that the oral absorption is low, for example in comparison with mercuric sulfate (NICNASb). However, chronic oral exposure to elemental mercury can lead to toxicity. Dermal absorption of elemental mercury can occur if it is applied in particular forms, e.g. as an ointment (HSE, 1995; IPCS, 1996; ATSDR, 1999; WHO, 2003).

Elemental mercury is lipid soluble, and can be distributed throughout the body, mainly accumulating in the brain and kidneys. Maximum levels occur within 24 hours of exposure for all organs except the brain, where the peak is within 2–3 days. Elemental mercury vapour reaches the brain before it is oxidised and is retained in the brain to a greater extent than other organs following oxidation. Mercury can also cross the placental–foetal barrier, and in neonates the chemical accumulates in organs that are highly perfused (e.g. heart, lungs and brain) (IPCS, 1996; ATSDR, 1999; WHO, 2003).

Elemental mercury dissolves in the blood. Dissolved elemental mercury and absorbed elemental mercury vapour are metabolised by oxidation. Oxidation of the chemical occurs primarily in the red blood cells, converting it to the inorganic divalent form. Oxidation can also occur in the brain, lungs and liver. Divalent cations can be reduced to the monovalent form, and be exhaled or re-oxidised. Divalent cations exist in an equilibrium between diffusible and non-diffusible forms. The diffusible form exists in blood and the non-diffusible form is protein-bound, in high molecular weight complexes found in organs (HSE, 1995; ATSDR, 1999; WHO, 2003).

Elimination and excretion of the chemical is mainly via the urine, faeces and exhalation. Sweat and saliva, in small proportions, also contribute to the elimination of mercury (WHO, 2003).

Conversion of elemental (inorganic) mercury to methylmercury has been reported to occur in vitro using human and rat intestinal microflora, as well as human oral bacteria (Rowland et al., 1975; Rowland et al., 1977; Heintze et al., 1983). There is limited evidence for mercury biotransformation in mammals. In guinea pigs (n = 18 males) administered mercuric chloride by subcutaneous injection at 0.6 mg mercury/kg bw for nine doses on alternate days, mercury methylation was reported to have occurred because 35–50 % of the total mercury measured in nine tissues (details not available) collected at the end of the study was methylmercury (Zorn & Smith, 1989).

In two case studies in humans, with intentional ingestion of a large volume (details not available) of mercuric chloride solution by a male, or dermal application of an ointment containing excess mercury bromide (due to incorrect formulation) by a female, mercury methylation was reported in the former instance only, as measured by methylmercury in liver and blood samples collected at autopsy (Triufante et al., 2009).

In a study in chloroalkali workers (n = 22 workers and n = 22 matched controls) exposed to inorganic mercury, erythrocyte methylmercury concentrations were similar, despite elevated urine, plasma and erythrocyte mercury concentrations in workers compared with controls (Barregard et al., 1994).

Acute Toxicity

Oral

No data are available.

Dermal

No data are available.

Inhalation

The chemical is classified as hazardous with the risk phrase ‘Very toxic by inhalation’ (T+; R26) in the HSIS (Safe Work Australia). The available data support this classification.

The median lethal concentration (LC50) in male Wistar rats exposed (whole body) to mercury vapours for two hours was <27 mg/m^3 (0.027 mg/L). Reported signs of toxicity included dyspnoea (laboured breathing) and asphyxia (suffocation) (ATSDR, 1999; REACH). Considering the standard acute inhalation toxicity test has a four-hour duration, the LC50 for four hours can be calculated to be approximately 0.014 mg/L.

Observation in humans

In case studies of oral exposure to elemental mercury, single ingestions of approximately 15 mL (204 g) or 220 mL (3000 g) of liquid mercury did not cause any toxicity. Elevated blood and urine mercury levels in the latter case returned to within the normal range by 10 months after exposure, and it was estimated that the majority of the mercury had been excreted in the faeces within 2–3 weeks (ATSDR, 1999).

In case studies, acute inhalation exposure to high levels (doses and duration not available) of elemental mercury vapour has resulted in death due to respiratory failure. Other signs of acute inhalation toxicity included stomatitis (inflammation of the oral cavity), abdominal pains, nausea, vomiting and diarrhoea (ATSDR, 1999).

