

Soluble cadmium salts: Human health tier II assessment

07 February 2014

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



Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Acetic acid, cadmium salt	543-90-8
Acetic acid, cadmium salt, dihydrate	5743-04-4
Benzoic acid, cadmium salt	3026-22-0
Nitric acid, cadmium salt, tetrahydrate	10022-68-1
Nitric acid, cadmium salt	10325-94-7
Cadmium bromide, tetrahydrate	13464-92-1
Borate(1-), tetrafluoro-, cadmium (2:1)	14486-19-2
Propanoic acid, cadmium salt	16986-83-7
Benzoic acid, cadmium salt, basic	90218-85-2
Propanoic acid, cadmium salt, basic	90529-78-5

Preface

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

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

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

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

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

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

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

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

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

Disclaimer

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

ACRONYMS & ABBREVIATIONS

Grouping Rationale

This group of ten chemical compounds consists of selected soluble cadmium salts, with or without water of hydration. On the AICS (Australian Inventory of Chemical Substances), hydrates are regarded as a mixture of the anhydrous form and water; therefore, anhydrous forms are taken to cover all hydrates and these chemicals should be considered equivalent. These compounds have been included in this group due to the expectation that the physico-chemical properties will not vary greatly, as all compounds are relatively water soluble, leading to the compounds within this group having related end uses. The toxicity is considered to result entirely from the presence of the cadmium component (cation). The acid components (anions) are not considered to contribute to any significant extent to the toxicity of the chemicals. In addition, information outlined in the Organisation for Economic Co-operation and Development (OECD) guideline on Grouping of Chemicals (OECD, 2007) provides guidance on grouping chemicals based on physico-chemical or toxicological criteria.

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacturing information has been identified.

International

Of the compounds in this group, no specific international use, import, or manufacture information has been reported for:

- Propanoic acid, cadmium salt (CAS No. 16986-83-7)
- Propanoic acid, cadmium salt, basic (CAS No. 90529-78-5)
- Benzoic acid, cadmium salt (CAS No. 3026-22-0)
- Benzoic acid, cadmium salt, basic (CAS No. 90218-85-2)

The remaining soluble cadmium compounds have one or more of the following reported uses, which have been identified through European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers; EU Risk Assessment Reports (EU RAR); Substances and Preparations in the Nordic countries (SPIN) database; the International Agency for Research on Cancer (IARC) report; the United States (US) National Toxicology Program's Report on Carcinogens (NTP RoC); Galleria Chemica and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB):

Reported commercial use including in:

- photography, e.g. photography emulsions and in manufacturing light sensitive paper;
- colouring agents for glass and assisting in dyeing and printing textiles;
- surface treatments, glaze for porcelains and ceramics where it produces iridescent effects;
- process engraving and lithography.
- corrosion inhibitors; and
- nickel-cadmium battery manufacturing.

Reported site-limited use including:

- as a laboratory reagent for sulfur, selenium and tellurium;
- in electroplating, e.g. as an alternative to the cyanide bath for cadmium electrolysis;
- in the manufacture of high strength steels;
- in preparing metallic soaps for PVC stabilisers;
- in the manufacture of laboratory chemicals, e.g. other cadmium salts; and
- in reactors to control rate of nuclear fission and as reactor poison.

Restrictions

Australian

Cadmium and cadmium compounds are listed in the *Poisons Standard* (the Standard for the Uniform Scheduling of Medicines and Poisons – SUSMP (SUSMP, 2012)) under the following Schedules:

Appendix I, The uniform paint standard

The following applies to paints containing cadmium or cadmium compounds at >0.1 %. 'The proportion of a substance for the purposes of this Schedule is calculated as a percentage of the element present in the non-volatile content of the paint' (SUSMP 2012).

'A person must not manufacture, sell, supply or use a paint containing >0.1 % of cadmium or cadmium compounds for application to:

- a roof or any surface to be used for the collection or storage of potable water; or
- furniture; or
- any fence, wall, post, gate or building (interior or exterior) other than a building which is used exclusively for industrial purposes or mining or any oil terminal; or
- any premises used for the manufacture, processing, preparation, packing or serving of products intended for human or animal consumption' (SUSMP, 2012).

Additionally, 'a person must not manufacture, sell, supply or use a paint for application to toys unless the paint complies with the specification for coating materials contained in Australian/New Zealand Standard AS/NZS ISO 8124.3:2012 entitled *Safety of toys Part 3: Migration of certain elements* (ISO 8124-03:2010, MOD)' (SUSMP, 2012).

'**Schedule 6** except when:

(a) included in Schedule 4; or

(b) in paints or tinters containing 0.1 per cent or less of cadmium calculated on the non-volatile content of the paint or tinter' (SUSMP, 2012).

Schedule 6 substances are considered to have 'moderate potential for causing harm, the extent of which can be reduced through the use of distinctive packaging with strong warnings and safety directions on the label' (SUSMP, 2012).

Cadmium and its compounds are also listed as restricted hazardous chemicals in the Australia work health and safety Regulations 2011 for 'use in abrasive blasting at a concentration of greater than 0.1 % as cadmium' (SafeWork Australia).

International

Cadmium and cadmium compounds are listed on the following (Galleria Chemica):

- EU Cosmetic Directive 76/768/EEC Annex II: List of substances which must not form part of the composition of cosmetic products;
- New Zealand Cosmetic Products Group Standard—Schedule 4: Components cosmetic products must not contain; and
- Health Canada list of prohibited and restricted cosmetic ingredients (The "Hotlist").

Cadmium and its compounds are also restricted in the EU under Annex XVII of the European Chemicals Agency (ECHA) REACH Regulation, including in:

- plastic materials;
- paints;
- metal plating; and
- brazing (soldering/welding) fillers.

Existing Worker Health and Safety Controls

Hazard Classification

The members of this group are not individually listed in the Hazardous Substances Information System (HSIS). Therefore, by default, they are covered by the generic 'cadmium compounds' classification as hazardous with the following risk phrases for human health (Safe Work Australia):

Xn; R20/21/22 (Harmful by inhalation, in contact with skin and if swallowed)

Exposure Standards

Australian

Cadmium and cadmium compounds have an exposure standard of 0.01 mg/m³ time weighted average (TWA).

International

For cadmium and cadmium compounds the following exposure limits were identified (Galleria Chemica).

An exposure limit (TWA) of 0.01 - 0.2 mg/m³ in different countries such as Canada, USA, Latvia and Switzerland.

