Aluminium chlorides: Human health tier II assessment

04 July 2014

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Aluminium chloride, basic	1327-41-9
Aluminium chloride, hexahydrate	7784-13-6
Aluminium chloride (AlCl3)	7446-70-0
Aluminium chloride hydroxide	10284-64-7
Aluminium chloride hydroxide (Al4Cl3(OH)9)	11089-92-2
Aluminium chloride hydroxide (Al2Cl(OH)5)	12042-91-0
Aluminium chloride hydroxide, AlCl2(OH)	14215-15-7

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

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

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

Disclaimer

ACRONYMS & ABBREVIATIONS

Grouping Rationale

This group consists of soluble aluminium chlorides, including one anhydrous compound and hydrates. The aluminium ion is considered to be the moiety responsible for systemic toxicity. This group of aluminium chemicals has similar bioaccessibility and bioavailability; that is, these aluminium chemicals release the aluminium ion into biological fluids at similar rates and, therefore, can be assessed collectively. Aluminium chloride ($AlCl_3$) has additional acute local hazards (corrosivity and irritation) when present as the pure compound or at high concentrations. Aluminium trichloride, hexahydrate will be intermediate in terms of irritancy between the anhydrous chloride and the remainder of the group due to its significant acidity.

Considering that aluminium chloride (hydrated) has similar bioaccessibility and bioavailability in biological fluids, data available for aluminium chloride can be "read across" when data are lacking for the chemicals in this group (OECD, 2014).

Hydrates are taken as being covered by listing as the anhydrous form for regulatory purposes, including AICS listing. For this reason the AICS entry for anhydrous $AlCl_3$ may also be used for hydrated forms, necessitating the assessment of these together. Other hydrous forms of these chemicals not listed on AICS are also covered by this assessment.

Import, Manufacture and Use

Australian

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

Aluminium chloride, basic has reported use as an odour agent and other (unspecified) uses. Aluminium chloride ($AlCl_3$) has reported use as fillers and process regulators. The total volume for both chemicals introduced into Australia, reported under previous mandatory and/or voluntary calls for information, was between 1000 and 9999 tonnes (NICNAS, 2006).

The following non-industrial use has been identified in Australia:

- drinking water treatment (aluminium chloride hydroxide ($Al_2Cl(OH)_5$).

International

The following international uses have been identified through European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers; Galleria Chemica; the Substances and Preparations in the Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database; the United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary; and the United States (US) Household Products Database.

All the chemicals in this group apart from aluminium chloride hydroxide, $AlCl_2(OH)$ have reported cosmetic use as:

- antiperspirants, deodorants and astringents in skin fresheners and other personal care products.

These chemicals have reported commercial use including:

- as process regulators;
- in surface treatment;
- in water purification and treatment of sewage and plant effluent;
- in the dyeing of fabrics;
- in the manufacture of parchment paper;
- as fixing agents;
- as odour agents;
- as cleaning and washing agents; and
- as adhesives and binding agents.

These chemicals have reported site-limited use including:

- as intermediates; and
- as complexing and flocculating agents.

Aluminium chloride ($AlCl_3$) has site-limited use including:

- as an acid catalyst, especially in Friedel-Crafts type reactions;
- in cracking of petroleum; and

- in the manufacture of rubbers and lubricants.

The following non-industrial uses have been identified internationally for aluminium chloride, hexahydrate and aluminium chloride hydroxide ($Al_2Cl(OH)_5$) respectively:

- wood preservative and therapeutic goods (antihyperphospataemic).

Restrictions

Australian

No known restrictions have been identified for these chemicals, except for a general limit on total aluminium intake under food standards.

Water authorities are strongly encouraged to keep acid-soluble aluminium concentrations as low as possible, preferably below 0.1 mg/L, to meet aesthetic requirements for drinking water (NHMRC, 2011).

International

The Joint Food and Agriculture Organization (FAO) of the United Nations/World Health Organization (WHO) Expert Committee on Food Additives (JECFA) established a provisional tolerable weekly intake (PTWI) of 2 mg Al/ kg bw/day, which is adopted in Australia by FSANZ.

The European Food Safety Agency set a Tolerable Weekly Intake of 1 mg Al/kg bw/day for all aluminium compounds (IPCS, 2012).

Existing Worker Health and Safety Controls

Hazard Classification

Apart from aluminium chloride ($AlCl_3$), the chemicals in this group are not listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia).

