Calcium chloride (CaCl2): Human health tier II assessment

27 November 2014

CAS Number: 10043-52-4

Preface

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

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

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

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

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

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

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

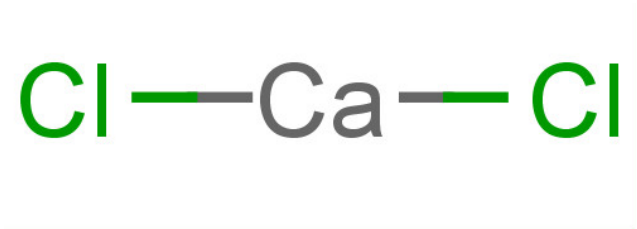
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

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

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	Calcium dichloride Calcium chloride anhydrous
Structural Formula	
Molecular Formula	CaCl2
Molecular Weight (g/mol)	110.98
Appearance and Odour (where available)	Odourless white powder
SMILES	_[Ca]{2+}_Cl{-}_Cl{-}

Import, Manufacture and Use

Australian

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

The chemical has reported site-limited uses, including as a construction material additive and in hydraulic fracturing.

The total volume introduced into Australia, reported under previous mandatory and/or voluntary calls for information, was less than 10 000 tonnes.

International

The following international uses have been identified through Galleria Chemica; Substances and Preparations in the Nordic countries (SPIN) database and the European Commission Cosmetic Ingredientsand Substances (CosIng).

The chemical has reported cosmetic use.

The chemical has reported domestic uses, including as a constituent of:

- cleaning/washing agents;
- adhesives and glues;
- fertilisers;
- fire retardants/fire extinguishers;
- paints, lacquers and varnishes;
- anti-condensation/coolant/de-icers; and
- surface treatment.

The chemical has reported commercial uses, including:

- as a viscosity controlling agent;
- as an absorbent and adsorbent;
- as an anti-freeze agent;
- as an anti-static agent;
- as a construction material;
- as a dust binding agent;
- in dyes and printing inks;
- as a softener;
- in paints, lacquers and varnishes;
- as a pH regulation agent;
- in photography/photocopiers;
- in plating and surface finishing;
- as a process regulator;
- as a construction materials additive;
- as a tanning agent; and
- in water and waste treatment.

The chemical has reported site-limited uses, including:

- in fillers;

- in manufacturing of other chemicals;
- as a stabiliser;
- as an intermediate;
- in heat transferring agents;
- in plastics and synthetic resins;
- in drilling mud additive/oil recovery agent/oil well treatments;
- in preserving wood;
- as a coagulant in rubber manufacturing;
- in the paper and pulp industry;
- as a humectant/dewatering aid/dehumidifier/dehydrating agent;
- in refrigerant brine (obsolescent); and
- as a complexing and flocculating agent.

The chemical has reported non-industrial uses, including as a constituent of:

- food/feed stuff flavourings and nutrients; and
- pesticides, pharmaceuticals and preservatives.

Restrictions

Australian

No known restrictions have been identified.

International

No known restrictions have been identified.

Existing Work Health and Safety Controls

Hazard Classification

Anhydrous calcium chloride is classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia, 2014):

Xi; R36 (irritation)

Exposure Standards

Australian

No specific exposure standards are available.

International

The following exposure standards are identified (Galleria Chemica):

- an occupational exposure limit (OEL) of 5 mg/m^3 for calcium chloride (CAS No. 10043-52-4) in Canada; and
- an OEL of 2 mg/m^3 for calcium chloride (CAS No. 10043-52-4) in Latvia.

Health Hazard Information

Toxicokinetics

Calcium chloride exists as anhydrous and hydrated forms. The anhydrous compound is hygroscopic and rapidly absorbs water to form mono-,di-, tetra- or hexa-hydrated calcium chloride. The hydrated forms are considered to have low hazard (OECD, 2002). Calcium chloride readily dissociates in water to calcium and chloride ions. Once absorbed, the calcium and chloride ions are regulated separately and the health effects in animals are attributable to either or both ions.

