Calcium hydroxide (Ca(OH)2): Human health tier II assessment

01 September 2015

CAS Number: 1305-62-0

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 dihydroxide calcium hydrate lime water hydrated lime slaked lime
Structural Formula	
Molecular Formula	CaH2O2
Molecular Weight (g/mol)	74.09
Appearance and Odour (where available)	Soft, white odourless crystalline powder
SMILES	O{-}.[Ca]{2+}.O{-}

Import, Manufacture and Use

Australian

The chemical is listed on the 2006 High Volume Industrial Chemicals List (HVICL) with a total reported volume in the range 10000–99999 tonnes.

The chemical has reported site-limited uses, including as a:

- construction materials additive;
- filler;
- pH-regulating agent; and
- softener.

The chemical has reported non-industrial use as a substance that may be used in listed medicines as an active ingredient or as an excipient (Therapeutic Goods Administration (TGA), 2007).

International

The following international uses have been identified through the European Union (EU) Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) dossiers; Galleria Chemica; the European Commission Cosmetic Ingredients and Substances (CosIng) database; the United States (US) Personal Care Products Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary; the United States (US) Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR); the US National Library of Medicine's Hazardous Substances Data Bank (HSDB); and the report from the Scientific Committee on Occupational Exposure Limits (SCOEL) for calcium oxide and calcium hydroxide (SCOEL, 2008).

The chemical has reported cosmetic use as a pH adjuster in many product types including bath oils, tablets and salts; bubble baths; body and hand preparations; cleansing products; depilatories; shaving products; skin fresheners; foundations; hair straighteners and other hair products.

The chemical has reported domestic/commercial uses as:

- an ingredient in building products such as cement, plaster and grout; and
- a pH adjuster for soil.

The chemical has reported site-limited uses, including:

- as a component of mixtures used for hydraulic fracturing; and
- manufacturing or formulating other chemicals.

The following non-industrial uses have been identified, including as:

- an antacid in pelleted feeds for ruminant animals;
- an antidote to tannin poisoning for ruminant animals;
- an ingredient in pesticides and water treatment products;
- a component of pool chemicals;
- a component of dental and bone cement;
- an inactive ingredient in approved drug products; and
- an astringent.

The chemical is also used as an edible paste or additive in chewing tobacco.

Restrictions

Australian

The chemical is a substance that may be used in listed medicines—'When used as an active, this ingredient is only listable as an uncompounded BP substance' (TGA, 2007). (BP refers to British Pharmacopoeia).

The chemical is on the Food Standards Australia New Zealand (FSANZ) Food Standards Code—Standard 1.3.1—Food Additives: The chemical must not be added to infant formula products except at a maximum permitted level determined by good manufacturing process (GMP).

International

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

- Association of Southeast Asian Nations (ASEAN) Cosmetic Directive Annex III—List of substances which cosmetic products must not contain except subject to restrictions and conditions laid down;
- EU Cosmetics Regulation 1223/2009 Annex II—List of substances which cosmetic products must not contain except subject to the restrictions laid down; and
- New Zealand Cosmetic Products Group Standard—Schedule 5: Components cosmetic products must not contain except subject to the restrictions and conditions laid down.

The chemical is restricted to a maximum concentration of 7 % (as calcium hydroxide) in hair straighteners; pH <12.7 in depilatories; pH <11 for other uses.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia) due to having an assigned exposure standard. No risk phrases are assigned.

Exposure Standards

Australian

The chemical has an exposure standard of 5 mg/m^3 time weighted average (TWA).

International

The following exposure standards are identified (Galleria Chemica):

- a TWA of 1–3 mg/m^3 in different countries such as Germany, Poland, Russia and Sweden;
- a TWA of 5 mg/m^3 in different countries such as Bulgaria, Canada, Denmark, Egypt, Estonia, France, Greece, Hungary, Iceland, Indonesia, Ireland, Latvia, Malaysia, Malta, Mexico, Norway, Singapore, South Africa, Spain, Switzerland, Taiwan, Turkey, the United Kingdom and the USA; and
- a short-term exposure limit (STEL) of 4–10 mg/m^3 in different countries such Canada, Poland and Sweden.

