



Lead oxides: Human health tier II assessment

12 September 2013

- Chemicals in this assessment
- Preface
- Grouping Rationale
- Import, Manufacture and Use
- Restrictions
- Existing Worker Health and Safety Controls
- Health Hazard Information
- Risk Characterisation
- NICNAS Recommendation
- References

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Lead oxide	1335-25-7
Lead oxide (PbO₂)	1309-60-0
Lead oxide (Pb₂O₃)	1314-27-8
Lead oxide (Pb₃O₄)	1314-41-6
Lead oxide (PbO)	1317-36-8
Plumbate (PbO₄⁴⁻), calcium (1:2), (T-4)-	12013-69-3

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

NICNAS has made every effort to assure the quality of information available in this report. However, before relying on it for a specific purpose, users should obtain advice relevant to their particular circumstances. This report has been prepared by NICNAS using a range of sources, including information from databases maintained by third parties, which include data supplied by industry. NICNAS has not verified and cannot guarantee the correctness of all information obtained from those databases. Reproduction or further distribution of this information may be subject to copyright protection. Use of this information without obtaining the permission from the owner(s) of the respective information might violate the rights of the owner. NICNAS does not take any responsibility whatsoever for any copyright or other infringements that may be caused by using this information.

ACRONYMS & ABBREVIATIONS

Grouping Rationale

This group of six chemical compounds consists of mixed lead oxides. These compounds have been included in this group due to the expectation that the physico-chemical properties will not vary greatly, leading to the compounds within this group having related end uses and their low water solubility. In addition, information outlined in the Organisation for Economic Co-operation and Development's (OECD) guideline on Grouping of Chemicals (OECD, 2007) provided guidance on the grouping of chemicals based on physico-chemical or toxicological criteria.

Import, Manufacture and Use

Australian

The following lead compounds have Australian industrial uses reported under previous mandatory and/or voluntary calls for information:

Lead oxide, red (CAS No. 1314-41-6) and **lead (II) oxide (CAS No. 1317-36-8)** are reported to have one or more of the following commercial uses including:

- in marine batteries;
- in the manufacture of glass and ceramics; and
- as flux agents for casting.

Lead (II) oxide (CAS No. 1317-36-8) has reported site-limited use including:

- in mining; and
- as a stabiliser.

The total volume introduced into Australia for **lead oxide, red (CAS No. 1314-41-6)** and **lead (II) oxide (CAS No. 1317-36-8)**, reported under previous mandatory and/or voluntary calls for information, was below 1000 tonnes for each chemical.

For **lead dioxide (CAS No. 1309-60-0)**, and **calcium plumbate (CAS No. 12013-69-3)** no Australian use, import, or manufacturing information was reported under previous mandatory calls for information.

International

For the majority of the group, the following international uses have been identified through European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers; Galleria Chemica; Substances and Preparations in the Nordic countries (SPIN) database; and eChemPortal: The Finnish Environment Institute; the US Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR); American Chemical Council Global Automotive Declarable Substance List (GADSL) and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB):

Domestic use including:

- in paints, lacquers and varnishes; and
- in adhesives and binding agents.

Commercial use including:

- in construction materials;
- in the manufacture of batteries;
- in the manufacture of matches and explosives;
- as lubricants and additives; and
- as process regulators.

Site-limited use including:

- as intermediates in the manufacture of pigments;
- as analytical or laboratory reagents;
- in metallurgy, e.g. bearing materials, brass, aluminium and steel used in the automotive industry; and
- as vulcanising agents in the manufacture of rubbers.

The following individual lead compounds have additional international uses identified from EU REACH dossiers; Galleria Chemica; SPIN database; and eChemPortal: The Finnish Environment Institute; ACToR; American Chemical Council Global Automotive Declarable Substance List (GADSL), the Color Handbook and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB):

Lead oxide, red (CAS No. 1314-41-6) and **lead (II) oxide (CAS No. 1317-36-8)** have one or more of the following reported uses:

Commercial use including:

- in the manufacture of non-metallic mineral products e.g. cement, coloured glass and ceramics; and
- in colouring agents/dyes, e.g. colouring rubber.

Lead oxide (CAS No. 1335-25-7) and **lead dioxide (CAS No. 1309-60-0)** have one or more of the following uses:

Domestic use including:

- cleaning/washing agents.

Commercial use including:

- insulating materials; and
- as absorbents and adsorbents.

Calcium Plumbate (CAS No. 12013-69-3) has the following reported use:

Domestic use including:

- as a corrosion-inhibiting pigment.

Restrictions

Australian

Lead and lead compounds are listed in the Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)) (SUSMP, 2012) in:

Appendix I, Uniform Paint Standard

Lead compounds are not permitted to be used in domestic or industrial paints at > 0.1 %.