Only limited data are available for any end-points, particularly for long-term exposure. However, given the essential role and high concentration of both calcium and chloride in the body, calcium chloride can be expected to have very low systemic toxicity.

The U.S. Food and Drug Administration has designated calcium chloride as 'generally recognized as safe' (GRAS). Calcium and chloride toxicokinetics have been well reviewed in standard textbooks.

Absorption

Calcium chloride is of low molecular weight and high water solubility. It readily dissociates in water to calcium and chloride ions. Calcium and chloride ions are absorbed efficiently from the intestine. Once absorbed, the calcium and chloride ions are regulated separately; the health effects in animals are attributable to either or both ions.

No data were available on the dermal absorption of calcium chloride. Absorption of ionic salts by the skin is essentially negligible (Schaefer & Redelmeier, 1996). Calcium chloride is not expected to be absorbed through the skin and be systemically available.

Information on inhalation absorption of calcium chloride is not available.

Distribution

Calcium and chloride ions are essential body constituents in all animal species. Calcium is the most abundant metallic element in all animal species with most of the body content located in the skeleton. It is an essential ion for the formation and maintenance of bone and teeth, and for regulating several important physiological functions such as blood coagulation, neuromuscular activity, enzyme activity and acid–base balance. Hormonal systems regulate plasma calcium concentrations at approximately 100 µg/mL by controlling intestinal absorption of dietary calcium, the release from bone, and renal absorption/excretion.

Chloride is the most abundant anion in animals and is important for maintaining osmotic and the acid–base balance. In the body, most chloride is located in extracellular fluids. Plasma concentrations are maintained at 3.6–3.9 mg/mL.

Metabolism

No data are available.

Excretion

Excess calcium is excreted in the urine via glomerular filtration. A significant increase in the calcium concentration in plasma will only occur after high calcium intake in conjunction with other disorders such as renal insufficiency or primary hyperthyroidism. Chloride is excreted from the renal tubules by active transport systems as well as by passive diffusion.

Acute Toxicity

Oral

Calcium chloride has low acute toxicity following oral exposure in animal tests. Acute oral toxicity of calcium chloride has been tested in several mice, rat and rabbit studies. The oral lethal median doses (LD50s) values range from 2120–3798 (male) and 2361–4179 (female) mg/kg bw in rats to 2045 (male) and 1940 (female) mg/kg bw in mice (Akatsuka, 1997).

In rabbits, acute oral toxicity studies were carried out by the method similar to the Organisation for Economic Cooperation and Development (OECD) Test Guideline (TG) 401 under good laboratory practice (GLP). Calcium chloride (anhydrous and di- and hexahydrate powder) was administered orally by gavage to groups of rabbits at doses of 250 to 2000 mg/kg bw. LD50 values of 500–1000 mg/kg bw were reported in these studies. Gross post-mortem examination revealed perforation and severe ulceration of the stomach in the dead animals (Koopman & Pot, 1986a).

Dermal

Calcium chloride has low acute toxicity from dermal exposure. An acute dermal toxicity study was conducted in rabbits by a scientifically accepted method (Carreon et al., 1981). No adverse effects were observed and no deaths occurred up to 5000 mg/kg bw, the highest applied dose. No significant change was found either at gross necropsy examination or at the site of application except for some skin lesions (see **Skin irritation**). The dermal LD50 from this study was >5000 mg/kg bw.

Inhalation

Reliable studies on acute inhalation toxicity of calcium chloride are not available. In one study, rats were exposed to 40 and 160 mg/m^3 anhydrous calcium chloride (CAS No. 10043-52-4) for four hours. Signs of irritation of the trachea were observed in the animals. No deaths were reported (Sukhanov et al., 1990). However, the reliability of this study is questioned due to insufficient information on the form of calcium chloride and methodology used.

Observation in humans

No data are available.

Corrosion / Irritation

Respiratory Irritation

No data are available. However, signs of irritation of the trachea were observed in animals in an acute inhalation study (Sukhanov et al., 1990), indicating that calcium chloride is likely to be a respiratory irritant.

