



Australian Government
Department of Health and Ageing
NICNAS

INVENTORY MULTI-TIERED ASSESSMENT AND PRIORITISATION (IMAP)



HUMAN HEALTH TIER II ASSESSMENT FOR Lead Salts of Selected Fatty Acids

Lead Salts of Selected Fatty Acids

Chemical name in AICS	CAS Number
Octadecanoic acid, lead(2+) salt	1072-35-1
9,12-Octadecadienoic acid, (Z,Z)-, lead salt	16996-51-3
9-Octadecenoic acid, lead(2+) salt, (Z)-	1120-46-3
Docosanoic acid, lead salt	3249-61-4
Octanoic acid, lead(2+) salt	7319-86-0
Octadecanoic acid, lead salt	7428-48-0
Lead, bis(octadecanoato)dioxotri-	12578-12-0
9-Octadecenoic acid, 12-hydroxy-, lead(2+) salt (2:1), [R-(Z)]-	13094-04-7
Dodecanoic acid, lead salt	15306-30-6
9-Octadecenoic acid, lead salt, (Z)-	15347-55-4
Octanoic acid, lead salt	15696-43-2
Decanoic acid, lead(2+) salt	15773-52-1
Dodecanoic acid, lead(2+) salt	15773-55-4
Hexadecanoic acid, lead(2+) salt	15773-56-5
Hexadecanoic acid, lead salt	19528-55-3
Tetradecanoic acid, lead salt	20403-41-2
Decanoic acid, lead salt	20403-42-3
Docosanoic acid, lead(2+) salt	29597-84-0
9,12-Octadecadienoic acid, (Z,Z)-, lead(2+) salt	33627-12-2
Lead, bis(octadecanoato)dioxodi-	56189-09-4
Octadecanoic acid, 12-hydroxy-, lead(2+) salt (2:1)	58405-97-3
9-Hexadecenoic acid, lead(2+) salt, (Z)-	93858-24-3
Tricosanoic acid, lead salt	93966-37-1
Tetracosanoic acid, lead salt	93966-38-2
Hexacosanoic acid, lead salt	94006-20-9
Eicosanoic acid, lead(2+) salt (2:1)	94266-31-6
Eicosanoic acid, lead salt	94266-32-7

PREFACE

As part of the reform regarding assessment of Existing Chemicals, the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is implementing a new framework to address the human health and environmental impacts of industrial chemicals, not yet assessed, on the Australian Inventory of Chemical Substances (AICS).

The framework provides a more rapid, flexible and transparent approach for the assessment of existing chemicals.

The Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework was developed, with significant input from stakeholders, and will be applied in stages.

Stage One of this program, which will take three years, started 1 July 2012 and is examining 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This includes chemicals for which NICNAS already holds exposure information, chemicals identified as a concern or for which regulatory action has been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

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.

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

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

Disclaimer

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ACRONYMS & ABBREVIATIONS

ACToR	Aggregated Computational Toxicology Resource (US)
AICS	Australian Inventory of Chemical Substances
ASTDR	Agency for Toxic Substances and Disease Registry (US)
bw	bodyweight
CAS	Chemical Abstracts Service
CFR	Code of Federal Regulations (US)
CHO	Chinese hamster ovary
CosIng	Cosmetic Ingredients and Substances database (EU)
d	day
DNA	Deoxyribonucleic acid
EC	European Commission
EC3	Estimated concentration three
ECHA	European Chemicals Agency
ESIS	European Chemical Substances Information System
EU	European Union
EU RAR	European Union Risk Assessment Report
FDA	Food and Drug Administration (US)
FSANZ	Food Standards Australia and New Zealand
g	gram
g/mol	grams per mole
GHS	Globally Harmonized System of Classification and Labelling of Chemicals*
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GPMT	Guinea Pig Maximisation Test
h	hour
HGPRT	hypoxanthine guanine phosphoribosyltransferase
HPV	high production volume
HSDB	Hazardous Substances Data Bank
HSIS	Hazardous Substances Information System
HVICL	High Volume Industrial Chemicals List
IARC	International Agency for Research on Cancer
INCHEM	International Programme on Chemical Safety (also known as IPCS)
INCI	International Nomenclature of Cosmetic Ingredients
ip	intraperitoneal
IRIS	Integrated Risk Information System (US)
IUCLID	International Uniform Chemical Information Database
iv	intravenous
kg	kilogram
L	litre
LC50	median lethal concentration
LD50	median lethal dose
LCLo	lowest published lethal concentration
LLNA	local lymph node assay
LOAEL	lowest observed adverse effect level
LOEL	lowest observed effect level
m ³	cubic metre
mg	milligram
mg/cm ³	milligrams per cubic centimetre
mg/kg bw/d	milligrams per kilogram bodyweight per day
min	minute
mL	millilitre
µg	microgram
µL	microlitre
(m)SDS	(material) Safety Data Sheet

