

Cadmium and Cadmium Compounds

CAS No. 7440-43-9 (Cadmium)

No separate CAS No. assigned for cadmium compounds as a class

Known to be human carcinogens

First listed in the *First Annual Report on Carcinogens* (1980)

Also known as Cd

Carcinogenicity

Cadmium and cadmium compounds are *known to be human carcinogens* based on sufficient evidence of carcinogenicity from studies in humans, including epidemiological and mechanistic studies. Cadmium and cadmium compounds were first listed as *reasonably anticipated to be human carcinogens* in the *First Annual Report on Carcinogens* in 1980, based on sufficient evidence of carcinogenicity from studies in experimental animals. The listing was revised to *known to be human carcinogens* in the *Ninth Report on Carcinogens* in 2000.

Cancer Studies in Humans

Several epidemiological cohort studies of workers found that exposure to various cadmium compounds increased the risk of death from lung cancer (IARC 1993). Although other factors that could increase the risk of cancer, such as co-exposure to arsenic, were present in several of these studies, it is unlikely that the increased risk of lung cancer was due entirely to confounding factors. Follow-up analysis of some of these cohorts has not definitively eliminated arsenic exposure as a possibly confounding factor, but has confirmed that cadmium exposure is associated with elevated lung-cancer risk under some industrial circumstances (Sorahan *et al.* 1995, Sorahan and Lancashire 1997). Some early cohort studies found an increased risk of death from prostate cancer among cadmium-exposed workers, but later cohort studies have not confirmed this observation. Additional epidemiological evidence (including case-control studies and geographic-distribution studies) suggests an association between cadmium exposure and cancer of the prostate (Bako *et al.* 1982, Shigematsu *et al.* 1982, Garcia Sanchez *et al.* 1992, van der Gulden *et al.* 1995), kidney (Kolonel 1976, Mandel *et al.* 1995), and urinary-bladder (Siemiątycki *et al.* 1994). The International Agency for Research on Cancer reevaluated the evidence for carcinogenicity of cadmium in 2009 and reaffirmed its earlier conclusion that there was sufficient evidence of cadmium's carcinogenicity in humans. The evidence was classified as sufficient for lung cancer and limited for prostate and kidney cancer (Straif *et al.* 2009).

Studies on Mechanisms of Carcinogenesis

Many studies of cultured mammalian cells have shown that cadmium compounds cause genetic damage, including gene mutations, DNA strand breaks, chromosomal damage, cell transformation, and disrupted DNA repair. Increased frequencies of chromosomal aberrations have been observed in the lymphocytes of workers occupationally exposed to cadmium. The accumulated information, including the carcinogenicity of a wide variety of cadmium compounds, supports the conclusion that ionic cadmium is the genotoxic form of cadmium and its compounds. Therefore, the carcinogenic potential of a given cadmium compound is expected to depend on the degree to which the compound releases ionic cadmium under the conditions of exposure (IARC 1993).

The sensitivity of cells or tissues to cadmium appears to be related, at least in part, to their ability to produce metallothionein, a protec-

tive protein that binds heavy metals, including cadmium. Activation of the *MT* gene in response to cadmium exposure results in production of metallothionein, which sequesters cadmium, thus limiting its genotoxic effects. The difference between rats and mice in sensitivity to cadmium as a lung carcinogen appears to be due to differential expression of *MT* in lung tissue following inhalation exposure to cadmium. Other tissues in which cadmium causes cancer in rodents also show minimal basal expression of the *MT* gene or limited activation of *MT* in response to cadmium exposure (Oberdörster *et al.* 1994). There is no evidence to suggest that mechanisms by which cadmium causes tumors in experimental animals would not also operate in humans.

Cancer Studies in Experimental Animals

Cadmium compounds caused tumors in several species of experimental animals, at several different tissue sites, and by several different routes of exposure. Exposure to various cadmium compounds by inhalation or intratracheal instillation caused lung cancer (pulmonary adenocarcinoma) in rats; tumor incidence increased with increasing exposure level. Lung tumors were also observed occasionally in mice exposed to cadmium compounds by inhalation (IARC 1993). When administered orally to rats, cadmium chloride caused dose-related increases in the incidences of leukemia and benign testicular tumors. In several studies with rats and mice, single or multiple injections (subcutaneous, intramuscular, or intraperitoneal) of various soluble and insoluble cadmium compounds caused tumors (sarcoma) at the injection site (IARC 1993, Waalkes and Rehm 1994a). Subcutaneous injection of cadmium compounds caused tumors at various tissue sites, including prostate tumors in rats, testicular tumors in rats and mice, lymphoma in mice, adrenal-gland tumors in hamsters and mice, and lung and liver tumors in mice (IARC 1993, Waalkes *et al.* 1994, Waalkes and Rehm 1994a,b,c).