Aluminium chloride ($AlCl_3$) (CAS No 7446-70-0) has the following classification:

C; R34

Exposure Standards

Australian

The chemicals in this group fall under the category 'Aluminium, soluble salts (as Al)' in HSIS, and have an exposure standard of 2 mg/m^3 time weighted average (TWA) (HSIS).

International

The following exposure standards are identified for the category 'Aluminium, soluble salts (as Al)' (Galleria Chemica):

An exposure limit (TWA) ranging from 0.5 mg/m^3 (Russia) to 5 mg/m^3 (France, USA) with an exposure limit of 2 mg/m^3 in most countries (in various states of the USA, various provinces of Canada, Greece and the United Kingdom).

Health Hazard Information

Toxicokinetics

Assessment of the bioavailability of aluminium compounds is confounded by limitations in the analytical methodology, particularly for older studies, by concurrent exposure to modifying factors and by dose-dependency (bioavailability varies according to exposure levels). Speciation appears to be an important factor in absorption and it is widely assumed that soluble aluminium compounds, such as the chloride and lactate salts, are more bioavailable than insoluble compounds, such as aluminium hydroxide or silicates. Studies in laboratory animals and in human volunteers generally show that absorption of aluminium is less than 1 % by any route. Concurrent intake of organic anions (particularly citrate) increases the absorption of aluminium, while other anions, such as silicates and phosphate, may reduce the absorption of aluminium (WHO, 2007).

Oral exposure

Aluminium is poorly absorbed following oral exposure (ATSDR, 2008; Environment Canada and Health Canada, 2010). Approximately 0.1–0.6 % of ingested aluminium is usually absorbed, depending on the dose. The observed relationship between dose and bioavailability is inconsistent: increased doses of aluminium decreased its bioavailability in some experimental studies while opposite results were observed in other work (Environment Canada and Health Canada, 2010). There are indications that the toxicokinetics of aluminium are dose-dependent and since high doses have been administered in many studies, the results of these studies, with respect to their relevance to humans, should be interpreted with caution (WHO, 2007).

Other factors influencing oral bioavailability include solubility of aluminium compounds, gastric pH, nutritional and medical status (for example, people with Down syndrome absorb aluminium at levels five times higher than people without the condition (EHC, 1997; Krewski 2007)).

Dermal exposure

There is some evidence from human case studies that small amounts of aluminium do reach the systemic circulation following dermal application. However, to date, no data for dermal bioavailability are available from controlled studies of more than one or two individuals (Environment Canada and Health Canada, 2010). A recent in vitro study of percutaneous absorption of aluminium from antiperspirants through human skin in the Franz™ diffusion cell found insignificant transdermal absorption of aluminium and particularly low cutaneous absorption which varied according to the formulations tested (aerosol base, stick and roll on). On stripped skin (mimicking damaged or freshly shaven skin), the measured uptake of aluminium was significantly higher (11.50 μg/cm^2 versus 1.81 μg/cm^2 for normal skin) using the stick formulation (Pineau, 2012).

Inhalation exposure

An investigation in New Zealand White rabbits exposed via the nasal-olfactory pathway (sponge soaked in aluminium solutions inserted into nasal recess for four weeks) provided evidence that inhaled aluminium in the olfactory tract can cross the nasal epithelium to reach the brain directly through axonal transport (Environment Canada and Health Canada, 2010).

Excretion

Following oral exposure, unabsorbed aluminium is excreted in the faeces. Absorbed aluminium is excreted principally in the urine and, to a lesser extent, in the bile. It was reported that the higher urinary excretion of aluminium in exposed workers, compared to the general population, demonstrates that some inhaled aluminium can reach the systemic circulation (Environment Canada and Health Canada, 2010).

Distribution

Aluminium binds to various ligands in the blood and distributes to every organ, with highest concentrations found in bone and lung tissues (ATSDR, 2008). It crosses the brain and placental barriers in very small amounts. Human and animal studies

demonstrate accumulation of aluminium in the brain and, in animal studies, in foetuses (ATSDR, 2008; Environment Canada and Health Canada, 2010).

Aluminium is efficiently transferred from blood to milk in lactating animals. Very low concentrations of aluminium are found in the milk of lactating humans. Two studies were undertaken in Canada to measure levels of aluminium in breast milk. They indicated that mean concentrations of aluminium in breast milk were of the same order of magnitude as elsewhere in the world with an average of approximately 0.11 mg/kg (Environment Canada and Health Canada, 2010).

There is evidence that with increasing age of humans, aluminium concentrations increase in the brain tissue, blood and bone. A number of studies indicate that removal of aluminium from the brain is low (Krewski, 2007). In humans, the aluminium levels are higher in the cerebral cortex and hippocampus than in other brain structures (Environment Canada and Health Canada, 2010; Walton, 2009).