NIOSH	National Institute for Occupational Safety and Health (US)
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOHSC	National Occupational Health and Safety Commission
NTP	National Toxicology Program (US)
OECD	Organisation for Economic Cooperation and Development
OEL	occupational exposure limit
PCBU	person conducting a business or undertaking
PEL	permissible exposure limit
PND	postnatal day
ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million
REACH	Registration Evaluation Authorisation of Chemicals (ECHA)
SD	Sprague Dawley
SIAP	SIDS Initial Assessment Profile (OECD)
SIAR	SIDS Initial Assessment Report (OECD)
SIDS	Screening Information Data Set (OECD)
SMILES	simplified molecular-input line-entry system
SPIN	Substances in Preparations In the Nordic countries
STEL	short-term exposure limits
STV	short-term value
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons (The Poisons Standard**)
TCLo	lowest published toxic concentration
TEEL	temporary emergency exposure limits
TSCA	Toxic Substances Control Act (US EPA)
TG	test guideline
TGA	Therapeutic Goods Administration
TLV	threshold limit values
TWA	time weighted average
UN	United Nations
US	United States of America
US EPA	United States Environmental Protection Agency
WHS	Work, Health and Safety
wt	weight
w/w	weight per weight

Glossary

NICNAS uses the IPCS Risk Assessment Terminology (IPCS, 2004) glossary, which includes:

Part 1: IPCS/OECD Key Generic Terms used in Chemical Hazard/Risk Assessment; and

Part 2: IPCS Glossary of Key Exposure Assessment Terminology.