Health Hazard Information

The main concern regarding effects on human health is expected to be driven by the cadmium component (cation) of these compounds. The compounds are expected to dissociate into the cadmium and their respective anions under physiological conditions. The anions of the chemicals in this group have been screened by NICNAS and are not considered to contribute to the final recommendations of this assessment.

While there are limited data available on these specific chemicals, data sources for determining the hazard of the cadmium cation include animal studies on well characterised cadmium compounds, particularly other soluble cadmium salts (cadmium chloride and cadmium sulfate) and a large amount of literature on observations of cadmium exposure in humans. The toxicity data for cadmium chloride and cadmium sulfate exposure are considered relevant to the cadmium compounds in this group, as the chloride and sulfate components have also been assessed by NICNAS and are not considered to contribute to the final recommendations (NICNAS).

Additionally, the health hazards identified in this report for acetic acid, cadmium salt (CAS No. 543-90-8) and nitric acid, cadmium salt (CAS No. 10325-94-7), are considered to apply to their respective hydrated forms.

Toxicokinetics

There is a large amount of information on the toxicokinetics of the cadmium ion in humans. This information is mostly related to general cadmium exposure in workers, and is not specific to particular cadmium compounds.

A study reported cadmium was detectable in the liver of male rats that were injected intraperitoneally (ip) with acetic acid, cadmium salt (CAS No. 543-90-8) at a dose equivalent to 1 mg cadmium/kg, daily for eight days (HSDB).

Dermal absorption of cadmium in rabbits following exposure to a cadmium chloride solution was considered to be substantial, resulting in accumulation of up to 0.8 % of the administered dose in the kidney and liver (EURAR, 2007).

In rodent dietary exposure studies using cadmium oxide, which is soluble at the low pH of gastric fluid, significant accumulation of cadmium was detected in the liver, kidneys, lungs and spleen. Levels in the liver and kidneys were reported to be dose-dependent. However, no significant increase in blood or urine levels of cadmium was detected. Absorption rates following oral exposure to low doses of the chemical were reported to be much greater than those determined for exposure to higher doses (EU RAR, 2007).

Animal studies have demonstrated that absorption of the chemical following inhalation exposure ranges from 30 % (dusts, size-dependent) to 50 % (fumes). In humans, inhalation absorption of 10-30 % (dusts, size-dependent) is reported (OECD, 2004). Specific data for soluble compounds are not available.

Following long-term low-level exposure, cadmium is reported to be widely distributed in the body and has a biological half-life of 10-20 years. The greatest accumulation occurs in the kidneys and liver, with only 0.005-0.02 % reported to be excreted in urine and faeces each day. Cadmium is also detectable in the placenta,

and can cross the placenta, although foetal concentrations are lower than placental concentrations. Concentrations of cadmium in newborn blood were 40-50 % lower than the levels in maternal blood (EU RAR, 2007). Cadmium is reported to be found in human breast milk at <1 µg/L (OECD, 2004). In tissue, cadmium is bound to metallothionein, a low molecular weight metal-binding protein that may play a key role in the metabolism and detoxification of cadmium (EU RAR, 2007).

Human data available on cadmium indicate that gastro-intestinal absorption rates are low (5-10 %), and vary depending on the source of the cadmium, presence of zinc in the diet, the body's iron stores (deficiencies linked with increased cadmium absorption) and the person's age and physiological condition (young or pregnant and

lactating animals have been shown to absorb more cadmium than non-pregnant adult animals) (EU RAR, 2007; OECD, 2004).

It should be noted that higher levels of cadmium (particularly in the kidney) are detected in smokers compared to non-smokers, as cadmium has been shown to accumulate in tobacco plant leaves (WHO, 2010).

Acute Toxicity

Oral

The compounds in this group are not individually listed in HSIS. Therefore, by default, they are covered by the generic 'cadmium compounds' hazard classification with the risk phrase 'Harmful if swallowed' (Xn; R22) in HSIS (Safe Work Australia). While there are no experimental data available for these specific chemicals, data from other soluble cadmium salts (cadmium chloride and cadmium sulfate) support a recommendation to amend the classification for the compounds in this group.

Cadmium chloride and cadmium sulfate are reported to be acutely toxic in animal tests following oral exposure. The oral median lethal dose (LD50) values are 107-327 and 280 mg/kg bw, respectively (NICNAS).

Additionally, cadmium chloride and cadmium sulfate are classified as hazardous following acute oral exposure, with the risk phrase 'Toxic if swallowed' (T; R25) in HSIS (Safe Work Australia).

There is sufficient evidence to warrant this classification applying to all compounds in this group.

Dermal

The compounds in this group are not individually listed in HSIS. Therefore, by default, they are covered by the generic 'cadmium compounds' hazard classification with the risk phrase 'Harmful in contact with skin' (Xn; R21) in HSIS (Safe Work Australia).

While there are no experimental dermal toxicity data available for these specific chemicals, a number of soluble cadmium salts are reported to be absorbed by the skin resulting in detectable levels of cadmium in the liver and kidney (see **Toxicokinetics** section).

In the absence of more comprehensive information, there is insufficient evidence to support a recommendation to amend the classification for this group of chemicals.

Inhalation

The compounds in this group are not individually listed in HSIS. Therefore, by default, they are covered by the generic 'cadmium compounds' hazard classification with the risk phrase 'Harmful if inhaled' (Xn; R20) in HSIS (Safe Work Australia).

While there are no experimental data available for these specific chemicals, data from other cadmium compounds support a recommendation to amend the classification for the compounds in this group.

Eight-hour inhalation exposure to cadmium levels of 5 mg/m³ is reported to be potentially lethal, while 1 mg/m³ is considered to be immediately dangerous to life (EU RAR, 2008).

Additionally, the soluble cadmium salts, cadmium chloride and cadmium sulfate, are classified as hazardous following acute inhalation exposure, with the risk phrase 'Very toxic by inhalation' (T+; R26) in HSIS (Safe Work Australia).

There is sufficient information about the chemical similarity to cadmium chloride and sulfate to warrant this classification applying to all compounds in this group.

Observation in humans

There are many case reports of acute poisoning following inhalation of cadmium oxide fumes, or fumes produced by heating cadmium-containing materials to high temperatures. Documented signs of toxicity include nausea, fever, difficulties in respiration and severe respiratory irritation. Pulmonary oedema, resulting in mortality, was commonly reported following acute exposure (EU RAR, 2007).

Several cases of cadmium poisoning (compound not specified) from ingesting contaminated food or drinks have been documented. Reported signs and symptoms of toxicity include nausea, vomiting, diarrhoea and abdominal cramps.