Acute Toxicity

Oral

The chemicals in this group generally have low acute oral toxicity. LD50 values for aluminium chloride, basic, and aluminium chloride hydroxide ($Al_2Cl(OH)_5$) were greater than 2000 mg/kg bw based on rat studies conducted in accordance with OECD Test Guideline (TG) 401 (REACH). Effects following oral administration could result from ingestion of anhydrous $AlCl_3$ due to its corrosive nature.

Dermal

The chemicals in this group have low acute dermal toxicity. LD50 values for aluminium chloride, basic, and aluminium chloride hydroxide ($Al_2Cl(OH)_5$) were greater than 2000 mg/kg bw based on rat studies conducted in accordance with OECD TG 402 (REACH).

Inhalation

No mortalities were found in studies involving inhalation exposure of humans or animals to various forms of aluminium (ASTDR, 2008).

Regarding aluminium chloride ($AlCl_3$), due to the corrosive properties of this chemical, acute inhalation testing is not required unless there are concerns regarding exposure at non-corrosive concentrations.

Observation in humans

No aluminium-related deaths in healthy humans have been reported after oral, dermal or inhalation exposure (ATSDR, 2008).

Corrosion / Irritation

Corrosivity

Aluminium chloride ($AlCl_3$) is classified as hazardous with the risk phrase "Causes burns" (C; R34) in HSIS (Safe Work Australia). This classification is supported by the physical-chemical properties of this chemical (it reacts violently and

exothermically with water to form hydrochloric acid). HSDB describes the chemical as " Irritating to eyes, nose and throat. Will burn skin and eyes" (HSDB).

Skin Irritation

Aluminium chloride, basic is reported to produce slight, reversible skin irritation in some rat studies. The effects were not sufficient to warrant a hazard classification. No effects were reported in a study conducted on aluminium chloride hydroxide ($Al_2Cl(OH)_5$). All studies were conducted in accordance with OECD TG 404 (REACH).

Data regarding aluminium chloride, hexahydrate can be read across from other salts producing the hexaaqua aluminium ion in water such as the alums, sulfuric acid, aluminium salt (3:2), sulfuric acid, aluminium potassium salt (2:1:1); and sulfuric acid aluminium ammonium salt (2:1:1). Tests on these compounds performed in accordance with OECD TG 404 found some skin irritation but the effects were not sufficient to warrant a hazard classification (NICNAS). Based on this, classification of aluminium chloride, hexahydrate is not warranted.

Eye Irritation

Aluminium chloride, basic and aluminium chloride hydroxide ($Al_2Cl(OH)_5$) are reported to produce reversible signs of eye irritation in some rabbit studies including corneal opacity, changes in the iris, conjunctival redness and swelling. One study involving exposure to aluminium chloride, basic reported a moderate degree of irreversible corneal opacity. However, the test solution was reported to have a pH of 0.4, much lower than expected for these chemicals. Thus the study results were questionable. All studies were conducted in accordance with OECD TG 405. The effects were not sufficient to warrant a hazard classification (REACH).

Data regarding aluminium chloride, hexahydrate can be read across from sulfuric acid, aluminium salt (3:2) because both salts produce the hexaaqua aluminium ion in water. Three studies on this compound performed in accordance with OECD TG 405 reported eye irritation. Two of the studies found conjunctival redness and swelling which was not reversible during the test periods (three and seven days). The third test reported conjunctivitis and purulent ophthalmitis which were reversible during the 21-day study (NICNAS). Based on this, classification of aluminium chloride, hexahydrate is warranted.

Regarding aluminium chloride ($AlCl_3$), corrosive chemicals are considered to cause irreversible effects on the eyes.

Sensitisation

Skin Sensitisation

The available data do not provide any evidence of skin sensitisation. Aluminium chloride, basic and aluminium chloride hydroxide ($Al_2Cl(OH)_5$) did not induce dermal sensitisation when tested in guinea pigs using the Guinea Pig Maximisation TEST according to OECD TG 406 (REACH).

Observation in humans

The data obtained from human studies of these chemicals and other relevant observations are consistent with those found in animal studies.

In 2011, the French agency for the safety of sanitary and health products (AFSSAPS) published a scientific opinion on the safety of aluminium from exposure to cosmetic sources concluding that additional data concerning the potential irritation of aluminium containing cosmetics are needed, but that human cases of sensitisation are rare (AFSSAPS, 2011; VKM, 2013).

The ATSDR reports that the dermal hypersensitivity to aluminium appears to be rare in humans (ATSDR, 2008).