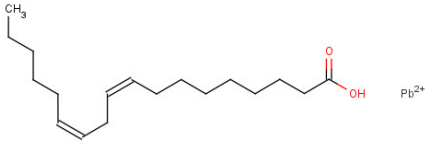
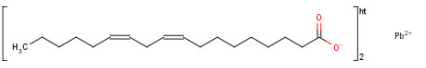
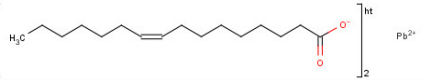
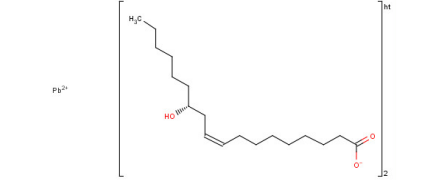
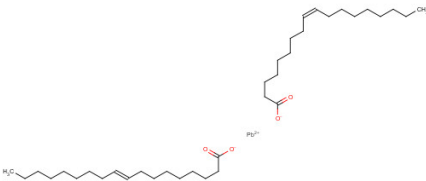
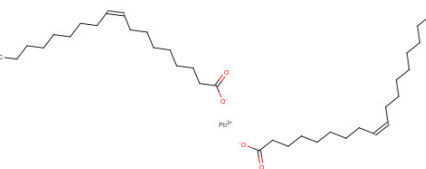
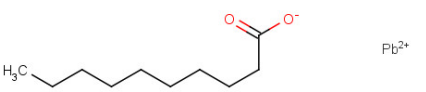
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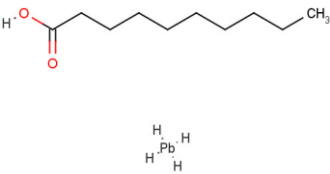
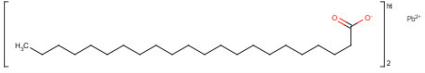
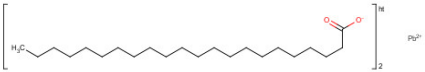
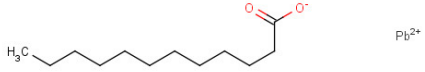
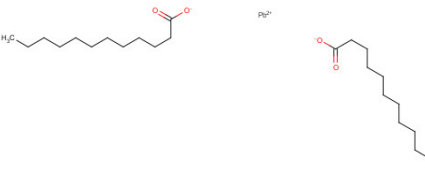
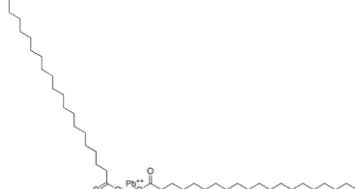
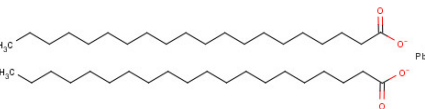
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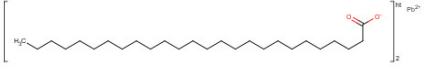
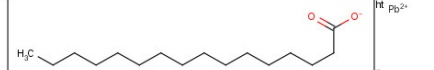
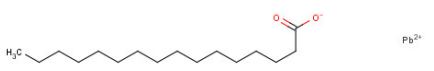
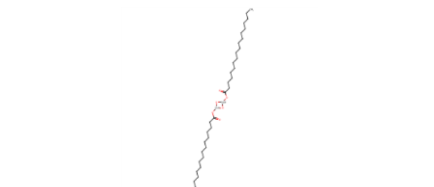

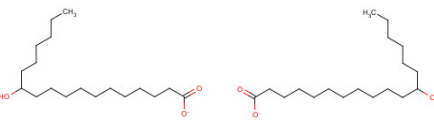
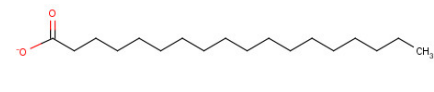
*Globally Harmonised System of Classification and Labelling of Chemicals (GHS) United Nations, 2009.

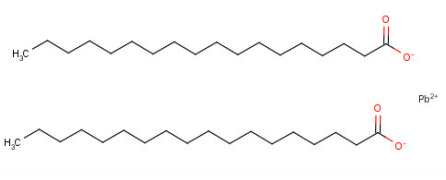
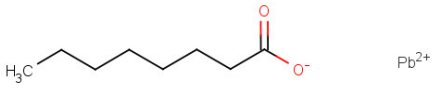
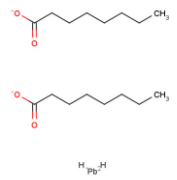
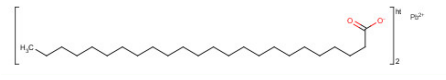
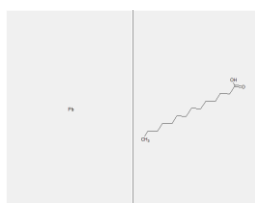
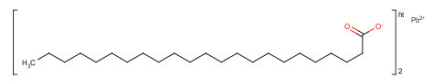
Third edition. Can be accessed at: http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html