In a group of workers (n = 6 males) exposed to elemental mercury vapours at up to approximately 44 mg/m^3 for 4–8 hours during an industrial accident, acute symptoms were reported which included chest pains, dyspnoea (breathlessness), cough with blood or bloody sputum, and pneumonitis. Chronic effects that lasted several years after the single exposure during the accident were also reported and included anxiety and irritability, reduced libido, fatigue and dental disease (HSE, 1995; ATSDR, 1999).

In maintenance workers at a chloroalkali plant (n = 53 males) exposed to extremely high concentrations of elemental mercury vapours (dose and duration not specified) during routine maintenance work, 26 men were later referred for hospital testing. Immediate symptoms reported were diagnosed as metal fume fever (chills, muscle pain, dry throat and headache), but central nervous system (CNS) effects ensued and included anxiety and irritability, mood alterations, aggression, impaired visual motor skills and muscle tremors (HSE, 1995).

Corrosion / Irritation

Respiratory Irritation

No animal data are available.

Respiratory tract irritation, including coughing and dry throat, was reported in four men exposed to elemental mercury vapours for up to five hours (HSE, 1995) (see **Observation in humans**). The available information is not sufficient to warrant hazard classification.

Skin Irritation

No animal data are available.

Exposure to elemental mercury vapours was reported to cause skin rashes and peeling skin in humans (ATSDR, 1999; WHO, 2003) (see **Observation in humans**). The available information is not sufficient to warrant hazard classification.

Eye Irritation

No animal data are available.

Exposure to elemental mercury vapours was reported to cause eye irritation (redness, burning sensation or conjunctivitis) in humans (ATSDR, 1999; WHO, 2003) (see **Observation in humans**). The available information is not sufficient to warrant hazard classification.

Observation in humans

Exposure to elemental mercury vapours has been reported to cause skin rashes, peeling skin of the palms of hands and soles of feet, heavy sweating and irritated eyes (redness, burning sensation or conjunctivitis) (ATSDR, 1999; WHO, 2003).

A syndrome known as acrodynia can occur, usually in children, and is a hypersensitive reaction following dermal exposure to mercury. It is characterised by body rash; chills; excessive sweating; swelling, irritation, skin peeling and ulceration of the hands, feet, cheeks or nose; hair loss; irritability and sleeplessness. The syndrome generally resolves once mercury exposure ceases (IPCS, 1996).

In four men exposed to elemental mercury vapours (estimated to be 1.1–3.3 mg mercury/m^3) for 2.5–5 hours, and in another case study on four men exposed to elemental mercury vapours (dose not specified) in a confined space for 4–5 hours, respiratory tract irritation was the main effect reported, with symptoms including coughing, chest tightness, dry throat and breathlessness. Anorexia and fever were also observed (HSE, 1995).

In a man exposed to elemental mercury vapours for seven hours per day for seven days during a 10-day period when cleaning broken thermometers, a non-allergic skin reaction (erythema exsudativum multiforme) was diagnosed, characterised by several vesicles and ulcerated lesions on the trunk and extremities, as well as purulent conjunctivitis. Fever, nausea, vomiting and anorexia were also reported. The skin lesions resolved within seven days when exposure ceased (HSE, 1995).

Sensitisation

Skin Sensitisation

No data are available.

Observation in humans

Dermal reactions were observed in people who had short-term accidental exposure to elemental mercury (e.g. from broken thermometers). Swelling and/or pustules were observed on the trunk, arms and legs. It was suggested that the response was systemic contact dermatitis due to inhaling the elemental mercury vapours (HSE, 1995).

Repeated Dose Toxicity

Oral

No data are available.

Dermal

No data are available.

Inhalation

The chemical is classified as hazardous with the risk phrase 'Toxic: Danger of serious damage to health by prolonged exposure through inhalation' (T; R48/23) in the HSIS (Safe Work Australia). The available data in animals and humans (see **Observation in humans** below and **Other health effects: Neurotoxicity** sections) support this classification.