Health Hazard Information

Calcium hydroxide is formed in an exothermic reaction when calcium oxide and water are combined. The chemical is an inorganic base, with a pH of 12.8 for a saturated solution at 25 °C (Clayton & Clayton, 1994).

Since the constituent ions of calcium hydroxide (Ca^{2+} and OH^-) are physiological components of the body and homeostatic mechanisms exist to regulate their levels, chronic systemic health effects from repeated dose exposure (e.g. carcinogenicity and reproductive toxicity) are not expected, apart from non-specific effects such as alkalosis. Available studies for these endpoints are not considered relevant to this assessment.

Toxicokinetics

Systemically absorbed calcium hydroxide rapidly dissociates into calcium ions and hydroxide ions. When assessing the potential systemic effects, the constituent ions (calcium and hydroxide) must be considered separately. Both ions are normal physiological components in humans.

The hydroxide ion is a natural constituent of aqueous solutions because of the self-ionisation reaction of water. Calcium is an abundant mineral in the body, primarily stored in the skeleton where it has a role in bone mineralisation. It is also involved in blood clotting, cardiac and skeletal muscle contraction, and general metabolic function (e.g. cellular signalling and neurotransmission). The physiological range of serum calcium is narrow, 2.2–2.6 mmol/L, and calcium homeostasis is maintained via hormone-mediated gut, kidney and bone transport (Peacock, 2010). Ingested calcium hydroxide is neutralised under the acidic conditions of the stomach, although alkalosis may occur at very high doses.

Acute Toxicity

Oral

The chemical has low acute toxicity based on results from animal tests following oral exposure.

The median lethal dose (LD50) in female Wistar rats was >2000 mg/kg bw (REACH). The LD50 values in the range 4830–11140 mg/kg bw in rats have also been reported (Clayton & Clayton, 1994; ACGIH, 2001).

Dermal

No data are available.

Inhalation

No data are available.

Corrosion / Irritation

Respiratory Irritation

No animal data are available. Occupational exposure to the chemical was reported to cause respiratory irritation in humans (see **Observation in humans** below). The available information is insufficient to classify the chemical as a respiratory irritant.

Skin Irritation

Based on the observations in animals and humans, and the high alkalinity of the chemical (pH = 12.8 for a saturated solution (Clayton & Clayton, 1994)), the chemical is considered to be a skin irritant, warranting hazard classification (see **Recommendation** section).

In an acute dermal irritation/corrosion study (according to the Organisation for Economic Cooperation and Development (OECD) test guideline (TG) 404), Himalayan rabbits (n = 3, sex not specified) were exposed (semi-occlusively) to 0.5 g of the chemical for four hours and observed at 24, 48 and 72 hours post-exposure. A mean erythema score of two was observed for two animals at all time-points and one animal also had a mean oedema score of one for all time-points. Erythema and oedema were reversible by 14 days after the termination of the study and it was concluded that the chemical was irritating to the skin (REACH).

However, in another acute dermal irritation/corrosion study (OECD TG 404), New Zealand White rabbits (n = 3, sex not specified) exposed (semi-occlusive) to 0.5 g of the chemical for four hours and observed at 24, 48 and 72 hours post-exposure had erythema and oedema scores of zero at all time-points (REACH).

In a long-term study in Swiss white mice (n = 53), an aqueous chewing tobacco extract that contained the chemical was painted on the ears of animals once daily for two years and the animals were assessed until their death. Thickening, hardening, partial ulceration, keratin-filled cysts and local infections were reported (Muir & Kirk, 1960).

Eye Irritation

Based on the available animal data and observations in humans (see below), the chemical is considered to causes severe eye irritation, warranting hazard classification (see **Recommendation** section).