**The Poisons Standard (the SUSMP) can be accessed at: <http://www.tga.gov.au/industry/scheduling-poisons-standard.htm>

Chemical Name in AICS (Including Synonyms)	CAS Number	Structural Formula	Molecular Formula	Weight (g/mol)
9,12-Octadecadienoic acid, (Z,Z)-, lead salt (9Z,12Z)-Octadeca-9,12-dienoic acid, lead (2+) salt 9,12-Octadecadienoic acid (9Z,12Z)-, lead salt 9,12-Octadecadienoic acid (9Z,12Z)-, lead salt (1:?) Lead linoleate	16996-51-3		C18H32O2.xPb	766.10
9,12-Octadecadienoic acid, (Z,Z)-, lead(2+) salt Linoleic acid, lead(2+) salt Lead dilinoleate	33627-12-2		C18H32O2.1/2Pb	766.10
9-Hexadecenoic acid, lead(2+) salt, (Z)- Lead(2+) (Z)-hexadec-9-enoate Lead dipalmitoleate	93858-24-3		C16H30O2.1/2Pb	714.00
9-Octadecenoic acid, 12-hydroxy-, lead(2+) salt (2:1), [R-(Z)]- Lead(2+) (R)-12-hydroxyoleate Lead diricinoleate	13094-04-7		C18H34O3.1/2Pb	802.10
9-Octadecenoic acid, lead salt, (Z)- 9-Octadecenoic acid (9Z)-, lead salt 9-Octadecenoic acid (9Z)-, lead salt (1:?) Lead oleate	15347-55-4		C18H34O2.xPb	770.10
9-Octadecenoic acid, lead(2+) salt, (Z)- Lead(II) oleate (2:1) 9-Octadecenoic acid (9Z)-, lead(2+) salt (2:1) Oleic acid lead salt Lead dioleate	1120-46-3		C18H34O2.1/2Pb	770.10
Decanoic acid, lead salt Decanoic acid, lead salt Lead caprate	20403-42-3		C10H20O2.xPb	378.50

Chemical Name in AICS (Including Synonyms)	CAS Number	Structural Formula	Molecular Formula	Weight (g/mol)
Decanoic acid, lead(2+) salt Lead(2+) decanoate Lead dicaprate	15773-52-1		C10H20O2.1/2Pb	383.50
Docosanoic acid, lead salt Docosanoic acid, lead salt lead behenate	3249-61-4		C22H44O2.xPb	886.40
Docosanoic acid, lead(2+) salt Lead didocosanoate Lead dibehenate	29597-84-0		C22H44O2.1/2Pb	886.40
Dodecanoic acid, lead salt Lauric acid, lead salt Lead laurate	15306-30-6		C12H24O2.xPb	406.50
Dodecanoic acid, lead(2+) salt Lauric acid, lead (2+) salt Dodecanoic acid, lead(2+) salt Dodecanoic acid, lead(2+) salt (2:1) Lead dilaurate	15773-55-4		C12H24O2.1/2Pb	605.80
Eicosanoic acid, lead salt Lead icosanoate Lead arachidate	94266-32-7		C20H40O2.xPb	830.20
Eicosanoic acid, lead(2+) salt (2:1) Lead icosanoate (1:2) Lead diarachidate	94266-31-6		C20H40O2.1/2Pb	830.30

Chemical Name in AICS (Including Synonyms)	CAS Number	Structural Formula	Molecular Formula	Weight (g/mol)
Hexacosanoic acid, lead salt Hexacosanoic acid, lead salt Lead cerotate	94006-20-9		C26H52O2.xPb	998.60
Hexadecanoic acid, lead salt Lead palmitate	19528-55-3		C16H32O2.xPb	718.00
Hexadecanoic acid, lead(2+) salt Palmitic acid, lead(2+) salt Lead dipalmitate	15773-56-5		C16H32O2.1/2Pb	462.60
Lead, bis(octadecanoato)dioxodi- Dibasic lead stearate Octadecanoic acid, lead salt, dibasic Dioxobis(stearato)dilead Stearic acid, lead salt, dibasic	56189-09-4		C36H70O6Pb2	1013.40
Lead, bis(octadecanoato)dioxotri- Lead, dioxobis(stearato)tri- Dioxobis(stearato)trilead Lead, bis(octadecanoato)dioxotri-	12578-12-0		C36H70O6Pb3	1220.50
Octadecanoic acid, 12-hydroxy-, lead(2+) salt (2:1) Lead bis(12-hydroxystearate)	58405-97-3		C18H36O3.1/2Pb	806.10
Octadecanoic acid, lead salt Stearic acid, lead salt Lead octadecanoate Lead stearate Octadecanoic acid, lead salt (1:?)	7428-48-0		C18H36O2.xPb	490.70