The proportion of a substance for the purposes of this Schedule is calculated as a percentage of the element present in the non-volatile content of paint.

Appendix C

Lead compounds in paints, tinters, inks or ink additives except in preparations containing ≤ 0.1 % of lead calculated on the non-volatile content of the paint, tinter, ink or ink additive.

Appendix C substances, other than those included in Schedule 9, are considered of such danger to health as to warrant prohibition of sale, supply and use. These substances are poisons prohibited from sale, supply or use because of their known potential for harm to human and/or animal health.

Schedule 6

Lead compounds unless specified in Appendix C or:

- (a) when included in Schedule 4 or 5;
- (b) in paints, tinters, inks or ink additives;

(c) in preparations for cosmetic use containing 100 mg/kg or less of lead;

(d) in pencil cores, finger colours, showcard colours, pastels, crayons, poster paints/colours or coloured chalks

containing 100 mg/kg or less of lead; or

(e) in ceramic glazes when labelled with the warning statement: *CAUTION - Harmful if swallowed. Do not use on surfaces which contact food or drink.* Written in letters not less than 1.5 mm in height.

Schedule 6 substances are considered to have moderate potential for causing harm, the extent of which can be reduced through the use of distinctive packaging with strong warnings and safety directions on the label.

Schedule 5

Lead compounds in preparations for use as hair cosmetics, unless specified in Appendix C.

Schedule 5 substances are considered to have low potential for causing harm, the extent of which can be reduced through the use of appropriate packaging with simple warnings and safety directions on the label.

In addition, under the *Customs (Prohibited Imports) Regulations 1956*, the importation of cosmetic products containing more than 250 mg/kg (0.025 % w/w) of lead or lead compounds (calculated as lead), except products containing more than 250 mg/kg of lead acetate designed for use in hair treatments, is prohibited

unless written permission is granted by the Minister (Australian Government, 2013).

International

The risk of exposure to lead and lead compounds has been recognised internationally, which has resulted in broad restrictions regarding occupational and public exposure.

Cosmetics

Lead compounds appear on the following:

- Health Canada List of Prohibited and Restricted Cosmetic Ingredients ("Hotlist").
- The EU Cosmetic Directive 76/768/EEC Annex II: List of Substances which must not form part of the Composition of Cosmetic Products.
- The New Zealand Cosmetic Products Group Standard - Schedule 4: Components Cosmetic Products Must Not Contain.
- The Thailand Cosmetic Act - Prohibited Substances.

Existing Worker Health and Safety Controls

Hazard Classification

The members of this group are not individually listed in the Hazardous Substances Information System (HSIS) and therefore, by default, are covered by the generic 'lead and lead compounds' classification as hazardous with the following risk phrases for human health:

Repr. Cat. 1; R61 (Reproductive toxicity - may cause harm to the unborn child)

Repr. Cat. 3; R62 (Reproductive toxicity - possible risk of impaired fertility)

Xn; R20/R22 (Harmful by inhalation and if swallowed)

Xn; R33 (Danger of cumulative effects)

Exposure Standards

Australian

Lead, inorganic dusts and fumes (as lead) have the following exposure standards reported in HSIS (Safe Work Australia). These exposure standards apply to the lead compounds in this assessment:

Time Weighted Average (TWA): 0.15 mg/m³ for lead compounds (as lead).

Short-Term Exposure Limits (STEL): No specific exposure standards are available.

International

For lead compounds in general the following exposure limits were identified:

TWA: 0.20 mg/m³ [Thailand, USA (Idaho)]

TWA: 0.15 mg/m³ [Argentina, Canada (Northwest Territories, Yukon), Egypt, European Union, Gibraltar, Hungary, India, Luxembourg, Malta, Singapore, Slovak Republic]

TWA: 0.12 mg/m³ [Chile]

TWA: 0.10 mg/m³ [Austria (Maximum Allowable Concentration (MAK)), New Zealand, Republic of South Africa, Sweden, Switzerland MAK]

TWA: 0.05 mg/m³ [Bulgaria, Canada (Alberta, British Columbia, Prince Edward Island, Nova Scotia, Ontario, Saskatchewan, Yukon), China, Italy, Malaysia, Peru, USA (Hawaii, Michigan, North Carolina, Oregon, Washington, Wyoming)]

TWA: 0.005 mg/m³ [Latvia]

STEL: 0.80 mg/m³ [Switzerland MAK]

STEL: 0.45 mg/m³ [Argentina, Canada (Northwest Territories, Yukon), Egypt]

STEL: 0.40 mg/m³ [Austria MAK]

STEL: 0.15 mg/m³ [Canada (Ontario, Saskatchewan)]

STEL: 0.01 mg/m³ [Latvia]

Health Hazard Information

Toxicokinetics

Inorganic lead compounds can be absorbed orally, dermally or via inhalation (NICNAS, 2007).