Corrosion / Irritation

Respiratory Irritation

While no data are available for the specific cadmium compounds in this group, based on sublethal symptoms observed in inhalation studies in animals and observations in humans, these compounds are expected to be irritating to the respiratory tract.

Skin Irritation

While no data are available for these specific cadmium compounds in this group, potential skin irritation was reported following exposure to cadmium chloride in humans (refer to **Observation in humans** section).

Eye Irritation

No data are available.

Observation in humans

Eczema patients were patch-tested with 0.06, 0.5, 1 or 2% doses of cadmium chloride in distilled water. At the 2% dose, skin irritation was reported in 25/1502 patients (1.7%), but no vesicular reactions (skin blisters) were observed. A lowest observed adverse effect level (LOAEL) value of 2 % was reported. No skin irritation was reported at 1 % in patients (EU RAR, 2007; REACH).

Sensitisation

Skin Sensitisation

While no data are available for the specific cadmium compounds in this group, there is evidence of skin sensitisation from human observations following exposure to cadmium chloride (refer to **Observation in humans** section).

In a guinea pig maximisation test, animals (20/dose) were intradermally administered a 0.007 % cadmium chloride solution in water. After an unreported period, a 5 % solution of the chemical (in petrolatum) was topically applied to the animals. When challenged three weeks later with 0.05 % cadmium chloride solution by intradermal injection, and with a 7.5 % topical application, no contact sensitisation was reported at 24 or 48 hours (EU RAR, 2007; REACH).

There is insufficient evidence to classify these chemicals as skin sensitisers.

Observation in humans

Skin patch tests using cadmium chloride and cadmium sulfate were positive in seven out of approximately 150 patients attending a dermatological department between 1979-1981 (EU RAR, 2007).

Repeated Dose Toxicity

Oral

While there are no data available for these specific chemicals, data from animal studies and observations in humans following exposure to soluble cadmium salts are provided in the following sections.

A chronic exposure study in male Wistar rats using cadmium chloride reported potential damage to the vertebrae. The animals (10/dose) were orally exposed to cadmium chloride through drinking water for 12 months at 1, 5, 50 mg/L. No treatment related signs were reported at 1 mg/L. At ≥ 5 mg/L, increased lumbar spine deformities and a decrease in lumbar spine mineralisation (including calcium, magnesium, zinc, copper, iron and phosphate) were reported. A decrease in mechanical strength of the vertebral column at the fourth lumbar vertebra (L4) was reported at 50 mg/L. The L4 was reported to be fractured in 30 % of animals in this

group, while 40 % were reported to have L4 deformities. The remaining animals in this group (30 %) had intact L4s. The NOAEL (no observed adverse effect level) and LOAEL (lowest observed adverse effect level) for this study were reported to be 0.2 mg/kg bw/day and 0.5 mg/kg bw/day, respectively (REACH).

Additionally, cadmium chloride and cadmium sulfate are classified as hazardous following repeat oral exposure, with the risk phrase 'Toxic: danger of serious damage to health by prolonged exposure if swallowed' (T; R48/R25) in HSIS (Safe Work Australia).

There is sufficient evidence from animal studies and observations in humans to warrant this classification applying to all compounds in this group.

Dermal

No data are available.

Inhalation

While there are no data available for these specific chemicals, data from animal studies and observations in humans following exposure to other cadmium compounds are provided in the following sections.

Effects observed in animal studies following repeated-dose exposure to cadmium oxide are reported to be similar to those observed in acute exposure studies including rales (abnormal respiratory sounds), laboured breathing and pneumonia, seen at low doses (EU RAR, 2008).

In a 13-week repeated-dose inhalation study in rats exposed to cadmium oxide, the NOAEL was reported to be 0.025 mg/m³. At higher doses (≥ 0.05 mg/m³), treatment-related lesions in the lungs, including inflammation and fibrosis, were observed. A dose-related increase in hyperplasia (elevated cell production) in the lungs was also reported (EU RAR, 2007).

Additionally, cadmium chloride and cadmium sulfate are classified as hazardous following repeat inhalation exposure, with the risk phrase 'Toxic: danger of serious damage to health by prolonged exposure through inhalation' (T; R48/R23) in HSIS (Safe Work Australia).

There is sufficient evidence from animal studies and observations in humans to warrant this classification applying to all compounds in this group.

Observation in humans

Exposure to low levels of cadmium over a long period of time has been linked to chronic cadmium poisoning. The effects of cadmium on specific target organs following exposure in humans are summarised and provided below.

Respiratory effects

There are a number of documented case studies of workers chronically exposed to the chemical fumes (EU RAR, 2007). Effects reported include fatigue, respiratory irritation, shortness of breath, decreased lung function and recurrent bronchitis.

It is suggested that an increase in residual levels of the chemical in lungs may lead to chronic obstructive airway disease and (in some cases) mortality, all of which have been documented following exposure (EU RAR, 2007). A lowest observed adverse effect concentration (LOAEC) of 0.0031 mg/L, based on lung effects (increased residual levels of the chemical), was derived from a study on workers exposed to the chemical fumes at <0.5 mg/m³ over several years.

Renal effects

The kidneys are considered to be the main target organ for cadmium toxicity following repeated oral and inhalation exposure (ATSDR, 2012; EU RAR, 2007). Initial signs of kidney effects following cadmium exposure include tubular dysfunction, a decreased glomerular filtration rate, and increased proteinuria and enzymuria. Renal dysfunction is considered to occur when renal cortex cadmium concentrations reach 200 ppm (equivalent to 5–10 µg/g creatinine) (EU RAR, 2007).

An increased frequency of kidney stones has also been reported in workers exposed to cadmium (18 %), compared with unexposed workers (3 %) (EU RAR, 2007).

Skeletal effects

Oral cadmium exposure is reported to cause bone disease in humans (EU RAR, 2008). While the underlying mechanism is not clearly understood, it is thought that cadmium-induced kidney damage and resulting hypercalcaemia (elevated levels of calcium in the urine) may promote osteoporotic effects in bone (EU RAR, 2007).

In a case study in Japan, a high incidence of Itai-Itai disease was diagnosed in patients from specific geographical locations. It was found that farms in these areas were irrigated by a river being polluted by cadmium sludge from an upstream mine, and the patients may have been exposed to cadmium for over 30 years. Samples of rice taken from those areas were reported to contain cadmium at 0.68 mg/kg, compared with 0.066 mg/kg in other areas (EU RAR, 2007). Itai-Itai disease is characterised by osteomalacia (softening of the bones), osteoporosis, severe renal tubular disease, and is associated with severe pain (WHO, 2011). A limited number of case reports have also documented clinical bone disease in workers exposed to cadmium compounds (EU RAR, 2007).