Chemical Name in AICS (Including Synonyms)	CAS Number	Structural Formula	Molecular	
			Formula	Weight (g/mol)
Octadecanoic acid, lead(2+) salt Lead distearate Lead(2+) octadecanoate Lead(II) octadecanoate Lead(2+) stearate Lead(II) stearate	1072-35-1		C18H36O2.1/2Pb	774.10
Octanoic acid, lead salt Lead octanoate Octanoic acid, lead salt Octanoic acid, lead salt (1:?) Lead caprylate	15696-43-2		C8H16O2.xPb	350.40
Octanoic acid, lead(2+) salt Lead dioctanoate Lead(II) octoate Lead(2+) octanoate Lead dicaprylate	7319-86-0		C8H16O2.1/2Pb	495.60
Tetracosanoic acid, lead salt Lignoceric acid, lead salt Lead tetracosanoate Lead lignocerate	93966-38-2		C24H48O2.xPb	942.50
Tetradecanoic acid, lead salt Lead tetradecanoate Myristic acid, lead salt Tetradecanoic acid, lead salt Tetradecanoic acid, lead salt (1:?) Lead myristate	20403-41-2		C14H28O2.xPb	436.60
Tricosanoic acid, lead salt Lead bis(tricosanoate)	93966-37-1		C23H46O2.xPb	914.40

Grouping Rationale

This group of 27 chemical compounds predominantly consists of lead salts of naturally occurring fatty acids. 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. The toxicity is considered to result entirely from the presence of the lead component (cation). The non-lead components (anions) are all included in the Identification of Chemicals of Low Concern to Human Health (NICNAS, 2012) and are not considered toxic. The lead compounds with an unspecified oxidation state will predominantly contain lead in the +2 oxidation state.

Data presented by the Lead REACH Consortium in the draft chemical safety report extract – self classification, in which lead salts of fatty acids (C16 – C18) were grouped together support the grouping of these 27

chemicals based on similarities in toxicological profiles. 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

Some lead compounds are listed in the 2006 High Volume Industrial Chemicals List (HVICL), however of the 27 lead compounds in the group assessed, no specific Australian use, import, or manufacture information have been identified, except in the following cases:

Octadecanoic acid, lead(2+) salt (CAS No: 1072-35-1)

Reported commercial use including:

- lubricants and additives.

Reported site-limited use including:

- stabilisers.

This lead compound is listed on the 2002 HVICL with a total reported volume between 1 000 and 9 999 tonnes.

Octanoic acid, lead(2+) salt (CAS No: 7319-86-0)

Due to the lead compound's historical use in paints, this compound was included in a NICNAS mandatory call for information (2006) regarding usage in industrial surface coatings and inks. The use in paints was reported to be zero.

International

For the majority of the group the following international uses have been identified from the Global Automotive Declarable Substance List (GADSL) via US Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR):

The lead compounds have reported domestic use including:

- pigments.

The lead compounds have reported site-limited use including:

- metallurgical, e.g. bearing metals, brass, aluminium and steel;
- stabilisers.

The following individual lead compounds have international uses identified from Galleria Chemica, European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) Dossiers, Substances and Preparations In the Nordic countries (SPIN) database & eChemPortal (European Commission IUCLID & OECD Chemical Data Sheets, EnviChem- Finnish Environment Institute), the Global Automotive Declarable Substance List (GADSL) via US Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR):

9-Octadecenoic acid, lead(2+) salt, (Z)- (CAS No: 1120-46-3);

Octanoic acid, lead salt (CAS No: 15696-43-2);

Octanoic acid, lead (2+) salt (CAS No: 7319-86-0);

Lead, bis(octadecanoato)dioxodi- (CAS No: 56189-09-4);

Octadecanoic acid, lead (2+) salt (CAS No:1072-35-1);

Octadecanoic acid, lead salt (CAS No: 7428-48-0);

Lead, bis(octadecanoato)dioxotri- (CAS No: 12578-12-0).

Each of these lead compounds have one of more of the following reported uses:

Domestic:

- paints, lacquers and varnishes;

- cleaning/washing agents.