When ingested, the absorption of inorganic lead compounds in the human gastrointestinal tract is influenced by different factors, the most significant being age. Children (up to the age of eight) are estimated to absorb up to

50 % of the lead dose they ingest while adults would absorb up to 10 % of the dose they ingest. This route of absorption can be dependent on solubility and particle size with smaller particles being absorbed more readily than larger ones. In addition, results from rodent feeding studies indicate that lead oxides are bioavailable (LDAI, 2008).

In an oral repeat dose toxicity study, rats were dosed with 0, 200, 500 or 1000 ppm lead acetate and tested for four, eight or 12 weeks. The blood lead concentration (PbB) level range was 40 - 100 µg/dL and the kidney lead levels were highest at four weeks. For all test groups the urinary lead excretion was highest at four weeks then decreased with continued exposure to lead (REACH).

If inhaled, the size of lead compound particles can dictate the site of deposition and rate of absorption (NICNAS, 2007).

Absorption via the dermal route has shown to be the least efficient (NICNAS, 2007). Less than 0.3 % of lead from lead acetate in cosmetics was absorbed dermally in human male volunteers over a 12 hour period. When lead nitrate was applied to the skin, 30 % of the dose was absorbed. It is not known if the absorption was systemic or confined to the layers of the skin.

The current lead compounds have low water solubility but are considered bioavailable (LDAI, 2008) as the small amount that can be absorbed from any route of dosing may be sufficient to lead to chronic effects.

Lead stored in bone can be released into the blood after exposure has ceased. Within bone, distribution is not uniform and lead accumulates in areas that are undergoing active calcification at the time of exposure (NICNAS, 2007). Inorganic lead is distributed in the body independently of source compound and route of exposure. The spatial distribution of lead in bone is similar between children and adults, although adults generally have a higher concentration. When in the blood, 99 % of lead is bound to proteins within erythrocytes (NICNAS, 2007).

Mobilisation of lead from bone increases during pregnancy when maternal bone is catabolised to produce the foetal skeleton. It has been shown that up to 80 % of lead in human cord blood comes from maternal bone stores and can be transferred into the foetal skeleton during its formation.

The PbB concentration is a reflection of recent exposure and does not capture the more significant impact and slower elimination kinetics of the chemical in bone (ASTDR, 2007). The accumulation of lead in bone is considered a biomarker for long-term exposure over a lifetime. As a result, the affinity of lead for bone would

suggest that lead levels in bone, rather than lead levels in blood, provide more relevant predictive information for some health effects associated with long term exposure.

Acute Toxicity

Oral

The members of this group are not listed in HSIS, and therefore, by default, are covered by the generic 'lead and lead compounds' hazard classification with the risk phrase 'Harmful if swallowed' (Xn; R22) in HSIS (Safe Work Australia). The available data do not support this classification for the lead oxides in this group, as presented below.

Lead oxides are demonstrated to be of low acute toxicity in animal tests following oral exposure. The rat oral median lethal doses (LD50s) for **lead dioxide (CAS No: 1309-60-0)**, **lead oxide, red (CAS No: 1314-41-6)** and **lead monoxide (CAS No: 1317-36-8)** are all reported to be > 2000 mg/kg bw for male and female rats (REACH). No clinical signs were reported.

Lead sesquioxide (CAS No: 1314-27-8) is reported to have similar solubility to the other lead compounds in this group (Schweitzer, G.K.), therefore, is not expected to exhibit greater toxicity than these compounds via the oral route (i.e. is expected to have a similar oral LD50 of > 2000 mg/kg bw).

Dermal

Lead oxide, red (CAS No: 1314-41-6) and **lead monoxide (CAS No: 1317-36-8)** exhibited low acute toxicity in animal tests as evidenced by reported LD50s in rats of > 2000 mg/kg bw (REACH).

Inhalation

The members of this group are not listed in HSIS, and therefore, by default, are covered by the generic 'lead and lead compounds' hazard classification with the risk phrase 'Harmful by inhalation' (Xn; R20) in HSIS (Safe Work Australia). While data available from observations in humans support this generic 'lead and lead compounds' classification, available experimental data support an amendment to this classification (refer to Recommendation section) to reflect the findings reported below.

Lead oxides are reported to be of low toxicity via inhalation; the rat median lethal concentration (LC50) was reported to be > 5.05 mg/L for male and female rats (REACH). The pulmonary deposition patterns and water solubility of **lead oxide, red (CAS No: 1314-41-6)** and **lead monoxide (CAS No: 1317-36-8)** are reported to be similar (LDAI, 2008). Therefore, the lead compounds in this group are unlikely to cause acutely toxic effects via inhalation.

Observation in humans

In this section, route specific data are not provided but exposure is reported in terms of absorbed dose. The concentration of lead in the blood is the most commonly reported value. However, lead in bone, hair and teeth are also reported in the literature.