Skin Irritation

In studies conducted according to OECD test guidelines, no or only slight skin irritation were observed in rabbits from four-hour exposures to anhydrous calcium chloride (CAS No. 10043-52-4), calcium chloride dihydrate (CAS No. 10035-04-8), and/or

calcium chloride hexahydrate (CAS No. 7774-34-7) (Koopman and Pot, 1986b-e).

Rabbits exposed for 24 hours to anhydrous calcium chloride and solid or 38 % calcium chloride dihydrate solution had slight to moderate irritation on intact skin and more severe irritation on abraded skin (Norris, 1971a, b; Carreon, Yano & New, 1981).

Eye Irritation

Anhydrous calcium chloride was a severe irritant to rabbit eyes. The cornea and conjunctivae were moderately to severely irritated from one hour until 14 days after treatment, and were still moderately irritated 21 days after treatment. Hydrated forms of calcium chloride were less irritating to the eyes. With the dihydrate form, the cornea and conjunctivae were moderately irritated from one hour to 72 hours post application, and in one rabbit for up to 14 days. The hexahydrate caused slight to moderate irritation of the cornea and conjuntivae, which persisted for up to 48 hours, and in one rabbit, for up to 14 days.

The 33 % and 38 % solutions of calcium chloride were slight to moderate eye irritants causing diffuse corneal opacity and slight to moderate conjunctival redness. Slight to moderate chemosis was also observed in some, but not all, rabbits (Norris, 1971a, b; Koopman & Pot, 1986f-i).

Observation in humans

No data are available.

Sensitisation

Respiratory Sensitisation

No data are available.

Skin Sensitisation

No data are available.

Observation in humans

No data are available.

Repeated Dose Toxicity

Oral

No reliable repeated dose oral studies are available.

In one study, which was not conducted according to OECD guidelines, 40-day-old rats were fed 20 mg/g of anhydrous calcium chloride for 12 months (Pamukcu, Yalciner & Bryan, 1977). No differences in mortality, weight gain, or daily food consumption were observed between the test and the control groups. No neoplastic lesions were observed in the gastrointestinal tract, urinary tract, liver, heart, brain or spleen of the animals. Based on food consumption, the daily intake of calcium chloride was estimated to be 440 mg. Considering that 1 mg/g in the diet is equivalent to 100 and 50 mg/kg bw/day for young and old rats, respectively, the dose used in this study corresponded to 1000 to 2000 mg/kg bw/day.

Dermal

No data are available.

Inhalation

No data are available.

Observation in humans

Cases of skin lesions, ulceration and calcinosis have been described from incidental repeated contact with calcium chloride powder or concentrated solutions (Botvinick, Sneddon & Archibald, 1958; Saeed et al., 1997).

Following inhalation of calcium chloride aerosols (2–5% aqueous solution) as therapy for pulmonary tuberculosis, several patients reported irritation of mucous membranes of the pharynx and throat (Vinnikov, Slepova & Sataev, 1962).

Genotoxicity

In an in vitro study, conducted according to OECD guidelines, doses of calcium chloride up to 5 mg/plate were examined in a *Salmonella typhimurium* mutation test using strains TA92, TA94, TA98, TA100, TA1535 and TA1537 with metabolic activation (Ishidate et al., 1984). In another reverse mutation test, doses up to 10 mg/plate were examined using *S. typhimurium* strains TA97 and TA102 with or without metabolic activation (Fujita & Sasaki, 1987). No significant increases in mutation frequencies were observed in either study.

In two additional bacterial genotoxicity studies, which were not conducted according to OECD test guidelines, no DNA damage was reported at calcium chloride concentrations of up to 0.5 molar (Kanematsu et al., 1980; Olivier & Marzin, 1987).

An in vitro chromosome aberration test comparable to OECD test guidelines, using Chinese hamster lung cells (CHL), has also been reported. Cells were exposed to calcium chloride at doses up to 4 mg/mL for 48 hours without metabolic activation. No significant increases in polyploid formation or structural chromosome aberration were observed (Ishidate et al., 1984).