Commercial:

- corrosion inhibitor for use in petroleum;
- lubricants and additives, such as high pressure solid, internal lubricants and a lubricant in extrusion of plastics;
- process regulators.

Site-limited:

- stabilisers, e.g. manufacture of vinyl polymers.

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 1, 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 the paint.

Appendix C

LEAD COMPOUNDS in paints, tinters, inks or ink additives except in preparations containing 0.1 per cent or less 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.

Given these restrictions, domestic use in paints identified from international sources can be considered to not be relevant to Australia.

Further information regarding the restriction of lead in cosmetics is provided in the NICNAS Existing Chemicals Information Sheet: Lead in Cosmetics (November, 2008).

International

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

Cosmetics

Lead compounds appear on the following:

- The Canadian List of Prohibited and Restricted Cosmetic Ingredients (The Cosmetic Ingredient "Hotlist").
- The EU Cosmetic Directive 76/768/EEC Annex II: List of Substances which must not form part of the Composition of Cosmetic Products (English).
- The New Zealand Cosmetic Products Group Standard - Schedule 4: Components Cosmetic Products Must Not Contain - Table 1.
- The Thailand Cosmetic Act - Prohibited Substances.

Existing Hazard Classification for Worker Health and Safety

Lead compounds with the exception of those specified elsewhere in the Hazardous Substances Information System (HSIS) are classified as hazardous with the following risk phrases for human health in HSIS (Safe Work Australia):

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; R20/22 (Harmful by inhalation / harmful if swallowed)

Xn; R33 (Danger of cumulative effects)

Exposure Standards

Australian

Lead compounds, with the exception of those specified elsewhere in the Hazardous Substances Information System (HSIS) including the lead compounds covered by this assessment, have the following exposure standards reported in HSIS (Safe Work Australia):

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

TWA: 0.20 mg/m³ [Thailand, USA]

TWA: 0.15 mg/m³ [Argentina, Canada, Egypt, European Union, Gibraltar, India, Malta, Singapore, Slovak Republic]

TWA: 0.10 mg/m³ [Austria MAK, New Zealand, Republic of South Africa, Sweden]

TWA: 0.05 mg/m³ [Bulgaria, Canada, China, Italy, Malaysia, USA]

STEL: 0.45 mg/m³ [Argentina, Canada, Egypt]

STEL: 0.15 mg/m³ [Canada]

STEL: 0.10 mg/m³ [Austria MAK]

Health Hazard Information

For this group of chemicals, the hazard associated with each health endpoint is considered to be due to the lead cation. While no experimental data were available on the lead compounds considered in this assessment, data sources for determining the hazard for the lead cation include animal studies on well characterised organic and inorganic lead compounds, and a large amount of literature on observations in humans.

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 8) 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 an oral repeat dose toxicity study, rats were dosed with 0, 200, 500 or 1000 ppm lead acetate and tested for 4, 8 and 12 weeks. The blood lead concentration (PbB) level range was 40 - 100 ug/dL and the kidney lead was highest at 4 weeks. For all test groups the urinary lead excretion was highest at 4 weeks and then decreased with continued exposure to lead (REACH, 2012).

If inhaled, the size of lead compound particulates 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 over a 12 hour (h) 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.

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; however, adults generally have a higher concentration. When in the blood, 99 % of lead is bound to proteins within erythrocytes (NICNAS, 2007).

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).

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 blood lead (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

Lead compounds (not listed elsewhere in HSIS) are classified as hazardous with the risk phrase 'Harmful if swallowed' (Xn; R22) in HSIS (Safe Work Australia). Data available from observations in humans support this classification and are presented in the following sections. The rat median lethal concentration (LD50) is >2000 mg/kg bw (REACH, 2012). Reported signs of toxicity from rats include raised fur, arched back and slightly decreased motor activities from approximately 4 hours to 9 days after dosing was observed. No other adverse effects were noted during the observation time.

Dermal

Several lead compounds were reported to exhibit low acute toxicity in animal tests as evidenced by reported LD50 in rats of > 2000 mg/kg bw (REACH, 2012).