Adult Exposure

The majority of the data have been collected from accidental or intentional exposure via ingestion or inhalation, and there are rich data regarding the dose-effect in humans (NICNAS, 2007; ASTDR, 2007). Exposure can cause encephalopathy (the signs of which include: hyperirritability, ataxia, convulsions, stupor and coma) in addition to gastrointestinal effects such as colic (the effects can be displayed as: abdominal pain, constipation, cramps, nausea, vomiting, anorexia and weight loss) (ASTDR, 2007; WHO, 1995). It was recorded that signs of acute toxicity were observed in adults with a PbB level ranging from 50 - 300 µg/dL. However, that is challenged in a more recent study that only noted signs of encephalopathy in adults with PbB levels greater than 460 µg/dL (NICNAS, 2007; ASTDR, 2007).

Colic is indicative of gastrointestinal impact and is typically displayed as an early sign of exposure to lead (NICNAS, 2007; ASTDR, 2007). Colic has been noted in individuals exposed to high levels of lead and can be evident as a result of occupational exposure where workers generally register PbB levels between 100 – 200 µg/dL, although symptoms have been reported by workers with PbB levels between 40 – 60 µg/dL.

Exposure to lead has been reported to cause proximal renal tubular damage in the kidney (NICNAS, 2007).

Paediatric Exposure

Data were compiled from a paediatric population regarding the dose-response after acute exposure to lead. Signs of encephalopathy were noted in children with PbB levels between 90 – 800 µg/dL. The mean value reported for PbB levels related to death (327 µg/dL) is similar to that noted for encephalopathy (330 µg/dL). Gastrointestinal effects (abdominal pain, constipation, cramps, nausea, vomiting, anorexia and weight loss) were reported at PbB levels between 60 – 450 µg/dL. Data collected from additional reports indicate that acute encephalopathy was noted in children with PbB levels of 80 – 100 µg/dL and infants at PbB levels of 74.5 µg/dL (NICNAS, 2007).

In paediatric populations, acute colic has also been reported as an effect of poisoning associated with exposure to lead and is noted to occur when the PbB level is greater than or equal to 60 µg/dL (NICNAS, 2007; ASTDR, 2007). In addition, it has been reported that exposure to lead can inhibit the formation of the haem-containing protein cytochrome P450 (NICNAS, 2007).

Corrosion / Irritation

Skin Irritation

In general, lead compounds are not considered irritating to skin (REACH). No effects were reported in skin irritation assays in rabbits citing OECD TG 404 for **lead dioxide (CAS No: 1309-60-0)**, **lead oxide, red (CAS No: 1314-41-6)** and **lead monoxide (CAS No: 1317-36-8)**.

Eye Irritation

In general, lead compounds were not reported to be irritating to eyes or having caused serious eye damage (REACH). No effects were reported in eye irritation assays in rabbits citing OECD TG 405 for **lead dioxide (CAS No: 1309-60-0)**, **lead oxide, red (CAS No: 1314-41-6)** and **lead monoxide (CAS No: 1317-36-8)**.

Observation in humans

No studies were located that recorded skin or eye irritation in humans as a result of exposure to lead compounds.

Sensitisation

Skin Sensitisation

Several lead compounds, including **lead dioxide (CAS No: 1309-60-0)**, **lead oxide, red (CAS No: 1314-41-6)** and **lead monoxide (CAS No: 1317-36-8)** were reported to be non-sensitisers (REACH). It was reported that the compounds gave negative results for skin sensitisation in guinea pigs when tested according to OECD TG 406.

Observation in humans

Although altered immune parameters were described in occupational and paediatric groups that were exposed to lead, there were no reports of skin or respiratory sensitisation to lead in humans (ASTDR, 2007).

Repeated Dose Toxicity

Oral

The compounds in this group are not individually listed in HSIS. Therefore, by default, they are covered by the generic 'lead and lead compounds' hazard classification with the risk phrase 'Danger of cumulative effects' (R33) in HSIS (Safe Work Australia).

While no data are available for the chemicals in this group, data available from animals studies on other lead compounds, and observations in humans, support this generic 'lead and lead compounds' classification and are presented in the following sections.

A lowest observed adverse effect level (LOAEL) of 200 ppm (corresponding to PbB levels of 40–60 µg/dL) was derived for lead acetate from a repeated dose toxicity study in Sprague Dawley (SD) rats following the guidelines set out in a US EPA chronic feeding study (REACH). Lead acetate was administered in drinking water (which was freely accessible [*ad libitum*]) to males rats (18 animals/dose group) at 0, 200, 500 or 1000 ppm per day for four, eight or 12 weeks. Decreased body weight and increased kidney weight as a percentage of body weight were reported at all dose ranges following four weeks exposure.