Carcinogenicity

No data are available.

Reproductive and Developmental Toxicity

No data are available on the effects of calcium chloride on fertility.

In a series of developmental toxicity studies conducted comparably to OECD TG 414, the effects of calcium chloride on embryo-lethality and teratogenicity were studied in mice, rats and rabbits at different dose levels. The maximum doses of calcium chloride were 189, 176, and 169 mg/kg bw/day in mice, rats and rabbits, respectively.

Calcium chloride had no discernible effect on implantation or on maternal or foetal survival. There were no differences in numbers of abnormalities in soft or skeletal tissues between test and control animals. The studies concluded that calcium chloride up to 189 mg/kg bw/day in the mouse, 176 mg/kg bw/day in the rat and 169 mg/kg bw/day in the rabbit had no developmentally toxic effects (Food and Drug Research Laboratories, 1974).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation are local effects (severe eye irritation). Observations in humans suggest that calcium chloride may be a slight respiratory irritant.

Public Risk Characterisation

The public may be exposed to calcium chloride through cosmetic and domestic use. In cosmetic products, calcium chloride will be present in an aqueous solution, and therefore have low eye irritation potential. Provided that normal precautions are taken to avoid eye contact, using cosmetic and domestic products containing calcium chloride is not considered to pose an unreasonable risk to public health.

Occupational Risk Characterisation

During product formulation, dermal, ocular and inhalation exposure of workers to the chemical might occur, particularly where manual or open processes are used. These can include transfer and blending activities, quality control analysis, and cleaning and maintenance of equipment. Worker exposure to the chemical at lower concentrations might also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the severe eye irritation effects of calcium chloride, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise eye exposure to the chemical are implemented. The chemical should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine appropriate controls.

The data available support an amendment to the hazard classification in HSIS (refer to **Recommendation** section).

NICNAS Recommendation

Current risk management measures are considered adequate to protect 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

Products containing the chemical should be labelled in accordance with state and territory legislation.

Work Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical hazards and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Irritation / Corrosivity	Irritating to eyes (Xi; R36)*	Causes serious eye irritation - Cat. 2A (H319)

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

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

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

Advice for consumers

Products containing the chemical should be used according to the instruction on the label.

Advice for industry

Control measures

Control measures to minimise the risk from ocular exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures which may minimise the risk include, but are not limited to:

- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to assist with meeting obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((m)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (m)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals— Code of practice* and *Labelling of workplace*

hazardous chemicals—Code of practice, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of the chemical has not been undertaken as part of this assessment.

References

Akatsuka K, Hashimoto T and Takeuchi K (1977) Pharmacological studies on Ca meso-tartrate I. Acute and subacute toxicity tests. Ouyou-Yakuri, 14, 963–975. (in Japanese).

Botvinick I, Smith RG and Stein SC (1961) Calcium chloride necrosis of the skin. J. Mich. Med. Soc. 60: 743–744.

Carreon RE, Yano BL and New MA (1981) Peladow calcium chloride (94–97%): acute toxicological properties and industrial handling hazards. Unpublished Dow Chemical Company report.

CosIng. Cosmetic Ingredients and Substances. Accessed November 2014 at http://ec.europa.eu/consumers/cosmetics/cosing/

Food and Drug Research Laboratories, Inc. (1974) Teratologic evaluation of FDA 71-87 (calcium chloride) in mice, rats and rabbits. Report No. FDABF-GRAS-251. NTIS PB-234879.

Fujita H and Sasaki M (1987) Mutagenicity test of food additives with Salmonella typhimurium TA97 and TA102 (II). Ann. Rep. Tokyo Metr. Res. Lab. P.H., 38, 423–430. (in Japanese).

Galleria Chemica. Accessed October 2014 at https://jr.chemwatch.net/galleria/

Ishidate M Jr., Sofumi T, Yoshikawa K, Hayashi M, Nohmi T, Sawada M and Matsuoka A (1984) Primary mutagenicity screening of food additives currently used in Japan. Fd. Chem. Toxic. 22: 623–636.