Rabbits (strain and sex not specified) were exposed to elemental mercury vapour at 0.1 mg/m^3 (0.1 µg/L; n = 18), 0.86 mg/m^3 (0.86 µg/L; n = 19) or 6 mg/m^3 (6 µg/L; n = 16) for seven hours per day, five days per week for 83, 12 and 11 weeks, respectively. Rats (strain and sex not specified; n = 25) and dogs (strain and sex not specified; n = 2) were also exposed at 0.1 mg/m^3 (0.1 µg/L) for seven hours per day, five days per week for up to 83 weeks. No tissue damage was observed in rabbits, rats or dogs exposed to elemental mercury vapours at 0.1 mg/m^3. Kidney function was also normal in dogs exposed to that dose. In rabbits exposed at 0.86 mg/m^3, moderate kidney damage, mild to moderate changes in the heart and unspecified changes in the brain were reported. At the highest dose, marked necrosis in the kidneys, mild necrosis in the liver and brain necrosis were observed in rabbits (HSE, 1995; ATSDR, 1999). A no observed adverse effect concentration (NOAEC) of 0.1 µg/L can be derived from this study based on the treatment-related effects reported at 0.86 mg/m^3.

Male rats (n = 26; strain not specified) were exposed to elemental mercury vapour at 0 or 3 mg/m^3 (3 µg/L) for three hours per day, five days per week for 12–42 weeks. From week 12 onwards, exposed rats had impaired behavioural responses in conditioned escape and conditioned avoidance tests; the impaired responses returned to normal within 10 weeks after ceasing exposure. From week 18 onwards, reduced weight gain or weight loss, and fine tremors of the head and legs were observed in exposed rats. Pathological changes were reported in the kidneys (dense deposits and lysosomal inclusions in the tubular epithelium) of exposed rats. The highest mercury accumulation was found in the brain (mainly in the cerebellum and brain stem) and kidneys of exposed rats. In the brain, mercury accumulation persisted even 12 weeks after exposure ceased; levels were approximately 50 % of those at the end of the exposure period (HSE, 1995; ATSDR, 1999).

Observation in humans

The main route of elemental mercury toxicity in humans is from chronic inhalation exposure of the vapours in occupational settings, eliciting neurobehavioural effects (see **Other health effects: Neurotoxicity** section) and renal toxicity.

A lowest observed adverse effect concentration (LOAEC) of 9 µg/m^3 was reported, based on human occupational inhalation studies where hand tremors, memory disturbance and autonomic dysfunction were observed. A reference concentration (RfC) of 0.3 µg/m^3 was derived, based on conversion factors and assumptions ('a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime') (US EPA IRIS). Based on the available human data, neurotoxicity occurs when urinary concentrations of mercury are above 20 µmol/mol creatinine, and blood concentrations are above 45 nM (HSE, 1995).

Renal toxicity has also been reported following occupational exposure to elemental mercury vapours. The effect of elemental mercury exposure on the kidneys has been assessed extensively in a variety of workers from the chloroalkali industry, thermometer manufacturers and mercury-zinc amalgam plants. Signs of kidney toxicity predominately included increased lysosomal enzymes in the plasma and urine, as well as albuminuria. A no observed adverse effect level (NOAEL) of approximately 20 µmol/mol creatinine for urinary mercury concentration has been determined based on the available human data (HSE, 2003).

Genotoxicity

Only limited human data are available, indicating no concerns for genotoxicity during occupational exposure.

Chloroalkali workers (n = 26 males) exposed to elemental mercury vapours at 25–50 µg/m^3 for a mean duration of 10 years did not have an increased frequency or size of micronuclei in peripheral lymphocytes compared with a matched control group (ATSDR, 1999).

Workers (n = 22 males) exposed to elemental mercury vapours (dose not specified) for a mean duration of four years did not have an increased frequency of structural aberrations (chromatid gaps, breaks and exchanges; chromosome fragments, dicentrics and translocations) in peripheral blood lymphocytes compared with unexposed controls (HSE, 1995; ATSDR, 1999).

Workers (sex not specified; n = 28) exposed to elemental mercury (dose not specified) for 1–11 years did not have any chromosomal abnormalities (aneuploidy, hyperploidy, hypoploidy) in whole blood lymphocytes compared with 12 unexposed controls (HSE, 1995; ATSDR, 1999).

Carcinogenicity

Only limited data are available. Therefore, no conclusion can be derived on the carcinogenicity of the chemical.