Dermal

While no data are available for the lead compounds in this group, no significant adverse effects were reported following repeated dermal exposure to several other lead compounds (REACH).

In a report available on repeat dose toxicity during dermal exposure, rats were exposed to lead acetate, lead oleate, lead arsenate or tetraethyl lead for 24 hours. The test groups had lead compounds applied either directly to the skin or to skin that had been mechanically injured. Dermal absorption of lead was shown to occur in both test groups. However, comparatively greater absorption of lead was reported in the groups where the skin had been mechanically injured.

Inhalation

While no data are available for the chemicals in this group, no significant adverse effects were reported following repeated inhalation exposure to lead nitrate (REACH).

Aerosolised lead nitrate was administered to mice (Swiss Webster) via inhalation at 2.5 mg/m³ per day for 14 or 28 days. It was determined, considering total retention of the inhaled lead, that each mouse received a dose of 80 µg/day of lead.

A statistically significant reduction in the relative size of the spleen and thymus in both test groups was reported when compared with the control group. Increased lung weight was noted in both test groups and an increase in lead concentration was reported in the liver, lung and kidney; although the 28 day group was noted to show a greater concentration. There were no apparent differences in body weight and food consumption noted for either test group.

Observation in humans

Lead has multiple modes of action in biological systems; as a result, any system or organ in the body can potentially be affected by lead exposure. For the purposes of this report, the effects of lead toxicity on the most sensitive target organs have been identified and summarised (NICNAS, 2007; ASTDR, 2007).

Neurological Effects

Lead encephalopathy is considered the most severe neurological effect of lead exposure in adults. Occupational lead exposure has also been linked to neurotoxicity and studies have shown that the following signs and symptoms have been noted in those recorded to have PbB levels of between 40 – 120 µg/dL: malaise, forgetfulness, irritability, lethargy, headache, fatigue, impotence, decreased libido, dizziness, weakness, paraesthesia, visual motor coordination impairment, cognitive performance impairment, decreased reaction time, mood and coping ability as well as affecting memory.

Haematological Effects

Lead exposure impacts the haematological system by inhibiting haem synthesis and decreasing the lifespan of erythrocytes, which results in the onset of microcytic and hypochromic anaemia (NICNAS, 2007). It has been estimated that the PbB threshold for a decrease in haemoglobin to be seen in occupationally exposed adults is 50 µg/dL. For children the threshold is estimated to be PbB 40 µg/dL.

Cardiovascular Effects

Studies investigating the effect of PbB on blood pressure in humans are not conclusive (NICNAS, 2007; ASTDR, 2007). The cardiovascular endpoint of concern for humans when exposed to low levels of lead is an increase in systemic blood pressure.

Longitudinal occupational studies investigating the possible relationship between low level lead exposure and blood pressure have been undertaken, with mixed results. Subsequently, based on the available literature, it is suggested that a relationship between low level exposure to lead and increased systemic blood pressure cannot be determined (NICNAS, 2007).

Renal Effects

Nephrotoxicity associated with lead is characterised by proximal tubular nephropathy, glomerular sclerosis and interstitial fibrosis. The deterioration in renal function is characterised by enzymuria, proteinuria and an impaired ability to transport organic anions and glucose, in addition to a decreased glomerular filtration rate. Studies summarised in ATSDR (2007) indicate that an increase in nephrotoxicity is proportional to an increase in PbB levels. Effects on glomerular filtration are reported at or below 20 µg/dL, enzymuria and proteinuria are reported at equal to or greater than 30 µg/dL and severe deficits in function and pathological changes are reported in association with PbB levels ≥ 50 µg/dL.

Genotoxicity

In general, lead compounds are considered genotoxic to mammalian cells.

The genotoxic effects of lead were reviewed and presented by the ATSDR (2007). The majority of the in vitro point mutation tests in bacteria were negative, while mammalian clastogenicity tests were generally positive.

It was reported that in bacterial reverse mutation assays, lead was negative both with and without metabolic activation (REACH). However, in vitro chromosomal aberration tests using Chinese hamster ovary (CHO) cells and human lymphocytes were positive without metabolic activation. An in vivo micronucleus assay using human peripheral lymphocytes (from those working with lead compounds) was positive below the maximum tolerated dose.

Carcinogenicity

A review conducted by the International Agency for Research on Cancer (IARC) in 1980, which was updated in 1987 and again in 2006, indicated that there was sufficient evidence in experimental animals for the carcinogenicity of inorganic lead compounds, that there is limited evidence in humans for the carcinogenicity of inorganic lead compounds and that there is inadequate evidence in experimental animals for the carcinogenicity of lead oxide (IARC 1980; IARC, 1987; IARC 2006). The review resulted in the IARC classification of inorganic lead compounds as 'Probably carcinogenic to humans' (Group 2A).