Genotoxicity

While there are limited experimental data available for these specific chemicals, data from other soluble cadmium salts (cadmium chloride and cadmium sulfate) are also provided below.

In vitro

Cadmium nitrate was reported to induce reversible mutations in four strains of *Salmonella typhimurium* bacterial strains TA 1535 and TA 1538 (HSDB).

Cadmium chloride was reported to not be mutagenic in *Salmonella typhimurium* bacterial strains TA 98, TA100, TA 1535 and TA 1537 with and without metabolic activation (REACH). However, cadmium ions have been shown to induce genotoxic effects in vitro (reduction in colony-forming ability and DNA strand breaks in *Escherichia coli*) (EU RAR, 2007).

Cadmium nitrate was reported to be mutagenic in Chinese hamster ovary (CHO) cells. Dose dependent effects observed included increased sister chromatid exchanges and chromosome aberrations which included breaks, acentrics (chromosome or chromosome fragment without a centromere), interchanges, and dicentrics (chromosome or chromatid with two centromeres). There was also a decrease in the mitotic index (the ratio between the number of cells in mitosis and the total number of cells). The inhibitory concentration (IC50) was determined to be 0.015 mM, indicating exposure to cadmium nitrate at that dose resulted in 50% inhibition of viable cells (Lin RH et al., 1994).

In another test using CHO cells, cadmium acetate was reported to induce large genomic deletions, base substitutions and splice mutations (HSDB).

Cadmium chloride and cadmium sulfate were clastogenic in tests using mammalian cells. An increase in sister chromatid exchanges was reported in male and female mouse splenocytes exposed to cadmium chloride, and in human lung fibroblasts exposed to either cadmium chloride or cadmium sulfate; chromosomal aberrations were observed in male and female Swiss mouse splenocytes following exposure to cadmium chloride; and DNA strand breaks and mutations at the K-ras gene were reported in human lung fibroblasts exposed to cadmium sulfate (REACH).

In vivo

Cadmium chloride was reported to be mutagenic in vivo in male albino rats that were injected intraperitoneally (ip) with a 4 mg/kg bw dose of the chemical. Single strand DNA breaks were observed following exposure, notably in the kidney (EU RAR, 2007).

Cadmium chloride was reported to be mutagenic in vivo in a study where the induction of micronuclei, sister chromatid exchanges in mouse bone marrow and chromosomal aberration were investigated, after a single ip treatment of the chemical at doses of 1.9, 5.7, 7.6 mg/kg bw.

A dose dependent increase of peripheral erythrocytes with micronuclei was reported, where doses of 5.7 and 7.6 mg/kg bw induced bone marrow toxicity as noted by a significant increase in the percentage of polychromatic erythrocytes relative to normal chromatic erythrocytes when compared to the control. The chemical was also reported to induce chromosomal aberrations (excluding metaphases with chromosome or chromatid gaps). The intensity of effects was dose-dependent, and at a maximum 24 hours post-treatment. A dose-dependent increase in the frequency of sister chromatid exchanges was reported at the two highest doses (EU RAR, 2007).

Additionally, cadmium chloride and cadmium sulfate are classified as hazardous, as Category 2 mutagens, with the risk phrase 'May cause heritable genetic damage' (T; R46) in HSIS (Safe Work Australia).

There is sufficient evidence to warrant this classification applying to all compounds in this group.

Observations in humans

Chromosomal aberrations, increased frequency of micronuclei, and sister chromatid exchanges have been detected in humans environmentally exposed to cadmium (EU RAR, 2007). However, the specific cadmium compounds involved are not identified.

Carcinogenicity

While there are no experimental data available for these specific chemicals, data from other soluble cadmium salts (cadmium chloride and cadmium sulfate) are provided below.

Oral administration of cadmium chloride to Wistar rats increased the incidence of large granular lymphocytes, leukaemia, prostate tumours, and testicular tumours. Prostate hyperplasia was also reported in Noble rats orally exposed to the chemical (NTP, 2011; REACH).

A non-guideline inhalation study reported an increase in lung tumours in male and female Wistar rats (20/sex/dose) exposed to aerosolised cadmium chloride, cadmium sulfate, cadmium oxide dusts, cadmium oxide fumes or cadmium sulfide (REACH).

Rats were exposed to cadmium chloride at 0.03 and 0.09 mg/m³ for 22 hours a day, seven days a week over an 18-month exposure period. The LOAEL for carcinogenicity was reported to be 0.03 mg/m³ air, as lung bronchioalveolar adenomas (benign glandular tumour of the lung), adenocarcinomas (malignant glandular

tumours) and squamous cell carcinomas (cancer of the outer layer of skin or of the lining of the internal organs) were noted at this dose. In male and female rats, a high incidence of lung nodules and lung tumours were reported for 0.03 mg/m³ exposure (lung nodules in 33/38 rats; primary lung tumours in 28/38 rats). Bronchioalveolar adenomas were observed in 6/38 animals, adenocarcinomas were observed in 19/38 animals and combined squamous cell carcinomas and adenocarcinomas were observed in 3/38 animals.

In another part of the study, rats were exposed to cadmium sulfate at 0.09 mg/m³ for 22 hours a day, seven days a week over an 18-month exposure period. Lung bronchioalveolar adenomas, adenocarcinomas and squamous cell carcinomas were noted. In another study using cadmium sulfate, a significant incidence of lung tumours was observed following chronic inhalation exposure to 0.09 mg/m³ over a 29-30 month period (REACH).

Additionally, cadmium chloride and cadmium sulfate are classified as hazardous, as Category 2 carcinogens, with risk phrase 'May cause cancer' (T; R45) in HSIS (Safe Work Australia).

There is sufficient evidence to warrant this classification applying to all compounds in this group.

Observations in humans

There are many case studies that explore the link between exposure to cadmium and increased incidences of cancer in workers (NTP, 2011; IARC, 2012).

The International Agency for Research on Cancer (IARC) has classified cadmium and cadmium compounds as 'Carcinogenic to humans (Group 1)' based on sufficient evidence in humans and experimental animals (IARC, 2012). Additionally, the US National Toxicology Program (NTP) has also classified cadmium and cadmium compounds as 'Known to be human carcinogens' (NTP, 2011).