In an eye irritation study (OECD TG 405), New Zealand White rabbits (n = 3 males) were administered 0.1 mL of an 150 g/L suspension of the chemical into the conjunctival sac and examined at one, 24, 48 and 72 hours after administration. The mean scores for all animals were 0.8 for corneal opacity, 0.8 for iris lesions, 2.3 for conjunctival redness and 2.3 for chemosis. Corneal opacity and iritis were reversible by day 7 in all animals. Conjunctival redness and chemosis were reversible by day 8 in two rabbits, but not reversible within the 21-day observation period in one rabbit (REACH).

One male New Zealand White rabbit was administered 100 mg of the chemical into the conjunctival sac of one eye and the animal was examined one hour after exposure (OECD TG 405). The corneal opacity score was four (total opacity) and the chemosis score was three, with the conjunctiva appearing necrotic and the iris not visible (REACH).

In another eye irritation study (similar to OECD TG 405), New Zealand White rabbits (n = 6–9/dose) were administered the chemical at 0.01, 0.03 or 0.10 g onto the cornea and examined up to 21 days after exposure. No irritation scores were available, but it was reported that the experiment was terminated on day 14 for the mid and high dose groups due to severe eye irritation and injury that was judged as unlikely to reverse. In the low dose group, it took more than 21 days for the lesions to reverse (REACH).

Observation in humans

Skin, eye and respiratory irritation can occur due to the high alkalinity of the chemical. Although corrosivity was indicated in some case studies, this occurred following exposure to the chemical in a mixture with other chemicals.

Accidental dermal exposure to the chemical as an aqueous suspension can cause loss of skin lipids and protein, resulting in dry and cracked skin, contact dermatitis, ulceration or skin burns. In several case studies of workers exposed to the chemical in cement preparation plants, ulcerative dermatitis or partial- to full-thickness skin burns were reported (SCOEL, 2008).

Accidental ocular exposure to the chemical can cause severe eye injuries. In several case studies of workers exposed to the chemical during its production or via cement splashes, reversible corneal damage (opacity) was reported (SCOEL, 2008).

When opening pouches of a chewing tobacco additive containing the chemical, irreversible eye burns with poor long-term prognoses were reported in children and adults (n = 21, age = 3.8–27 years) (SCOEL, 2008).

Respiratory irritation may coincide with coughing, pains and burns of the mucous membranes, as well as pulmonary oedema, low blood pressure and altered pulse rate in severe cases of acute exposure (Clayton & Clayton, 1994). However, adverse effects from controlled occupational exposure have been limited (ACGIH, 2001).

Workers (n = 315) from 23 factories extracting chemicals, including calcium hydroxide from limestone, were assessed after a single exposure. Twelve percent of the workers assessed were exposed to calcium hydroxide only and 40 % were not exposed to any chemicals. Exposed workers had higher risk ratios for eye, nose and throat irritation and acute cough (1.9, 4.7, 3.0 and 3.1, respectively) compared with workers who were not exposed to any chemicals (SCOEL, 2008).

Chronic exposure to the chemical may cause inflammation and ulceration of the mouth and oesophagus (Clayton & Clayton, 1994). It was concluded in the SCOEL (2008) report that long-term inhalation exposure to the chemical affected lung function.

Workers (n = 580) from 31 factories producing chemicals, including calcium hydroxide from limestone, were assessed for chronic effects. Exposed workers had higher risk ratios for chronic cough, phlegm, bronchitis, wheeze, chest tightness and dyspnoea (1.5, 1.3, 1.4, 2.2, 1.7 and 2.2, respectively) compared with workers that were not exposed. The specific contribution of the chemical to these effects is not known (SCOEL, 2008).

Exposure to cement dust was used as a surrogate for chronic inhalation exposure to the chemical. Numerous epidemiological studies on cement dust exposure have determined that there was no consistent dose-response effect in the respirable dust range of 0.57–1.5 mg/m^3 (<3.3 mg/m^3 total dust), but that lung impairment (e.g. reduced lung function, chronic cough, phlegm, dyspnoea, asthma) occurred in the respirable dust range of 1.6–3.9 mg/m^3 (>5.7 mg/m^3 total dust). An exposure level of 1 mg/m^3 (0.001 mg/L) respirable dust was determined as the cut-off to prevent lung dysfunction from cement dust and this level was reported to be applicable for the chemical as well (SCOEL, 2008).