Repeated Dose Toxicity

Oral

The lowest observed adverse effect level (LOAEL) of 0.9 mg aluminium chloride, hexahydrate /kg bw/day was found in a chronic rat study (greater than 28 months). Neurotoxic effects and the neuropathology observed at and above this concentration are described in the neurotoxicity section.

Effects apart from neurotoxicity have only been observed at much higher doses.

Dermal

No data are available.

Inhalation

Results from human and animal studies investigating the toxicity of soluble and insoluble forms of aluminium suggest that the respiratory tract, particularly the lung, is a sensitive target of airborne aluminium toxicity. The lung effects observed in humans and animals are suggestive of dust overload (ATSDR, 2008).

Observation in humans

Aluminium has been shown to have neurotoxic effects in addition to bone and blood toxicity in humans during medical treatment in which the gastrointestinal barrier is bypassed (e.g. aluminium-induced encephalopathy through dialysis treatment in patients with renal failure) (ATSDR, 2008).

Interpretation of the human inhalation data is complicated by the lack of exposure assessment and the potential for exposure to both soluble and insoluble aluminium compounds, and concomitant exposure to other toxic compounds. Numerous studies have found impaired lung function in a variety of aluminium workers. Other effects that have been observed include occupational asthma and pulmonary fibrosis (ASTDR, 2008).

Neurotoxicity data are discussed in the neurotoxicity section.

Genotoxicity

The weight of evidence does not support classification of these chemicals for genotoxicity.

Negative results were observed for aluminium compounds in most short-term in vitro mutagenic assays for reverse mutations and forward mutations in bacteria as well as assays for morphological transformation in Syrian hamster cells. Positive results were found in in vivo tests for chromosome aberrations in bone marrow cells in mice and rats (ATSDR, 2008; Environment Canada and Health Canada, 2010).

Carcinogenicity

The available data do not support classification of these chemicals as carcinogens.

The aluminium ion has not been shown to be carcinogenic in epidemiological studies in humans, nor animal toxicity studies using inhalation, oral and other exposure routes (ATSDR, 2008). The literature concerning oral exposure bioassays for carcinogenicity is very limited and results are mixed. An increase in gross tumours was reported in male rats and female mice in a one-dose study conducted over at least two years but few study details were reported. Two other studies conducted over 20

and 24 months reported no increased incidence of tumours in mice and rats respectively exposed orally to aluminium compounds (Environment Canada and Health Canada, 2010; ATSDR, 2008).

Reproductive and Developmental Toxicity

Animal studies

There are many animal studies investigating the oral reproductive and developmental toxicity of aluminium salts; in particular, the more bioavailable salts such as aluminium lactate and citrate. As a result of the limitations of the animal study data, both WHO and the Canadian assessments based their evaluations on the combined evidence from many studies, concluding that the lowest observed effect levels (LOELs) for total aluminium (Al) exposures for mice, rats and dogs were in the region of 50–75 mg Al/kg bw/day. Effects include histopathological changes in testes, delays in maturation, and neurodevelopmental effects such as decreases in forelimb and hindlimb grip strength (Environment Canada and Health Canada, 2010; IPCS, 2007; ATSDR, 2008).

Significant alterations in motor function, sensory function, and cognitive function have been detected following gestational and/or lactational exposure of rats and mice to aluminium lactate, aluminium nitrate, and aluminium chloride. Neurodevelopmental effects have been observed in rats and mice at doses of 103–330 mg Al/kg bw/day (ATSDR, 2008). This is equivalent to 665–2132 mg aluminium chloride, basic.

Fifteen studies on neurodevelopmental toxicity of aluminium chloride were summarised in a report by Health Canada and Environment Canada. It was difficult to draw conclusions because different endpoints were studied using different test conditions (observation periods and dosing protocols). Lowest observed effect levels ranged from 19-36 mg Al/kg bw/d for markers of toxicity and 43-183 mg Al/kg bw/d for adverse effects such as impaired reflexes or performance in the Morris water maze (Environment Canada and Health Canada, 2010).