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' and 'There is *inadequate evidence* in experimental animals for the carcinogenicity of metallic mercury'. The overall conclusion of IARC was that 'Metallic mercury and inorganic mercury compounds are not classifiable as to their carcinogenicity to humans (Group 3)' (IARC, 1993).

In BD III and BD IV rats (n = 39 males and females) exposed to 0.1 mL elemental mercury by two intraperitoneal (i.p.) injections, local sarcomas were observed in 5/12 rats that survived longer than 22 months (ATSDR, 1999; US EPA IRIS). However, these data were considered inadequate due to poor documentation of the control rats and statistics used in the study (SCOEL, 2007).

Increased incidence of glioblastoma (brain cancer) was reported in Swedish dental workers (n = 1125 female dentists; n = 3454 male dentists; n = 4662 female dental nurses). All categories of dental workers were affected, and mercury amalgam, chloroform and radiography were considered to be contributing factors (HSE, 1995; WHO, 2003; US EPA IRIS). However, dentists and dental technicians who were US Armed Forces veterans did not have increased incidence of brain cancer (WHO, 2003). A case-control study of brain tumours and amalgam fillings in Australia reported 'a decreased risk for gliomas and no effect was seen with regard to meningiomas' (IARC, 1993).

In Swedish chloroalkali workers (n = 1190 males) studied over 24 years, lung cancer incidence was significantly increased compared with the expected incidence in the general Swedish male population. However, there were confounding factors such as previous asbestos exposure in 9/10 cases and unknown smoking status. Cancer incidence at all other sites was not increased (HSE, 1995; US EPA IRIS).

Norwegian chloroalkali workers (n = 674 males), exposed to elemental mercury vapours (doses not specified) for more than one year, showed no increased incidences of kidney or nervous system cancers compared with the general male Norwegian population (WHO, 2003). Lung cancer incidence was significantly increased, but data linking this to mercury exposure were lacking. Smoking and asbestos were confounding factors (US EPA IRIS).

Reproductive and Developmental Toxicity

The chemical is classified as hazardous—Category 2 substance toxic to reproduction—with the risk phrase ‘May cause harm to the unborn child’ (T; R61) in the HSIS (Safe Work Australia). The neurobehavioural effects in the offspring of squirrel monkeys exposed to the chemical at ≥0.5 mg/m^3 support this classification. Based on the reproductive toxicity effects observed in female rats exposed to the chemical (hormone level changes, prolonged oestrus cycle and decreased number of live pups), hazard classification for toxicity to fertility is also warranted (see **Recommendation** section).

Female Sprague Dawley (SD) rats (n = 6–18/dose) were exposed (nose only) to elemental mercury vapour at 0, 1, 2 or 4 mg/m^3 for two hours per day for 1, 4, 7 or 11 days. Prolonged oestrus cycles and morphological changes in the corpora lutea were observed in rats at ≥2 mg/m^3. At 4 mg/m^3, circulating oestrogen levels were decreased and progesterone levels were increased, compared with control rats, and body weights were also significantly reduced (8–12 %) from day seven. Ovulation, implantation and pregnancy were not affected (Davis et al., 2001).

Pregnant Long-Evans rats (n = 25/dose) were exposed (nose only) to elemental mercury vapour at 0, 1, 2, 4 or 8 mg/m^3 for two hours per day during gestation days (GD) 6–15. Maternal toxicity was observed at doses ≥4 mg/m^3 (significantly increased kidney weights and decreased weight gain). Increased resorptions, decreased litter sizes and decreased neonatal body weights were reported at 8 mg/m^3. Developmental toxicity was only observed at doses that were considered maternally toxic (Morgan et al., 2002). In female rats (n = 12; strain not specified) exposed to elemental mercury vapour at 0 or 0.1 mg/m^3 from GD 1–21, resorption rates and foetal body weights were similar between exposed and unexposed animals (HSE, 1995).

Female rats (n = 12/dose; strain not specified) were exposed to elemental mercury vapour at 0 or 2.5 mg/m^3 for six hours per day for 21 days before mating and on GD 7–20. Exposed dams showed signs of neurotoxicity including agitation, body tremors and fits from the second week of exposure, and prolonged oestrus cycle compared with control rats. There was a decrease in the number of live pups born to exposed dams and all pups born to exposed dams died by post natal day (PND) 6. There were no differences in developmental abnormalities in pups born to exposed dams compared with pups born to control dams, although a failure of lactation and poor health of the exposed dams could have contributed to the pup mortalities (ATSDR, 1999; WHO, 2003; REACH).