A subsequent review by the International Lead Association (LDAI, 2008) concluded that lead oxide exhibits high bioavailability as evidenced by animal feeding studies and when tested in vitro via gastric simulation systems. There is consistent evidence from studies in rodents that soluble lead compounds or those that are considered bioavailable are carcinogenic in animals; notably, reproducible renal tumours in male rats following administration of high levels of lead via food or water.

This evidence is sufficient to classify the chemicals in this group as potential carcinogens.

Reproductive and Developmental Toxicity

The lead compounds in this group are not individually listed in HSIS. Therefore, by default, they are covered by the generic 'lead and lead compounds' hazard classifications with the risk phrases 'Possible risk of impaired fertility' (R62) and 'May cause harm to the unborn child' (R61) in HSIS (Safe Work Australia). While no data are available for the lead compounds in this group, the available data on other lead compounds support these classifications.

In a reproductive and developmental toxicity screening test in SD rats, lead acetate was administered via drinking water to nine females at 0.6 % weight per volume (w/v) (equivalent to 502 mg/kg bw/day) at gestation days 5–21 (Ronis et al, 1996; LDAI, 2008). A stillbirth rate of 19 % was recorded in the test group compared with a 2 % rate noted in the control group. The dams and offspring had PbB levels >200 µg/dL.

In a subsequent reproductive and developmental toxicity screening test in SD rats, lead acetate was administered via drinking water to 10 females at 0.05 % w/v, eight females at 0.15 % w/v and nine females at 0.45% w/v, during gestation days 5–21 (Ronis et al, 1998). Stillbirth rates of 3(±3), 10(±6) and 28(±8) % were recorded for increasing dose groups respectively. This was compared with a 4(±3) % rate noted in the control group. At birth, the male pups had PbB levels of 40(±1), 83(±8) and 120(±120) µg/dL for increasing dose groups respectively, while the female pups had PbB levels of 42(±7), 67(±16) and 197(±82) µg/dL. A developmental LOAEL of 0.05 % (equivalent to 42 mg/kg bw/day) was reported for this study (LDAI, 2008).

Reproductive toxicity observations in humans

Recent studies have investigated the effect of lead exposure in occupational groups and general populations living near industrial plants. Although the evidence reported is predominantly qualitative and dose-effect relationships have largely not been established (NICNAS, 2007; WHO, 1995), it has been suggested that moderately high PbB levels in humans could result in spontaneous abortion, pre-term delivery, alterations in sperm and decreased male fertility (ASTDR, 2007).

Developmental toxicity observations in humans

Data pertaining to low level exposure to lead contributing to developmental toxicity in infants and young children were recently reviewed. Consensus exists between the reports, which suggest that PbB levels in humans >10 µg/dL can affect paediatric intellectual development (ASTDR, 2007; Donovan, J, 1996).

In addition, data regarding the effects on children of higher levels of lead exposure were reviewed. Although neurobehavioural deficits were reported in children with PbB levels <10 µg/dL, there is uncertainty attached to these estimates of reported effects

(ASTDR, 2007). Even so, the US Centers for Disease Control and Prevention (CDC) has a reference level of 5 µg/dL, above which it is recommended that public health action be initiated (CDC).

Risk Characterisation

Critical Health Effects

The acute toxicity of the chemicals in this group is limited by their low water solubility. However, they are considered bioavailable with respect to long term effects. The critical health effects for risk characterisation include systemic long-term effects (carcinogenicity, mutagenicity, reproductive toxicity and developmental toxicity). The lead compounds may also cause harmful effects following repeated exposure and harmful systemic effects following a single exposure via inhalation.

Public Risk Characterisation

The restrictions on the use of lead and lead compounds in products available to the public in Australia are listed in the Poisons Standard (SUSMP, 2012). These restrictions will prevent risks from domestic use of these compounds.

Given these restrictions, historical reports of cosmetic use of these chemicals, i.e. in anti-persperants identified from international sources (HSDB, 2013) can be considered to not be relevant to Australia.

Historical use of lead compounds in surface coatings suggests that the potential for the public to be exposed, through flaking paint and during home renovation, still exists. While it is possible that the public will be exposed to lead or lead compounds, the risk can be managed by following appropriate guidelines.

Occupational Risk Characterisation

Given the critical health effects, the risk to workers from this chemical is considered high if adequate control measures to minimise occupational exposure to the chemical are not 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.

NICNAS Recommendation

Current risk management measures are considered adequate for the protection of public and workers' health and safety, provided that all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory. No further assessment is required.

Regulatory Control

Public Health

Current restrictions control the use of lead and lead compounds in cosmetics, paint, tinters, inks or ink additives, which effectively reduces the risk of public exposure.

The availability and permissible lead content in products, such as paint, are regulated in terms of availability and concentration (SUSMP, 2012). Products that historically contained lead or lead compounds still pose an exposure risk to the public due to their existence in the public domain.