The highest quality developmental toxicity study of aluminium salts was conducted on aluminium citrate using Sprague Dawley (SD) rats in accordance with Good Laboratory Practice (GLP) and OECD TG 426. Aluminium citrate was administered in drinking-water to groups of pregnant rats, commencing on gestational day 6, at concentrations aiming to deliver aluminium doses of 30, 100 and 300 mg/kg bw/day, based on an expected water intake of 120 mL/kg bw/day. Half of the pups of each group were processed for neurohistopathological examination, and the other half were subjected to a regular necropsy followed by brain weight measurement, clinical chemistry, haematology, and collection of tissues and blood for measurement of aluminium and other metals. Overall, the authors concluded that the study indicated a LOAEL of 100 mg Al/kg bw/day and a no observed adverse effect level (NOAEL) of 30 mg Al/kg bw/day based on dose-related effects on hindlimb and forelimb grip strength in both male and female pups (Poierer, 2011; IPCS, 2012). These findings support previous studies; where the most consistently affected performance tests include forelimb and/or hindlimb grip strength (ATSDR, 2008).

While the aluminium ion (Al^{3+}) is the species considered to give rise to toxicity, the studies on aluminium citrate and lactate (which found effects at the lowest levels with NOAELs of 240 mg citrate/kg bw/day and 283 mg lactate/kg bw/day) are known to be highly bioavailable compared to the chemicals in this group (Poierer, 2011: ATSDR, 2008). The studies on other soluble aluminium salts show similar types of effects to those undertaken on the more bioavailable aluminium compounds (Environment Canada and Health Canada, 2010; ATSDR, 2008).

Human studies

A small study of the offspring of 88 pregnant women who were exposed to elevated levels of aluminium sulfate accidentally added to the local water supply in north Cornwall, England in 1988 found no evidence of major problems apparent from birth (REACH).

There is some epidemiological evidence for long-term cognitive impairment in pre-term infants receiving aluminium-containing nutritional solution intravenously (ATSDR, 2008).

Other Health Effects

Neurotoxicity

Although the neurotoxicity of aluminium has not been established in humans with normal renal function, the data for dialysis encephalopathy (as well as some occupational studies) establish that the human nervous system is susceptible to aluminium toxicity. In addition, neurotoxicity is a well-documented effect of aluminium in orally-exposed mice and rats (ATSDR, 2008).

Animal studies

There is an extensive database on the toxicity of aluminium in animals. These studies clearly identify the nervous system as the most sensitive target of aluminium toxicity and most of the animal studies have focused on neurotoxicity and neurodevelopmental toxicity. Neurodevelopmental toxicity is covered in the reproductive and developmental toxicity section of this report.

Overt signs of neurotoxicity are rarely reported at the doses tested in the available animal studies (less than or equal to 330 mg Al/kg bw/day for bioavailable aluminium salts); rather, exposure to these doses is associated with subtle neurological effects detected with neurobehavioural performance tests (ATSDR, 2008).

A small number of chronic animal studies of aluminium toxicity have been undertaken, although very little research has been undertaken using aged animals (ATSDR, 2008; WHO, 2007; NHMRC, 2013). Neurodegenerative changes in the brain with cognitive deficits are a characteristic response to aluminium in certain species for non-natural exposure situations generally involving direct application to brain tissue through injection of aluminium solutions and in vitro incubation in rabbits, cats, ferrets, and nonhuman primates (ATSDR, 2008).

One long-term chronic oral toxicity study investigated neurodegeneration in aged rats at aluminium levels relevant to total human intake. Thirty Wistar rats (10 per dose) were orally exposed to 0.4 mg, 0.5 mg and 1.7 mg Al/kg bw/day in their food (0.4 mg Al/kg bw/day for all groups) and water (as 0, 2 and 20 ppm Al, equivalent to 0, 0.9 and 11.6 mg $AlCl_3.6H_2O$/kg bw/day). Dosing for the rats commenced from 12 months old (equivalent to 35 year old humans) until the end of their natural life (28 to 37.5 months, equivalent to 82-109 year old humans) and cognitive function was evaluated using the T-maze task. By age 28 months, none of the rats (0/10) in the low Al dose group, two of the rats (2/10) receiving the intermediate Al dose and seven rats (7/10) that consumed Al at the high end of the human range for total dietary Al exhibited significantly lower mean scores on their T-maze task in old age than in middle age, as well as showing dementia-like behaviours such as confusion, inability to focus attention on the task, perseverative activities and incontinence in the T-maze. This study established a no observed effect level (NOEL) of 0.4 mg Al/kg bw/day and LOAEL of 0.5 mg Al/kg bw/day in rats (equivalent to 0 and 0.9 mg $AlCl_3.6H_2O$) based on significant cognitive deterioration and neuropathology (brain lesions) (Walton, 2009).

Findings included a significant inverse correlation between memory scores and plasma Al; high relative concentrations of Al and lesions in brain regions associated with memory function (equivalent to where Al and tissue damage has been found in humans with Alzheimer's disease); elevated markers of oxidative stress and other biochemical changes that precede and lead to hallmarks associated with Alzheimer's disease in humans (plaques, tangles, granulovacuolar degeneration) (Walton, 2014).