Significantly increased mortalities due to lung cancer were reported in workers in cadmium-processing plants, cadmium recovery plants and those who worked in the nickel-cadmium battery production industry (IARC, 2012). An increased risk of lung cancer was identified in workers with long-term employment in high cadmium-exposure jobs.

A few cases of cancer of the prostate, pancreas and kidney have also been reported following exposure to cadmium (either from occupational exposure or by contamination).

In some of these cases, workers may have been exposed to other chemicals, including arsenic and nickel. Both IARC and the US NTP concluded that the increase in lung cancers could not be solely due to co-exposure to other chemicals (NTP, 2011; IARC, 2012). However, the Agency for Toxic Substances and Disease Registry (ATSDR) concluded that the interpretation of these observations in humans is complicated by co-exposure with other metals, and that there is a 'lack of significant relationship between cadmium exposure and duration' (ASTDR, 2012). Based on these data, there is only limited evidence of human carcinogenicity of soluble cadmium compounds.

Reproductive and Developmental Toxicity

While there are limited experimental data available for these specific chemicals, data from other soluble cadmium salts (cadmium chloride and cadmium sulfate) are also provided below.

Reproductive toxicity

In a study in female Wistar rats, animals were exposed to cadmium chloride by oral gavage at 0.04, 0.4, 4 and 40 mg/kg bw/day for 14 weeks. Increased oestrous cycle lengths and decreased body weights when compared to the control group animals, were reported in the highest dose group (40 mg/kg bw/day) after six weeks of treatment; this was not reported for other dose groups. A reproductive NOAEL of 4 mg/kg bw/day and LOAEL of 40 mg/kg bw/day were reported for this study (REACH; EU RAR, 2007).

Developmental toxicity

A study using pregnant Sprague Dawley (SD) rats reported developmental effects following exposure to cadmium acetate from gestation day 1 through to lactation day 21 at doses of 5-8 mg/kg bw/day. Pup body weights were significantly decreased in the cadmium exposed pups during lactation. No details on maternal toxicity are reported, although the developmental LOAEL was reported to be 3.1 mg cadmium/kg bw/day (EU RAR, 2007).

Effects of cadmium exposure on maternal and foetal zinc metabolism were reported to be investigated in a non-guideline developmental toxicity study. SD rats were orally exposed to cadmium chloride in drinking water at daily doses of 0, 5, 50 and 100 ppm on gestation days 6-20. Exposure-related reduced maternal weights and weight gains were reported at the highest dose groups at 50 and 100 ppm but not in the 5 ppm group. In the 100 ppm dose group, reduced foetal weights were reported to be a secondary effect to decreased maternal weights (attributed to maternal reduced food and water intake). A significant difference in the foetal weight to maternal weight ratio (as compared to the controls) was only observed in the 50 ppm group.

It was reported at the 50 ppm dose that cadmium-induced zinc retention was the cause of impaired foetal growth as zinc retention in maternal liver and kidney and decreased concentration of zinc in the foetal liver were observed. A maternal and developmental NOAEL of 5 ppm (0.63 mg/kg bw/day) and a maternal and developmental LOAEL of 50 ppm (4.7 mg/kg bw/day) were reported (REACH; EU RAR 2007).

In another study, cadmium chloride was administered intragastrically at 2, 12 and 40 mg/kg bw/day, to pregnant rats. At the two highest dose groups, reduced foetal body weights and reduced skeletal ossification, compared to controls, were reported. However, reduced body weight gains during pregnancy of treated females at all dose

levels were also reported. NOAEL or LOAEL estimates were not reported for this study (EU RAR 2007).

Additionally, cadmium chloride and cadmium sulfate are both individually listed in HSIS and are classified as hazardous, as Category 2 reproductive and developmental toxins, with the risk phrases 'May impair fertility' (T; R60) and 'May cause harm to the unborn child' (Xn; R61) in HSIS (Safe Work Australia).

There is sufficient evidence to warrant this classification applying to all compounds in this group.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects (carcinogenicity, mutagenicity, reproductive toxicity and developmental toxicity), systemic acute effects (acute toxicity by the oral and inhalation route of exposure), and toxic effects resulting from repeated exposure following ingestion or inhalation. The chemicals are also potential respiratory irritants.

Public Risk Characterisation

Given the uses identified for these chemicals, it is unlikely that the public will be exposed. Hence, the public risk from these chemicals is not considered to be unreasonable.

Occupational Risk Characterisation

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

NICNAS Recommendation

Assessment of the chemicals is considered to be sufficient, provided that the recommended amendments to the classification are 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.

Regulatory Control

Public Health

Products containing the chemicals should be labelled in accordance with state and territory legislation (SUSMP).

Work Health and Safety

The chemicals 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.

The classification proposed below is based on read across principles (refer to section on Grouping Rationale). It should be used as a default for all members of the group. If empirical data become available for any member of the group indicating that a lower (or higher) classification is appropriate for the specific chemical, these may be used to amend the default classification for that chemical.

Hazard	Approved Criteria (HSIS) ^a	GHS Classification (HCIS) ^b
Acute Toxicity	Toxic if swallowed (T; R25) Harmful in contact with skin (Xn; R21)* Very toxic by inhalation (T+; R26)	Toxic if swallowed - Cat. 3 (H301) Harmful in contact with skin - Cat. 4 (H312) Fatal if inhaled - Cat. 1 (H330)
Repeat Dose Toxicity	Toxic: danger of serious damage to health by prolonged exposure through inhalation (T; R48/23) Toxic: Danger of serious damage to health by prolonged exposure if swallowed (T; R48/25)	Causes damage to organs through prolonged or repeated exposure - Cat. 1 (H372)
Genotoxicity	Muta. Cat 2 - May cause heritable genetic damage (T; R46)	May cause genetic defects - Cat. 1B (H340)
Carcinogenicity	Carc. Cat 2 - May cause cancer (T; R45)	May cause cancer - Cat. 1B (H350)

Hazard	Approved Criteria (HSIS) ^a	GHS Classification (HCIS) ^b
Reproductive and Developmental Toxicity	Repro. Cat 2 - May impair fertility (T; R60) Repro. Cat 2 - May cause harm to the unborn child (T; R61)	May damage fertility or the unborn child - Cat. 1B (H360F) May damage fertility or the unborn child - Cat. 1B (H360D)

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

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

* Existing Hazard Classification. No change recommended to this classification

Advice for consumers

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

Advice for industry

Control measures

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

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

Guidance on managing risks from hazardous chemicals are provided in the *Managing Risks of Hazardous Chemicals in the Workplace—Code of Practice* available on the Safe Work Australia website.