Kanematsu N, Hara M and Kada T (1980) Rec assay and mutagenicity studies on metal compounds. Mutation Res. 77: 109–116.

Koopman TSM and Pot TE (1986a) Acute oral toxicity study with anhydrous calcium chloride in male rabbits. Duphar Report No. 56645/52/86.

Koopman TSM and Pot TE (1986b) Primary irritation study of anhydrous calcium chloride to the skin of the male rabbit. Duphar Report No. 56645/30/86

Koopman TSM and Pot TE (1986c) Primary irritation study of calcium chloride 33% to the skin of the male rabbit. Duphar Report No. 56645/31/86.

Koopman TSM and Pot TE (1986d) Primary irritation study of calcium chloride dihydrate to the skin of the male rabbit. Duphar Report No. 56645/29/86.

Koopman TSM and Pot TE (1986e) Primary irritation study of calcium chloride hexahydrate to the skin of the male rabbit. Duphar Report No. 56645/32/86.

Koopman TSM and Pot TE (1986f) Primary irritation study of anhydrous calcium chloride to the eye of the male rabbit. Duphar Report No. 56645/42/86.

Koopman TSM and Pot TE (1986g) Primary irritation study of calcium chloride 33% to the eye of the male rabbit. Duphar Report No. 56645/45/86.

Koopman TSM and Pot TE (1986h) Primary irritation study of calcium chloride dihydrate to the eye of the male rabbit. Duphar Report No. 56645/43/86.

Koopman TSM and Pot TE (1986i) Primary irritation study of calcium chloride hexahydrate to the eye of the male rabbit. Duphar Report No. 56645/44/86.

Norris JM (1971a) Eye and skin irritation properties of DOWFLAKE calcium chloride. Unpublished Dow Chemical Company report.

Norris JM (1971b) Eye and skin irritation properties of LIQUIDOW liquid calcium chloride. Unpublished Dow Chemical Company report.

OECD (2002) SIDS Initial Assessment Report for SIAM 15. Calcium chloride.

Olivier PH and Marzin D (1987) Study of the genotoxic potential of 48 inorganic derivatives with the SOS chromotest. Mutation Res. 189: 263–269.

Pamukcu AM, Yalciner S and Bryan GT (1977) Inhibition of carcinogenic effect of bracken fern (Pteridium aquilinum) by various chemicals. Cancer 40: 2450–2454.

Saeed WR, Distante S, Holmes JD and Kolhe PS (1997) Skin injuries afflicting three oil workers following contact with calcium bromide and/or calcium chloride. Burns 23(7/8): 634–637.

Safe Work Australia (SWA). Hazardous Substances Information System (HSIS). Accessed October 2014 at http://hsis.safeworkaustralia.gov.au/HazardousSubstance

Schaefer H and Redelmeier TE (1996) Skin barrier: principles of percutaneous absorption. Karger AG, Basel and New York.

Sneddon IB and Archibald RMcL (1958) Traumatic calcinosis of the skin. Br. J. Dermatol. 70: 211–214.

SPIN (Substances in Preparations in Nordic Countries) Database. Available: http://195.215.202.233/DotNetNuke/default.aspx

Substances in Preparations in Nordic Countries (SPIN). Accessed October 2014 at http://188.183.47.4/dotnetnuke/Home/tabid/58/Default.aspx

Sukhanov VV, Petul'ko SN, Bolonova LN and Yulish NR (1990) Toxicological assessment of calcium chloride and calcium chloride-containing products. Gigiena Truda I Professional'nye Zabolevaniya (Labor Hygiene and Occupational Diseases) 34(5): 51–52.

Vinnikov PL, Slepova RI and Sataev IF (1962) Inhalation of calcium chloride aerosols in complex therapy of pulmonary tuberculosis. Kazan Med Zh. 4: 7–9.

Last update 27 November 2014

Share this page