Pregnant squirrel monkeys (n = 11) were exposed to elemental mercury vapour at 0, 0.5 or 1.0 mg/m^3 for four or seven hours per day, five days per week, for at least the last two trimesters of the gestation period. Neurobehavioural testing (reinforcement learning in a lever pressing test) in the offspring showed impairments in prenatally exposed monkeys compared with unexposed monkeys (ATSDR, 1999; WHO, 2003).

Observations in humans

In women exposed to mercury (doses not available), there are conflicting reports on reproductive toxicity. One study reported an increased rate of spontaneous abortions (17 % in 168 exposed workers from a mercury smelting ore plant compared with 5 % in 178 unexposed controls) and toxaemia in pregnancy (35 % compared with 2 % in 178 controls). However, three other studies reported no difference in the spontaneous abortion rate between mercury exposed women (lamp factory workers and dental staff) and unexposed age-matched controls (IPCS, 2006).

A study in dental staff (n = 115 women: 45 dentists; 36 dental assistants; and 34 unexposed controls) showed an increased incidence of spontaneous abortion, stillbirth and developmental defects in 28/117 pregnancies in 19 women exposed to mercury (doses not available). In the unexposed controls,

7/63 pregnancies in five women resulted in adverse outcomes (no details available). Menstrual disorders (irregularity, pain or heavy bleeding) were reported in 31 % of exposed women and 19 % of unexposed women under the age of 40. Statistical analysis was not undertaken and confounding factors for adverse pregnancy outcomes were not taken into account (HSE, 1995; ATSDR, 1999; IPCS, 2006).

In a retrospective analysis of male chloroalkali workers and their wives (n = 118 couples), and unexposed male workers and their wives (n = 283 couples), increasing paternal elemental mercury vapour exposure was significantly associated with an increased rate of spontaneous abortion. When risk factors for spontaneous abortion were accounted for, the correlation still held, although statistical significance was borderline (p = 0.07). Maternal mercury exposure was not assessed, so it was not possible to align the increased spontaneous abortion rate to male or female related mechanisms (HSE, 1995).

However, in another retrospective analysis of American Department of Energy plant workers (n = 496 males: 241 mercury exposed workers and 254 unexposed matched controls), no link between male occupational exposure to elemental mercury for at least four months and adverse reproductive or pregnancy outcomes (including infertility, miscarriage, developmental defects, serious childhood illness) were observed (HSE, 1995; ATSDR, 1999; WHO, 2003).

In a fertility study in Belgian factory workers (n = 204 males: 103 mercury exposed and 101 controls), the number of children born to mercury-exposed men was similar to the number of children born to unexposed control men (HSE, 1995).

Other Health Effects

Neurotoxicity

Neurotoxicity has been reported in humans following occupational inhalation exposure to elemental mercury vapour. The chemical accumulates in the brain causing adverse effects, warranting hazard classification for cumulative effects similar to (organic) phenylmercury compounds (NICNASa) and mercuric sulfate (NICNASb) (see **Recommendation** section).

Elemental mercury is lipid soluble, able to cross the blood–brain barrier, and elemental mercury vapour reaches the brain before it is oxidised. The chemical is retained in the brain to a greater extent than other organs following oxidation (ATSDR, 1999). Based on data from human occupational inhalation studies, an LOAEC of 9 μg/m^3 and an RfC of 0.3 μg/m^3 has been reported (US EPA IRIS) (see **Repeat dose toxicity: Observation in humans**), supporting this classification.

Workers from various industries (n = 26 males: Seven from fluorescent tube factories, 12 from chloroalkali plants and seven from acetaldehyde production factories) who were exposed to low levels (0.026 mg/m^3) of elemental mercury vapour for 1–41 years (median 15.3 years) were compared with unexposed controls from the same factories (n = 25 males). Increased incidence of tremor was reported in exposed workers compared with unexposed workers and this was correlated with years of exposure. The impairments were reported to be similar to those that can arise from mercury accumulation in the cerebellum and basal ganglia regions of the brain, which are responsible for motor function (ATSDR, 1999; US EPA IRIS).