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

Obligations under workplace health and safety legislation

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

- ensuring that hazardous chemicals are correctly classified and labelled;

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

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

Information on how to prepare an (m)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of Safety Data Sheets for Hazardous Chemicals— Code of Practice* and *Labelling of Workplace Hazardous Chemicals—Code of Practice*, respectively. These codes of practice are available from the Safe Work Australia website.

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

References

Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profile for Cadmium. Accessed January 2014 at <http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=48&tid=15>

Cosmetics Directive (CosIng). Accessed January 2014 at <http://ec.europa.eu/consumers/cosmetics/cosing/>

eChemPortal. Accessed January 2014 at <http://www.echemportal.org/echemportal/substancesearch/substancesearchlink.action>.

European Union Risk Assessment Report (EU RAR) 2007. Final report for cadmium oxide. Part II - Human Health. Accessed January 2014 at <http://esis.jrc.ec.europa.eu/>

European Union Risk Assessment Report (EU RAR) 2008. Summary report for cadmium metal and cadmium oxide. Accessed September 2013 at <http://esis.jrc.ec.europa.eu/>

Galleria Chemica. Accessed January 2014 at <https://jr.chemwatch.net/galleria/>

Hazardous Substances Data Bank (HSDB). National Library of Medicine. Accessed January 2014 at <http://toxnet.nlm.nih.gov>

International Agency for Research on Cancer (IARC) 2012. IARC monographs on the evaluation of carcinogenic risks to humans. A Review of Human Carcinogens: Cadmium. Volume 100 C. Accessed January 2014 at <http://monographs.iarc.fr/ENG/Monographs/vol100C/index.php>

Lin RH, Lee CH, Chen WK, Lin-Shiau SY, 1994. Studies on cytotoxic and genotoxic effects of cadmium nitrate and lead nitrate in Chinese hamster ovary cells. *Environ Mol Mutagen*. 1994;23(2):143-9. Abstract available at <http://www.ncbi.nlm.nih.gov/pubmed/8143703>

National Industrial Chemicals Notification and Assessment Scheme (NICNAS). Inventory Multi-tiered Assessment and Prioritisation (IMAP) Human Health Tier II Assessment for Cadmium chlorides and sulfates. Available at <http://www.nicnas.gov.au>

National Toxicology Program (NTP) 2011. Report on Carcinogens, Twelfth Edition: Cadmium and cadmium compounds. U.S. Department of Health and Human Services. Accessed January 2014 at <http://ntp.niehs.nih.gov/?objectid=03C9AF75-E1BF-FF40-DBA9EC0928DF8B15>

OECD (2004). SIDS Initial Assessment Profile (SIAP): Cadmium oxide and cadmium metal. Accessed January 2013 at <http://webnet.oecd.org/HPV/>

Personal Care Product Council (INCI Dictionary). Accessed January 2014 at <http://www.ctfa.gov.org/jsp/gov/GovHomePage.jsp>

REACH Dossier. Cadmium chloride (CAS No. 10108-64-2). Accessed January 2014 at <http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances>

REACH Dossier. Cadmium sulfate (CAS No. 10124-36-4). Accessed January 2014 at <http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances>

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

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

The Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)) 2013. Accessed January 2014 at <http://www.comlaw.gov.au/Details/F2013L01607/Download>

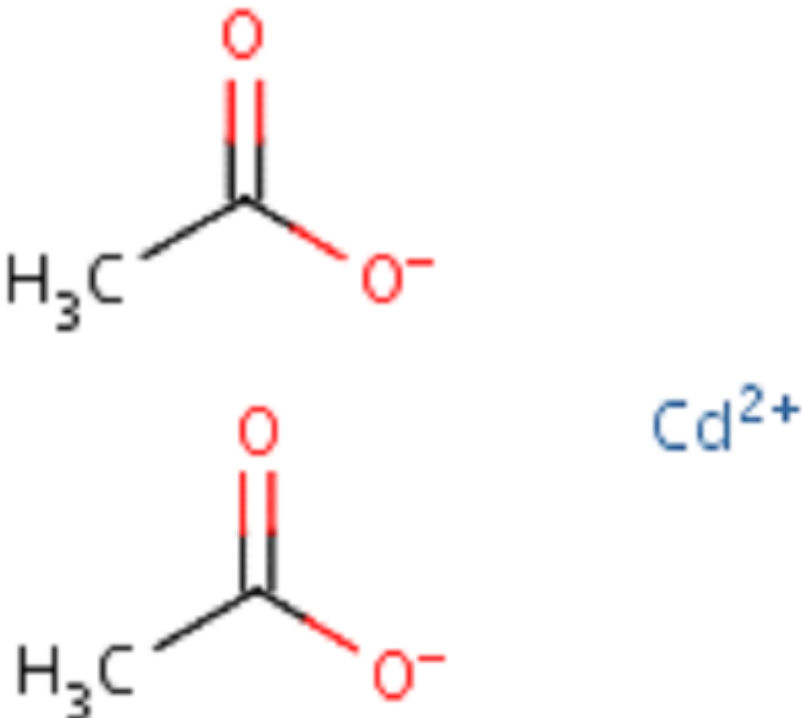
US National Library of Medicines (NLM) Household Products Database, Health & Safety Information on Household Products. Accessed January 2014 at <http://householdproducts.nlm.nih.gov/>

World Health Organisation (WHO) 2010. Exposure to cadmium: A major public health concern. International Programme on Chemical Safety. Accessed January 2014 at http://www.who.int/ipcs/assessment/public_health/cadmium/en/

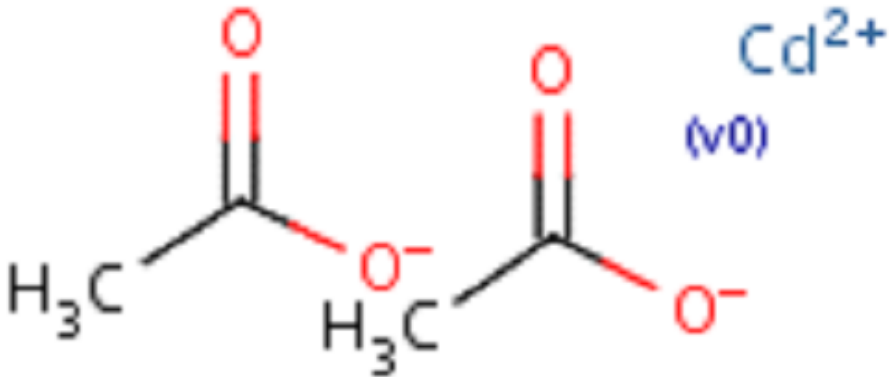
World Health Organisation (WHO) 2011. Cadmium in Drinking-water. Background document for the development of WHO Guidelines for Drinking-water Quality, Fourth edition. Accessed January 2014 at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