Sensitisation

Skin Sensitisation

No data are available.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include irritation effects (respiratory, dermal and ocular) due to the high alkalinity of the chemical.

Public Risk Characterisation

The chemical is used only as a buffering agent in cosmetics (CosIng) and therefore cosmetic use is not expected to expose the public to high concentrations. If the concentrations in cosmetics are low, irritation effects are not expected; therefore, the risk to public health is not considered to be unreasonable and further risk management is not considered necessary for public safety.

Occupational Risk Characterisation

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

Exposure to the chemical as a fine powder may occur in some applications.

The data available support an amendment to the hazard classification in the HSIS (Safe Work Australia) (see **Recommendation** section).

NICNAS Recommendation

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

However, it is recommended that Safe Work Australia consider whether the current exposure controls offer adequate protection to workers.

Regulatory Control

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 and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Irritation / Corrosivity	Risk of serious eye damage (Xi; R41) Irritating to skin (Xi; R38)	Causes serious eye damage - Cat. 1 (H318) Causes skin irritation - Cat. 2 (H315)

[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 industry

Control measures

Control measures to minimise the risk from inhalation, dermal and 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 that could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

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

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

Obligations under workplace health and safety legislation

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

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

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

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

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

References

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

Clayton GD and Clayton FE (eds.) 1994. Patty's Industrial Hygiene and Toxicology. Volume II Part A: Toxicology. 4th edition, pp. 762–764. John Wiley& Sons.

Dunham LJ, Muir CS& Hamner JE 3rd 1966. Epithelial atypia in hamster cheek pouches treated repeatedly with calcium hydroxide. Br J Cancer 20(3) pp. 588-593

European Commission Cosmetic Ingredients and Substances (CosIng) Database. Accessed July 2015 at http://ec.europa.eu/consumers/cosmetics/cosing/

Food Standards Australia New Zealand (FSANZ) 2014. Australia New Zealand Food Standards Code - Standard 1.3.1 - Food Additives. Accessed July 2015 at http://www.comlaw.gov.au/Details/F2014C01335

Galleria Chemica. Accessed July 2015 at http://jr.chemwatch.net/galleria/

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

Muir CS& Kirk R 1960. Betel, tobacco, and cancer of the mouth. Br J Cancer 14 pp. 597-608

National Institute for Working Life 1999. Scientific Basis for Swedish Occupational Standards XX: Consensus report for calcium oxide and calcium hydroxide. Available at http://www.inchem.org/documents/kemi/kemi/ah1999_26.pdf

NICNAS 2006. Australian High Volume Industrial Chemicals List (AHVICL). Available at http://www.nicnas.gov.au/__data/assets/pdf_file/0019/6661/NICNAS_AHVICL_2006_PDF.pdf

Peacock M 2010. Calcium metabolism in health and disease. Clin J Am Soc Nephrol 5 pp. S23–S30.

Recommendation from the Scientific Committee on Occupational Exposure Limits (SCOEL) for Calcium oxide (CaO) and calcium hydroxide (Ca(OH)2) 2008. SCOEL/SUM/137. Available at http://ec.europa.eu/social/BlobServlet?docId=3866&langId=en

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Dossier. 1305-62-0. Accessed July 2015 at http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

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

Therapeutic Goods Administration (TGA) 2007. Substances that may be used in Listed medicines in Australia. Available at https://www.tga.gov.au/sites/default/files/cm-listed-substances.pdf

Thomas SJ& MacLennan R 1992. Slaked lime and betel nut cancer in Papua New Guinea. Lancet 340(8819) pp. 577-8.

United States (US) Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) dictionary. Accessed July 2015 at http://gov.personalcarecouncil.org/jsp/gov/GovHomePage.jsp

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

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

Last update 01 September 2015