Human studies

As noted previously, patients with renal failure are at risk of neurotoxicity from aluminium (EHC, 1997). There is also some epidemiological evidence for long-term cognitive impairment in pre-term infants receiving aluminium-containing nutritional solution intravenously, and associated with occupational exposures (ATSDR, 2008). Patients with renal failure and infants receiving parenteral nutrition were exposed to aluminium salts directly through dialysis and intravenous injections, thereby by-passing the gastrointestinal system which effectively excludes most orally ingested aluminium.

With respect to the conditions of exposure in the general population, the most relevant available information is provided by the epidemiological investigations into the association between exposure to aluminium through drinking water and Alzheimer's disease and other forms of dementia (ATSDR, 2008). Most epidemiological studies addressed the potential neurotoxicity of aluminium in drinking-water or antacids. The results are mixed. Some of the drinking-water studies showed an association of aluminium with dementia or Alzheimer's disease, whereas others reported an absence of neuropsychological effects measured in several ways (IPCS, 2012). Nine out of 13 published epidemiological studies of aluminium in drinking water and Alzheimer's disease have shown statistically significant positive relations (Flatten, 2001).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects (reproductive and developmental toxicity, neurotoxicity) and, in the case of auminium chloride ($AlCl_3$), local acute effects on skin and eyes. Aluminium chloride, hexahydrate is irritating to eyes.

Public Risk Characterisation

Given the health effects identified, in particular neurodevelopmental and neurodegenerative effects, further investigation of the exposures from cosmetics, antiperspirants and deodorants in particular, is warranted.

Although use in cosmetic and domestic products in Australia is not known, this group of chemicals is reported to be used extensively in cosmetic products overseas. Exposure through dermal contact and inhalation with these products is expected to be relatively low for intact skin, although French, German and Norwegian risk assessments based on very conservative assumptions suggest it could be of similar magnitude to exposures through food (BfR 2014a and 2014b; AFSSAPS, 2011; and VKM, 2013). The French agency for the safety of sanitary and health products (AFSSAPS) subsequently recommended that the concentration of aluminium in consumer products should be restricted to 0.6 % and that aluminium-containing cosmetics should not be used on impaired skin (AFSSAPS, 2011).

NICNAS Recommendation

This group of chemicals is recommended for Tier III assessment to better characterise all aluminium exposures from cosmetics, antiperspirants and deodorants in particular and whether these exposures are significant contributors to exceeding tolerable weekly intakes for aluminium.

Regulatory Control

Public Health

The need for any regulatory controls for public health will be determined as part of the Tier III assessment.

Work Health and Safety

Aluminium chloride ($AlCl_3$) and aluminium chloride, hexahydrate are recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical hazards and environmental hazards. In the absence of specific data on chemicals in this group, data have been read-across from the data available for members of this group. Should 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 that chemical.

No single classification for irritation/corrosivity can be made for this group of chemicals because one of the chemicals, aluminium chloride ($AlCl_3$) is corrosive as the pure anhydrous substance. Aluminium chloride, hexahydrate is classified as irritating to eyes based on reading across from data available for sulfuric acid, aluminium salt (3:2).

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Irritation / Corrosivity	Irritating to eyes (Xi; R36) Causes burns (C; R34)*	Causes serious eye irritation - Cat. 2A (H319) Causes severe skin burns and eye damage - Cat. 1 (H314)

[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 these chemicals 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 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;
- 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.

The airborne concentrations of these chemicals should be kept as low as practically possible and in accordance with the exposure standards to minimise risk.

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 chemicals has not been undertaken as part of this assessment.