Last Update 07 February 2014

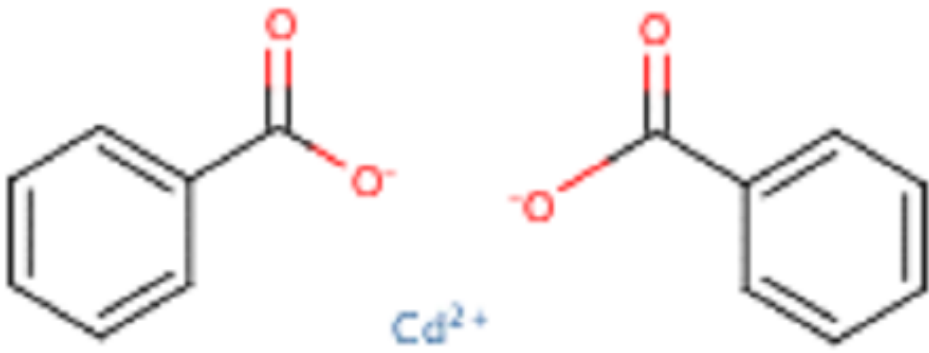
Chemical Identities


Chemical Name in the Inventory and Synonyms	Acetic acid, cadmium salt Cadmium acetate Cadmium diacetate Acetic acid, cadmium salt (2:1) Bis(acetoxy)cadmium Cadmium ethanoate
CAS Number	543-90-8
Structural Formula	 <p>The structural formula shows two acetate ions (CH₃COO⁻) coordinated to a central cadmium ion (Cd²⁺). Each acetate ion consists of a central carbon atom double-bonded to an oxygen atom and single-bonded to a methyl group (H₃C) and an oxygen atom with a negative charge (O⁻). The cadmium ion is represented as Cd²⁺ in blue text to the right of the acetate ions.</p>

Molecular Formula	C ₂ H ₄ O ₂ .1/2Cd
Molecular Weight	230.50

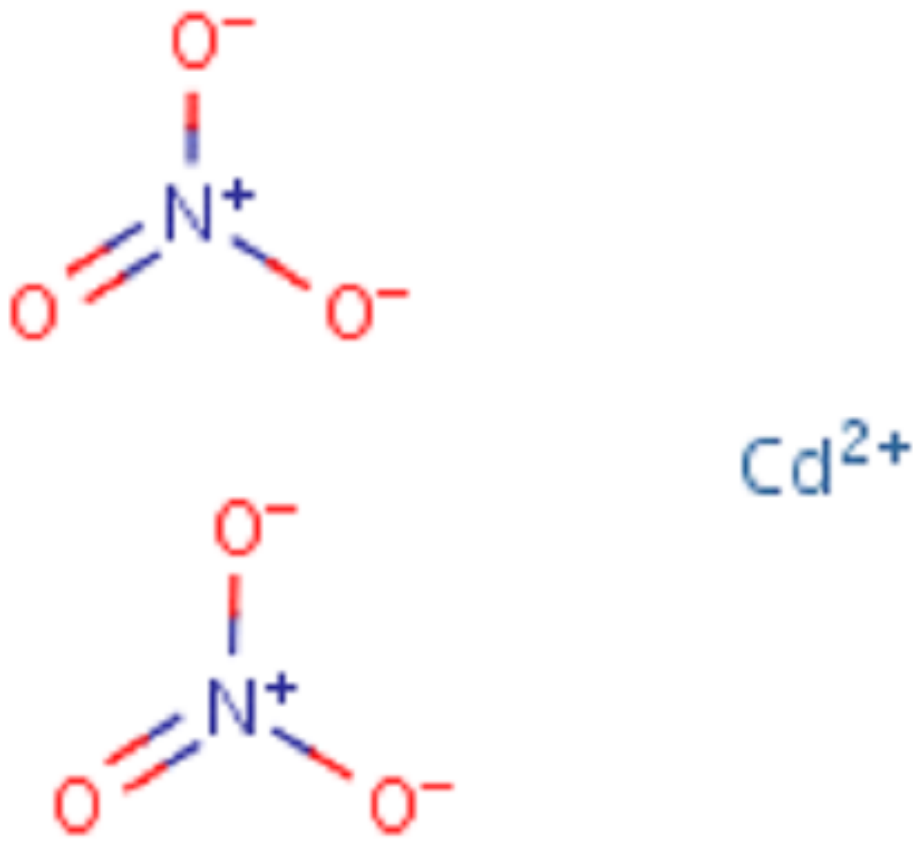
Chemical Name in the Inventory and Synonyms	Acetic acid, cadmium salt, dihydrate Cadmium acetate dihydrate Cadmium diacetate dihydrate
CAS Number	5743-04-4
Structural Formula	
Molecular Formula	C ₂ H ₄ O ₂ .1/2Cd.H ₂ O
Molecular Weight	30.50

Chemical Name in the Inventory and Synonyms	Benzoic acid, cadmium salt Cadmium benzoate (1:2)
CAS Number	3026-22-0
Structural Formula	

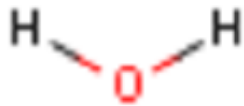
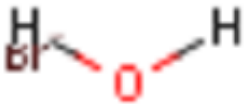
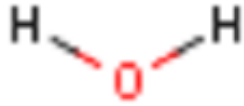
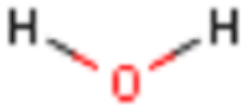

	
Molecular Formula	C ₇ H ₆ O ₂ .1/2Cd
Molecular Weight	

Chemical Name in the Inventory and Synonyms	Nitric acid, cadmium salt, tetrahydrate Cadmium nitrate tetrahydrate Cadmium dinitrate tetrahydrate Cadmium(II) nitrate, tetrahydrate (1:2:4) C.I. 77192
CAS Number	10022-68-1
Structural Formula	
Molecular Formula	Cd.4H ₂ O.2HNO ₃
Molecular Weight	238.43

Chemical Name in the Inventory and Synonyms	Nitric acid, cadmium salt Cadmium nitrate Cadmium dinitrate
---	--