The National Health and Medical Research Council (NHMRC) of Australia has published recommendations regarding how the public can manage exposure to lead by mitigating the risk (NHMRC, 2009). Methods for the safe approach to painting a house (when there is a likelihood of lead paint having been used previously) have been published by the Department of Sustainability, Environment, Water, Population and Communities (DSEWPaC, 2009).

Work Health and Safety

The health risk to workers from these chemicals is controlled when correct classification and labelling are considered, and adequate control measures to minimise occupational exposure and protective clothing are implemented. Safe Work Australia (SWA) encourages working safely with lead and promotes the *National Code of Practice for the Control and Safe Use of Inorganic Lead at Work [NOHSC: 2015 (1994)]* and the *National Standard for the Control of Inorganic Lead at Work [NOHSC:1012 (1994)]*. These Codes of Practice, in addition to the *Model Work Health and Safety Regulations, 2011* are available from the SWA website.

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

If empirical data become available for any member of the group indicating that a lower (or higher) classification is appropriate for the specific chemical, this may be used to amend the default classification for the chemical.

Hazard	Approved Criteria (HSIS) ^a	GHS Classification (HCIS) ^b
Repeat Dose Toxicity	Danger of cumulative effects (R33)*	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)
Carcinogenicity	Carc. Cat 3 - Limited evidence of a carcinogenic effect (Xn; R40)	Suspected of causing cancer - Cat. 2 (H351)
Reproductive and Developmental Toxicity	Repro. Cat 1 - May cause harm to the unborn child (T; R61)* Repro. Cat 3 - Possible risk of impaired fertility (Xn; R62)*	May damage the unborn child. Suspected of damaging fertility - Repr. 1A (H360Df)

^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 oral/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 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

Agency for Toxic Substances & Disease Registry (ATSDR) Toxicological Profile for Lead. Accessed September 2012 at <http://www.atsdr.cdc.gov/toxprofiles/tp13.pdf>

American Chemical Council: Global Automotive Declarable Substance List (GADSL). Accessed June 2013 at: <http://www.gadsl.org/>.

Australian Government, Customs (Prohibited Imports) Regulations 1956 (The Customs Act 1901). Accessed in June 2013 at <http://www.comlaw.gov.au/Details/F2013C00003>

Color Handbook. Accessed September 2013 at <http://www.specialchem4coatings.com/tc/color-handbook/?id=corrosionplumb>

Donovan J (1996). Lead in Australian Children: Report on the National Survey of Lead in Children. Canberra: Australian Institute of Health and Welfare. Accessed September 2012 at http://www.lead.org.au/Lead_in_Australian_Children.pdf

eChemPortal. Accessed June 2013 at <http://www.echemportal.org/echemportal/substancesearch/substancesearchlink.action>.

Galleria Chemica. Accessed June 2012. <http://jr.chemwatch.net/galleria/>

Hazardous Substances Data Bank (HSDB). US National Library of Medicine. Accessed June 2013 at <http://toxnet.nlm.nih.gov>

International Agency for Research on Cancer (IARC) (1980). Some metals and metallic compounds, IARC Monograph Volume 23. Accessed September 2012 at <http://monographs.iarc.fr/ENG/Monographs/vol23/volume23.pdf>

International Agency for Research on Cancer (IARC) (1987). Overall evaluations of carcinogenicity: An updating of IARC Monographs Volumes 1 to 42. Supplement 7. Accessed September 2012 at

International Agency for Research on Cancer (IARC) (2006). Inorganic and Organic Lead Compounds, IARC Monographs 87. Accessed September 2012 at <http://monographs.iarc.fr/ENG/Monographs/vol87/index.php>

Lead Development Association International (LDAI). 2008. Voluntary Risk Assessment Report on Lead and some Inorganic Lead Compounds. (LDAI now known as the International Lead Association). Accessed June 2013 at <http://echa.europa.eu/web/guest/information-on-chemicals/transitional-measures/voluntary-risk-assessment-reports>

NICNAS Priority Existing Chemical Report for Lead Compounds in Industrial Surface Coatings and Inks 2007. Electronic version for the web, accessed in September 2012 at www.nicnas.gov.au.

REACH Dossier. Lead oxide (Pb₃O₄) (1314-41-6). Accessed June 2013 at <http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances>

REACH Dossier. Lead oxide (PbO) (1317-36-8). Accessed June 2013 at <http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances>

REACH Dossier. Lead oxide (PbO₂) (1309-60-0). Accessed June 2013 at <http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances>

Ronis MJ, Badger TM, Shema SJ, Roberson PK & Shaikh F (1996). Reproductive toxicity and growth effects in rats exposed to lead at different periods during development. *Toxicology and Applied Pharmacology* 136(2) pp 361-371.