In chloroalkali workers (n = 41 males) exposed to elemental mercury vapour at 0.025–0.030 mg/m^3 (derived exposure based on blood mercury levels) for approximately 15.6 years, significantly slower and lower brain electrical activity was detected by electroencephalograms (EEG) in 15 % of exposed workers compared with matched controls. The EEG showed changes that correlated with mercury content in the occipital cortex (and to a lesser extent the parietal cortex, but not the frontal cortex), a region of the brain responsible for processing visual input (US EPA IRIS). In chloroalkali workers (n = 60 males) exposed to elemental mercury vapour at 0.025 mg/m^3 (derived based on blood mercury levels) for approximately 13.7 years, there was increased self-reporting of memory disturbance, sleep disorders, anger, fatigue and confusion in exposed workers compared with matched controls (no details available). However, objective measures of neurobehavioural parameters (perceptual motor function, memory and learning) were not significantly different between the groups (US EPA IRIS).

Neurobehavioural performance (motor speed, visual scanning, visuomotor coordination and concentration, visual memory) was affected in dentists (n = 98) exposed to elemental mercury vapour at 0.014 mg/m^3 (derived based on blood mercury levels) for 0.7–24 years (average 5.5 years), compared with matched controls. Impairment was reported to be consistent with central and peripheral neurotoxicity (ATSDR, 1999; US EPA IRIS). Significantly impaired neurobehavioural functions (such as finger tapping, switching attention and visual reaction time) were observed in workers at a fluorescent lamp factory (n = 88) exposed to elemental mercury vapour at an average of 0.033 mg/m^3 for an average of 15.8 years, compared with unexposed workers (US EPA IRIS).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include:

- systemic acute effects from inhalation exposure; and
- systemic long-term effects (reproductive and developmental toxicity, neurotoxicity and cumulative effects).

The chemical can also cause systemic toxicity effects following repeated inhalation exposure.

Public Risk Characterisation

The chemical is not expected to be used in cosmetics or domestic products in Australia. Although sealed articles such as thermometers and floodlights containing the chemical are available to consumers, direct exposure to the chemical is not expected during their intended use.

The chemical is listed on Schedules 2, 4 and 7 of the SUSMP (SUSMP, 2015). These controls are considered adequate to minimise the risk to public health and, therefore, the chemical is not considered to pose an unreasonable risk to public health.

Occupational Risk Characterisation

Given the critical health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise inhalation 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) (see **Recommendation** section).

NICNAS Recommendation

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

Regulatory Control

Public Health

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

Work Health and Safety

Workers exposed to mercury require health monitoring according to Schedule 14 of the *Work Health and Safety Regulations* (2011). The type of health monitoring required is: 'Demographic, medical and occupational history. Physical examination with emphasis on dermatological, gastrointestinal, neurological and renal systems. Urinary inorganic mercury' (Work Health and Safety Regulations, 2011).

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	Very toxic by inhalation (T+; R26)*	Fatal if inhaled - Cat. 1 (H330)
Repeat Dose Toxicity	Toxic: danger of serious damage to health by prolonged exposure through inhalation (T; R48/23)*	Causes damage to organs through prolonged or repeated exposure through inhalation - Cat. 1 (H372)
Reproductive and Developmental Toxicity	Repro. Cat 2 - May cause harm to the unborn child (T; R61)* Repro. Cat 2 - May impair fertility (T; R60)	May damage fertility. May damage the unborn child - Cat. 1B (H360FD)
Other Health Effects	Danger of cumulative effects (R33)	

[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 the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from 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 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

Agency for Toxic Substances and Disease Registry (ATSDR) 1999. Toxicological profile for mercury. Accessed at http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=115&tid=24

Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)]. Third edition [NOHSC:1008 (2004)]. Accessed at http://www.safeworkaustralia.gov.au/sites/swa/about/publications/Documents/258/ApprovedCriteria_Classifying_Hazardous_Substances_NOHSC1008-2004_PDF.pdf

Barregard L, Horvat M and Schutz A 1994. No indication of in vivo methylation of inorganic mercury in chloroalkali workers. Environmental Research 67(2) pp. 160–167.

Davis BJ, Price HC, O'Connor RW, Fernando R, Rowland AS, Morgan DL 2001. Mercury vapor and female reproductive toxicity. Toxicological Sciences 59(2) pp. 291–6.