	Cadmium(II) nitrate Nitric acid, cadmium salt (2:1)
CAS Number	10325-94-7
Structural Formula	 <p>The structural formula shows two nitrate ions (NO₃⁻) and one cadmium ion (Cd²⁺). Each nitrate ion consists of a central nitrogen atom (N⁺) bonded to three oxygen atoms (O⁻), with one double bond and two single bonds. The cadmium ion is represented as Cd²⁺.</p>
Molecular Formula	Cd.2HNO ₃
Molecular Weight	236.42

Chemical Name in the Inventory and Synonyms	Cadmium bromide, tetrahydrate Cadmium dibromide tetrahydrate
CAS Number	13464-92-1
Structural Formula	

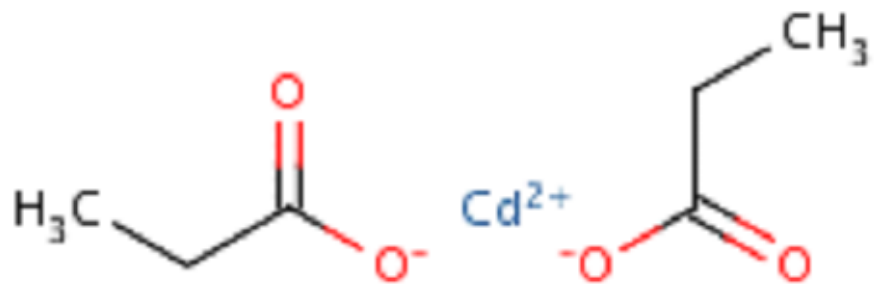
	    
Molecular Formula	Br ₂ Cd.4H ₂ O
Molecular Weight	344.28

Chemical Name in the Inventory and Synonyms	Borate(1-), tetrafluoro-, cadmium (2:1) Cadmium fluoroborate Borate(1-), tetrafluoro-, cadmium Borate(1-), tetrafluoro-, cadmium (2:1) Cadmium tetrafluoroborate Tetrafluoroborate(1-) cadmium (2:1)
CAS Number	14486-19-2
Structural Formula	



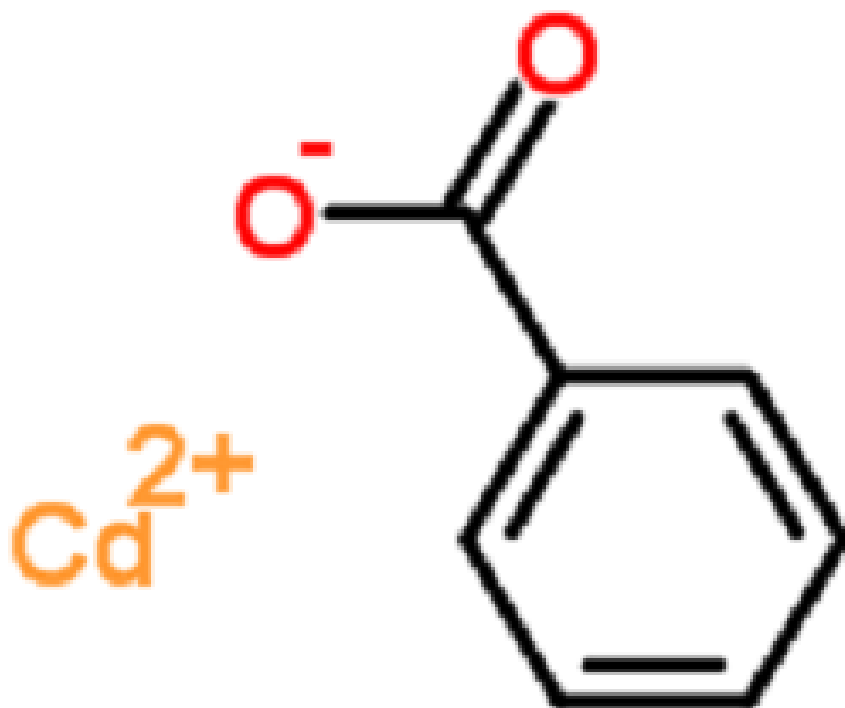
Molecular Formula	BF ₄ .1/2Cd
Molecular Weight	86.02

Chemical Name in the Inventory and Synonyms	Propanoic acid, cadmium salt Cadmium dipropionate Cadmium propionate
CAS Number	16986-83-7
Structural Formula	

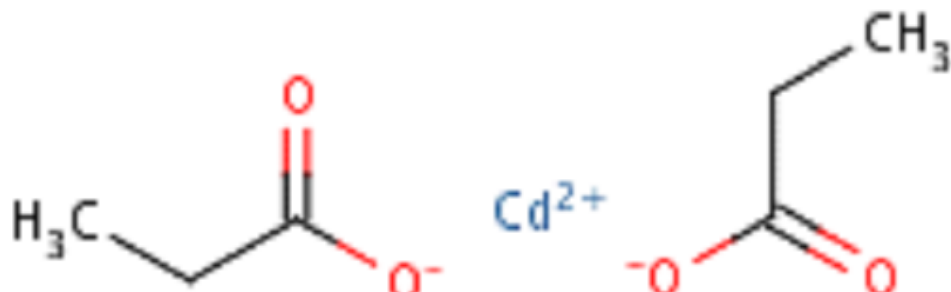


Molecular Formula	C ₃ H ₆ O ₂ .1/2Cd
Molecular Weight	258.55

Chemical Name in the Inventory and Synonyms	Benzoic acid, cadmium salt, basic Cadmium benzoate (1:1)
CAS Number	90218-85-2
Structural Formula	



Molecular Formula	Unspecified
Molecular Weight	

Chemical Name in the Inventory and Synonyms	Propanoic acid, cadmium salt, basic
CAS Number	90529-78-5
Structural Formula	 <p>The structural formula shows the propanoate ion on the left, consisting of a methyl group (H_3C) attached to a methylene group, which is then attached to a carboxylate group. The carboxylate group is shown with a central carbon atom double-bonded to one oxygen atom and single-bonded to another oxygen atom with a negative charge. To the right of the propanoate ion is the cadmium ion, Cd^{2+}, shown in blue text. Further to the right is another propanoate ion, shown with a methyl group (CH_3) attached to a methylene group, which is then attached to a carboxylate group. The carboxylate group is shown with a central carbon atom double-bonded to one oxygen atom and single-bonded to another oxygen atom with a negative charge.</p>

Molecular Formula	Unspecified
Molecular Weight	58.55

Share this page