Inhalation

Lead compounds (not listed elsewhere in HSIS) are classified as hazardous with the risk phrase 'Harmful by inhalation' (Xn; R20) in HSIS (Safe Work Australia). The data available from observations in humans support this classification given that lead compounds are absorbed systemically following inhalation (NICNAS, 2007). The rat median lethal concentration LC50 is > 5.05 mg/L in air (REACH, 2012). No clinical signs of toxicity were reported.

Observation in humans

The primary source for the data provided in this section recognises that the toxic effects of lead compounds are the same regardless of the route of exposure (ASTDR, 2007). Therefore route specific data is 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 has been collected from accidental or intentional exposure via ingestion or inhalation, and there is rich data regarding the dose-effect in humans (NICNAS 2007; ASTDR 2007). Exposure can cause encephalopathy (the symptoms of which include: hyperirritability, ataxia, convulsions, stupor and coma) in addition to gastrointestinal effects such as colic (the symptoms can be displayed as: abdominal pain, constipation, cramps, nausea, vomiting, anorexia and weight loss) (ASTDR 2007; WHO 1995). It was recorded that symptoms 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 symptom 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 recorded in 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. Symptoms 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). Notably some of the population with recorded PbB levels between 60 – 300 µg/dL after exposure did not report any symptoms. Other symptoms of acute lead poisoning recorded included gastrointestinal effects (abdominal pain, constipation, cramps, nausea, vomiting, anorexia and weight loss) were associated with 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 a symptom 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 haem-containing protein cytochrome P-450 (NICNAS, 2007).

Irritation / Corrosivity

Skin Irritation

In general, lead compounds are not considered irritating to skin (REACH, 2012). No effects were reported in skin irritation assays in rabbits citing OECD TG 404 using lead oxide, dibasic lead phosphite and dibasic lead phthalate.

Eye Irritation

In general lead compounds were not reported to be irritating to eyes or having caused serious eye damage (REACH, 2012). In an eye irritation assay (OECD TG 405) in rabbits (New Zealand White) using dibasic lead phthalate, all symptoms reported were fully reversible within 7 days.

Observation in humans

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

Sensitisation

Skin sensitisation

Several lead compounds were reported to be non-sensitisers (REACH, 2012). 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).

Repeat dose toxicity

Oral

The lead compounds (unless listed elsewhere in HSIS) are currently classified as hazardous with the risk phrase 'Danger of cumulative effects' (R33) in HSIS. This is not specific to the route of exposure. The data available from observation in humans support this classification.

A lowest observed adverse effect level (LOAEL) in rats of 200 ppm (equivalent to a mean daily intake of 3.1 mg/kg bw/day) was derived based on body and kidney weights (REACH, 2012).

In a repeated dose toxicity study with Sprague-Dawley rats following the guidelines set out in an EPA chronic feeding study, the chemical was administered via drinking water (ad libitum) to 18 male rats per dose group at 0, 200, 500 and 1000 ppm per day for 4, 8 and 12 weeks. Decreased body weight and increased kidney weight as a percentage of body weight were reported at all dose ranges from 4 weeks.

Dermal

No significant adverse effects were reported following repeated dermal exposure to several lead compounds in a weight of evidence report (REACH, 2012).

In a weight of evidence report available on repeat dose toxicity during dermal exposure, rats were exposed to lead oleate, lead acetate, lead arsenate or tetraethyl lead for 24 hs. The test groups had lead compounds applied either directly to the skin or to skin that had been mechanically injured. Comparatively, greater absorption of lead was reported in the groups where the skin had been mechanically injured. Dermal absorption of lead was shown to occur in all the test groups, although the concentration of tissue lead in the group exposed to tetraethyl lead was significantly greater than the groups exposed to non-volatile lead compounds.

Inhalation

No significant adverse effects were reported by weight of evidence following repeated inhalation exposure to lead nitrate (REACH, 2012).