Ronis MJ, Gandy J & Badger TM (1998). Endocrine mechanisms underlying reproductive toxicity in the developing rat chronically exposed to dietary lead. *Journal Toxicology and Environmental Health* 54 pp 77-87.

Safe Work Australia (SWA). Hazardous Substances Information System (HSIS). Accessed June 2013 at <http://hsis.safeworkaustralia.gov.au/HazardousSubstance>

Substances in Preparations in Nordic Countries (SPIN). Accessed June 2013 at <http://188.183.47.4/dotnetnuke/Home/tabid/58/Default.aspx>

United States Centers for Disease Control and Prevention (CDC). Accessed December 2012 at <http://www.cdc.gov/nceh/lead/>

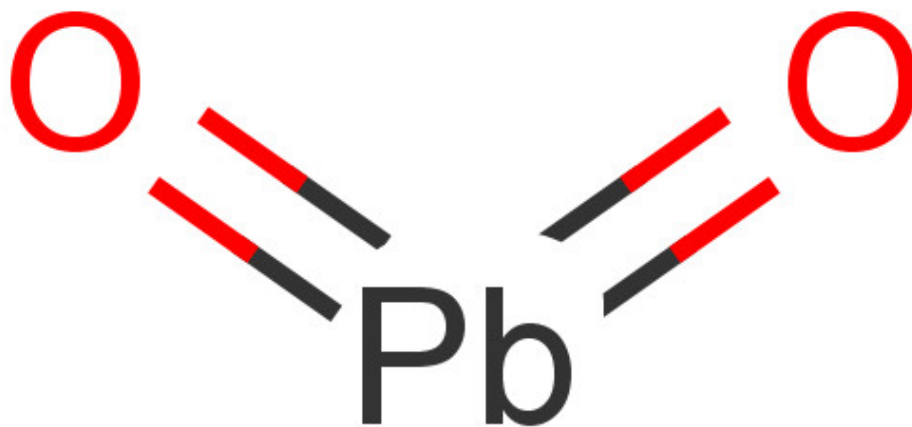
World Health Organisation (WHO) (1995) International Programme on chemical Safety (IPCS) Environmental Health Criteria 165 - Inorganic Lead. Accessed September 2012 at <http://www.inchem.org/documents/ehc/ehc/ehc165.htm>

Last Update 12 September 2013

Chemical Identities

Chemical Name in the Inventory and Synonyms	Lead oxide
CAS Number	1335-25-7
Structural Formula	$\text{Pb}^{2+} \quad \text{O}^{2-}$
Molecular Formula	Unspecified
Molecular Weight	

Chemical Name in the Inventory and Synonyms	Lead oxide (PbO₂) Lead dioxide Lead peroxide Lead oxide brown Lead superoxide Lead (IV) oxide
CAS Number	1309-60-0
Structural Formula	



Molecular Formula	O2Pb
Molecular Weight	239.20

Chemical Name in the Inventory and Synonyms	Lead oxide (Pb2O3) Lead sesquioxide Lead trioxide
CAS Number	1314-27-8
Structural Formula	Pb^{2+} Pb^{4+} O^{2-}
Molecular Formula	O.Pb
Molecular Weight	

Chemical Name in the Inventory and Synonyms	Lead oxide (Pb3O4) Lead oxide, red
---	--

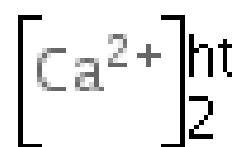
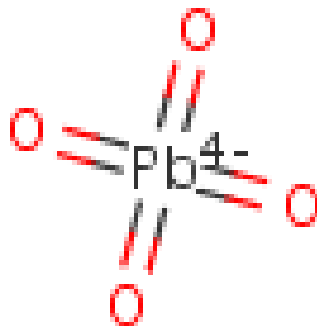
	Red lead Lead tetroxide Lead tetraoxide
CAS Number	1314-41-6
Structural Formula	<p>The structural formula shows three lead (Pb) atoms and four oxygen (O) atoms. Two lead atoms are at the top, and one is at the bottom. They are connected by red lines representing bonds. The oxygen atoms are also connected by red lines, forming a cyclic structure. The lead atoms are labeled with oxidation states (v3).</p>
Molecular Formula	O ₄ Pb ₃
Molecular Weight	685.60

Chemical Name in the Inventory and Synonyms	Lead oxide (PbO) Lead(II) oxide Litharge Lead monoxide
CAS Number	1317-36-8
Structural Formula	



Molecular Formula	OPb
Molecular Weight	223.20

Chemical Name in the Inventory and Synonyms	Plumbate (PbO₄⁴⁻), calcium (1:2), (T-4)- Calcium plumbate Dicalcium lead tetraoxide Calcium lead oxide
CAS Number	12013-69-3
Structural Formula	



Molecular Formula	Ca.1/2O4Pb
Molecular Weight	351.35

Share this page