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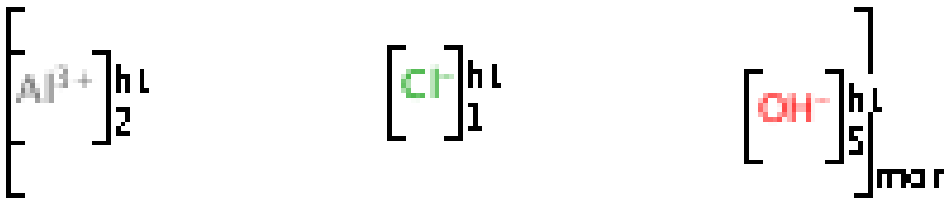
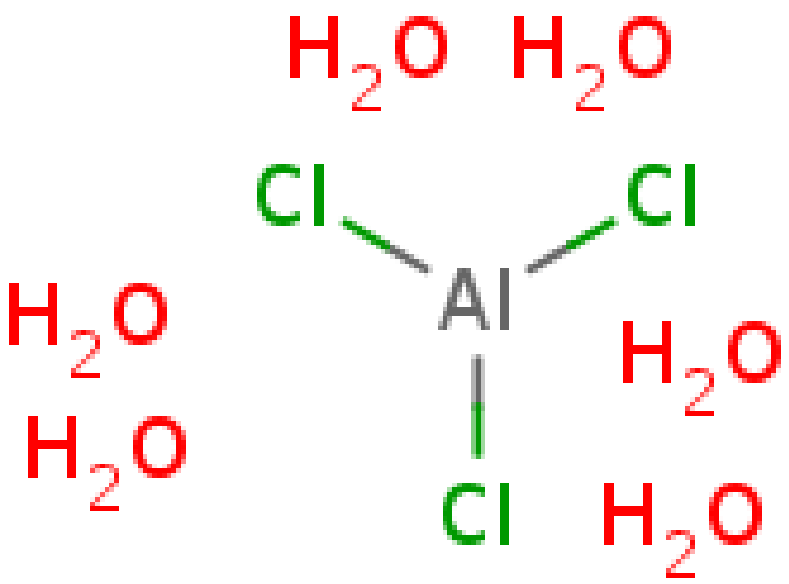
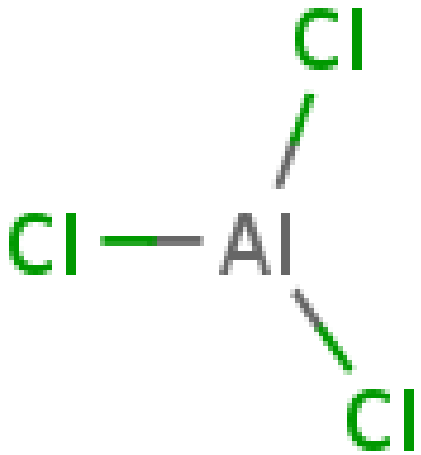
Last Update 04 July 2014

Chemical Identities

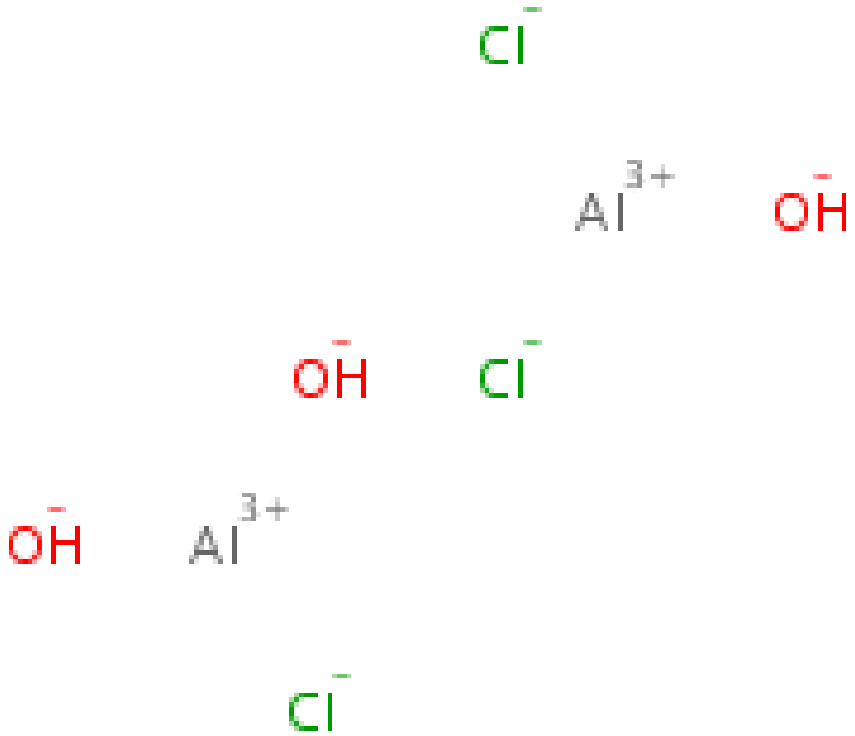
Chemical Name in the Inventory and Synonyms	**Aluminium chloride, basic** Aluminium hydroxide chloride Aluminium chlorohydrate Aluminum sesquichlorohydrate Polyaluminum chloride Aluminium hydroxychloride
CAS Number	1327-41-9
Structural Formula	
Molecular Formula	Unspecified
Molecular Weight	174.45