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

A statistically significant reduction in the relative size of the spleen and thymus in the 14 day and 28 day test groups was reported. Increased lung weight was noted in the 14 day and 28 day test groups and an increase lead concentration was reported in the liver, lung and kidney, although the 28 day inhalation group was noted to show a greater concentration. There were no apparent differences in body weight and food consumption noted in 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 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 for a decrease in haemoglobin to be seen.

- *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 illustrated 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 \geq 50 µg/dL.

Genotoxicity

Lead compounds are considered genotoxic for mammalian cells.

The genotoxic effects of lead were reviewed and presented by the Agency for Toxic Substances and Disease Registry (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, 2012). 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, resulted in the classification of inorganic lead compounds as probably carcinogenic to humans (Group 2A) (IARC 1980; IARC, 1987; IARC 2006).

The review indicated that there was sufficient evidence in experimental animals for the carcinogenicity of inorganic lead compounds, lead acetate, lead subacetate, lead chromate and lead phosphate. It was also indicated that there was insufficient evidence in experimental animals for the carcinogenicity of organic lead compounds, lead oxide and lead arsenate, tetraethyl lead and lead powder.

Reproductive and developmental toxicity

Reproductive toxicity

Lead compounds (unless listed elsewhere in HSIS) are currently classified as hazardous with the risk phrase 'Possible risk of impaired fertility' (R62) in HSIS (Safe Work Australia). The available data support this classification.

In a reproductive and developmental toxicity screening test in Sprague-Dawley rats, lead acetate was administered via drinking water to nine females at 0.6 % weight per volume (w/v) at gestation days 5 – 21 (Ronis et al, 1996). 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 Sprague-Dawley 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) µg/dL, 83(±8) µg/dL and 120(±120) µg/dL for increasing dose groups respectively, while the female pups had PbB levels of 42(±7) µg/dL, 67(±16) µg/dL and 197(±82) µg/dL.

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 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 could result in spontaneous abortion, pre-term delivery, alterations in sperm and decreasing male fertility (ASTDR, 2007).

Developmental toxicity observations in humans

Lead compounds (unless listed elsewhere in HSIS) are currently classified as hazardous with the risk phrase 'May cause harm to the unborn child' (R61) in HSIS (Safe Work Australia). The available data support this classification.

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 greater than 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 less than 10 µg/dL, there is uncertainty attached to these estimates of reported effects (ASTDR, 2007). Even so, the US Center for Disease Control (CDC) has a reference level of 5 µg/dL, above which they recommend that public health action be initiated (CDC).

Risk Characterisation

Critical Health Effects

The main critical effects to human health are reproductive and developmental toxicity, potential genotoxicity, and limited carcinogenicity. The chemical is also expected to have acute and repeated dose toxicity.

Public Risk Characterisation

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

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 an employee at a workplace 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) has been published by the Department of Sustainability, Environment, Water, Population and Communities (DSEWPoC, 2009).

Occupational 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 National Standard for the Control of Inorganic Lead at Work [NOHSC:1012 (1994)]. These Codes of Practice, in addition the Model Work Health Safety Regulations, 2011 are available from the SWA website.

	<i>Approved Criteria (HSIS)^a</i>	<i>GHS Classification</i>
Acute Toxicity	Harmful if swallowed (Xn; R22)* Harmful by inhalation (Xn; R20)*	Harmful if swallowed - Cat. 4 (H302) Harmful if inhaled - Cat. 4 (H332)
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)
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)	

^a Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

* Existing Hazard Classification. No change recommended to this classification.

Advice for consumers

Products containing the chemical should be used according to label instructions.

Advice for industry

Control measures

Control measures to minimise the risk from dermal, ocular and inhalation exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate or minimise risk arising from storage, handling and use of a hazardous chemical are dependent 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:

- use of closed systems or isolation of operations;
- use of 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;
- minimisation of manual processes and work tasks through automation of processes;
- work procedures that minimise splashes and spills;
- regular cleaning of equipment and work areas; and
- use of 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 be relied upon on its own to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selection of 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 hazardous chemical are prepared; and
- management of risks arising from storage, handling and use of 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 physical hazards of the chemical has not been undertaken as part of this assessment.

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