Galleria Chemica. Accessed May 2015 at http://jr.chemwatch.net/galeria/

Globally Harmonised System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third edition. Accessed at http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html

Health and Safety Executive (HSE) 1995. Mercury and its inorganic divalent compounds. Accessed at http://www.hse.gov.uk/research/crr_pdf/1995/crr95076.pdf

Heintze U, Edwardsson S, Derand T and Birkhed D 1983. Methylation of mercury from dental amalgam and mercuric chloride by oral streptococci in vitro. Scandinavian Journal of Dental Research 91(2) pp. 150–152.

International Agency for Research on Cancer (IARC) 1993. Beryllium, Cadmium, Mercury, and Exposures in the Glass Manufacturing Industry, IARC Monographs Volume 58. Accessed at http://monographs.iarc.fr/ENG/Monographs/vol58/

Morgan DL, Chanda SM, Price HC, Fernando R, Liu J, Brambila E, O'Connor RW, Beliles RP, Barone S Jr 2002. Disposition of inhaled mercury vapor in pregnant rats: maternal toxicity and effects on developmental outcome. Toxicological Sciences 66(2) pp. 261–73.

National Industrial Chemical Notification and Assessment Scheme (NICNASa). Human health Tier II assessment for the group Phenylmercury Compounds. Australian Government Department of Health. Accessed at http://www.nicnas.gov.au

National Industrial Chemical Notification and Assessment Scheme (NICNASb). Human health Tier II assessment for Mercuric Sulfate: CAS No. 7783-35-9. Australian Government Department of Health. Accessed at http://www.nicnas.gov.au

Recommendation from the Scientific Committee on Occupational Exposure Limits (SCOEL) for elemental mercury and inorganic divalent mercury compounds 2007. SCOEL/SUM/84. Accessed at http://ec.europa.eu/social/BlobServlet?docId=3852&langId=en SCOEL 2007 mercury

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Dossier. 7439-97-6. Accessed May 2015 at http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

Rowland I, Davies M and Grasso P 1977. Biosynthesis of methylmercury compounds by the intestinal flora of the rat. Archives of Environmental Health 32(1) pp. 24–28.

Rowland IR, Grasso P and Davies MJ 1975. The methylation of mercuric chloride by human intestinal bacteria. Experientia 31(9) pp. 1064–1065.

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

Standard for the Uniform Scheduling of Medicines and Poisons No. 6 (the SUSMP 6) 2015. Therapeutic Goods Administration–Department of Health. Accessed at http://www.comlaw.gov.au/Details/F2012L01200, downloaded 5 February 2015.

Substances in Preparations in Nordic Countries (SPIN). Accessed May 2015 at http://188.183.47.4/dotnetnuke/Home/tabid/58/Default.aspx

The International Programme on Chemical Safety (IPCS) 1996. Mercury. Monograph for UKPID. World Health Organization, Geneva. Accessed at http://www.inchem.org/documents/ukpids/ukpids/ukpid27.htm

Triufante P, Soares ME, Santos A, Tavares S, Carmo H and Bastos Mde L 2009. Mercury fatal intoxication: two case reports. Forensic Science International 184(1-3) pp. e1–6.

US Environmental Protection Agency's (EPA) Aggregated Computational Toxicology Resource (ACToR). Accessed May 2015 at http://actor.epa.gov/actor/faces/ACToRHome.jsp

US EPA Integrated Risk Information System (IRIS). Mercury, elemental (CAS No. 7439-97-6). Accessed May 2015 at http://www.epa.gov/iris/subst/0370.htm

US National Library of Medicine's Hazardous Substances Data Bank (HSDB). Accessed May 2015 at http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

Work Health and Safety (WHS) Regulations 2011. Accessed May 2015 at http://www.comlaw.gov.au/Details/F2011L02664

World Health Organisation (WHO) 2003. Concise International Chemical Assessment Document 50 (CICAD). Elemental mercury and inorganic mercury compounds: Human health aspects. Accessed at http://www.who.int/ipcs/publications/cicad/en/cicad50.pdf

Zorn NE and Smith JT 1989. In vivo methylation of inorganic mercury in guinea pigs. Biochemical Archives 5(2) pp. 141–146.

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