Chemical Name in the Inventory and Synonyms	**Aluminium chloride, hexahydrate** Aluminum chloride Aluminum trichloride hexahydrate Aluminum chloride hydrate
CAS Number	7784-13-6
Structural Formula	
Molecular Formula	AlCl3.6H2O
Molecular Weight	241.43

Chemical Name in the Inventory and Synonyms	**Aluminium chloride (AlCl3)** Aluminum chloride Aluminum chloride anhydrous Trichloroaluminum Aluminum trichloride
CAS Number	7446-70-0
Structural Formula	

	
Molecular Formula	AlCl3
Molecular Weight	133.34

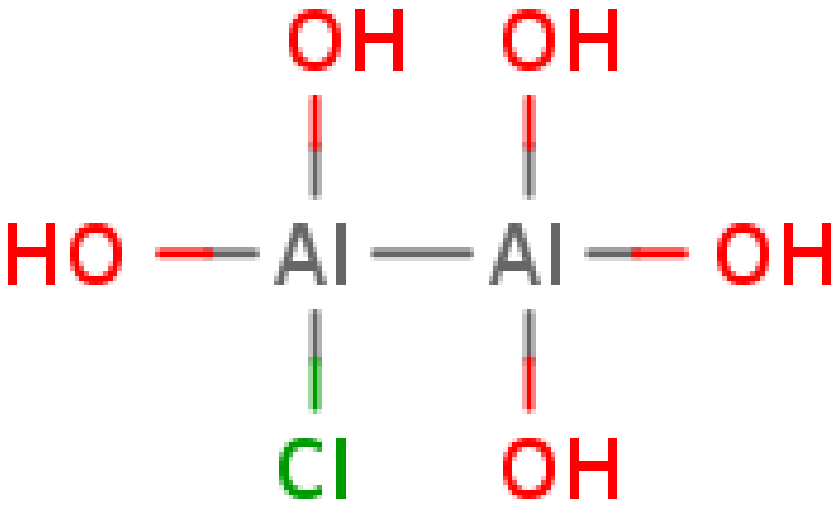
Chemical Name in the Inventory and Synonyms	**Aluminium chloride hydroxide** Aluminum dichlorohydrate Aluminium chloride dihydroxide Basic aluminium chloride Chlorodihydroxyaluminium Dichlorotetrahydroxydialuminium
CAS Number	10284-64-7
Structural Formula	

	
Molecular Formula	AlClH2O2
Molecular Weight	211.34

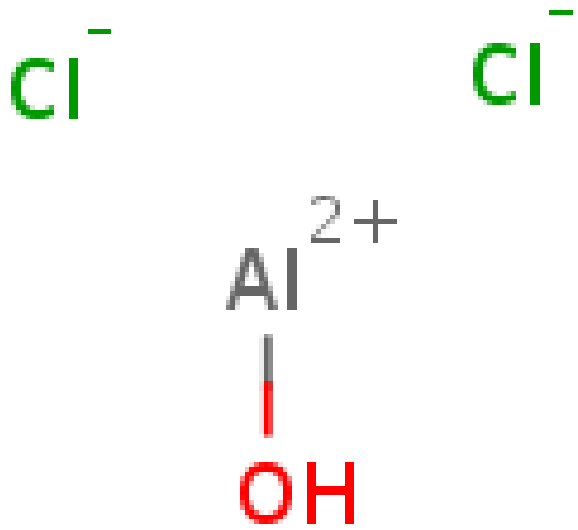
Chemical Name in the Inventory and Synonyms	**Aluminium chloride hydroxide (Al4Cl3(OH)9)** Aluminum sesquichlorohydrate Tetraaluminium trichloride nonahydroxide
CAS Number	11089-92-2
Structural Formula	

	
Molecular Formula	Al.Cl.HO
Molecular Weight	367.35

Chemical Name in the Inventory and Synonyms	**Aluminium chloride hydroxide (Al2Cl(OH)5)** Aluminum chlorohydrate Aluminium hydroxide chloride Aluminium monochloride pentahydroxide Aluminum chlorhydroxide Basic aluminum chlorate
CAS Number	12042-91-0
Structural Formula	

	
Molecular Formula	Al.Cl.HO
Molecular Weight	174.45

Chemical Name in the Inventory and Synonyms	**Aluminium chloride hydroxide, AlCl2(OH)** Aluminium dichloride hydroxide
CAS Number	14215-15-7
Structural Formula	

	
Molecular Formula	AlCl2HO
Molecular Weight	114.90

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