Since cadmium and cadmium compounds were listed in the *Ninth Report on Carcinogens*, additional studies in rats have been identified. Subcutaneous administration of cadmium chloride to rats caused pituitary-gland tumors (Waalkes *et al.* 1999a). In rats orally exposed to cadmium chloride, the incidence of kidney tumors increased with increasing exposure level; however, the tumor incidence was not significantly higher at the highest dose than in the unexposed control animals (Waalkes *et al.* 1999b).

Properties

Cadmium is an odorless, silver-white, blue-tinged malleable metal or grayish-white powder. It has an atomic weight of 112.4 and belongs to group IIB of the periodic table. Almost all cadmium compounds have an oxidation state of +2. Cadmium is soluble in dilute nitric acid, ammonium nitrate, and hot sulfuric acid and insoluble in water. It is slowly oxidized in moist air but forms cadmium oxide fumes when heated. Cadmium and cadmium compounds are not combustible but may decompose in fires and release corrosive and toxic fumes. Hot cadmium metal reacts with halogens, phosphorus, selenium, sulfur, and tellurium, and cadmium vapor reacts with oxygen, carbon dioxide, water vapor, sulfur dioxide, sulfur trioxide, and hydrogen chloride. Cadmium is commercially available in purities ranging from 99% to 99.9999%, as powders, foils, ingots, slabs, sticks, and crystals (IARC 1993, Llewellyn 1994, HSDB 2009).

Commercially important cadmium salts include cadmium chloride, cadmium sulfate, and cadmium nitrate. Cadmium chloride occurs as small colorless-to-white rhombohedral or hexagonal crystals. It is soluble in water and acetone, slightly soluble in methanol and ethanol, and insoluble in diethyl ether. Commercial cadmium chloride is a mixture of hydrates similar to the dihydrate form of cadmium chlo-

ride. It is available in purities ranging from 95.0% to 99.999%. Cadmium sulfate occurs as colorless to white orthorhombic crystals. It is soluble in water but insoluble in ethanol, acetone, and ammonia, and is available in purities ranging from 98% to 99.999%. Cadmium nitrate occurs as a colorless solid. It is soluble in water, ethanol, acetone, diethyl ether, and ethyl acetate, and very soluble in dilute acids. Cadmium nitrate is available in technical and reagent grades with a purity of 99% or higher (IARC 1993, HSDB 2009).

Other commercially important cadmium compounds include cadmium oxide and cadmium sulfide. Cadmium oxide occurs as a colorless amorphous powder or dark-brown crystals. It is practically insoluble in water, soluble in dilute acids and ammonium salts, and insoluble in alkalis. Commercial-grade cadmium oxide is available in purities ranging from 99% to 99.9999%. Cadmium sulfide occurs as yellow-orange hexagonal or cubic dimorphic semitransparent crystals or as a yellow-brown powder, but may be prepared to range in color from white to deep orange-red. It is practically insoluble in water, insoluble in alkalis, slightly soluble in ammonium hydroxide, and soluble in concentrated or warm dilute mineral acids, with evolution of hydrogen sulfide. Cadmium sulfide is available in purities ranging from 98% to 99.999%; however, many cadmium sulfide products are complex mixtures that contain other metal compounds (IARC 1973, 1993, HSDB 2009).

Use

Cadmium was discovered in 1817 but was not used commercially until the end of the 19th century. The earliest use of cadmium, primarily in the sulfide form, was in paint pigments. Minor amounts were used in dental amalgams in the early 1900s. During World War I, cadmium was used as a substitute for tin. Since World War II, almost all cadmium has been used in batteries, pigments, alloys, electroplating and coating, and stabilizers for plastics (IARC 1993, Llewellyn 1994). However, in the late 20th century, the percentage of cadmium consumed globally in the production of nickel-cadmium (NiCd) batteries increased, while the percentages used in other traditional end uses declined dramatically because of environmental and health concerns (Tolcin 2009b). Electroplating and coating accounted for more than half of cadmium consumption in 1960 but declined to 8% by 2000. Cadmium pigments accounted for 20% to 30% of cadmium consumption between 1970 and 1990 but declined to 12% in 2000. From 1970 to 2000, cadmium's use in stabilizers decreased from 23% to 4%, and its use in alloys from 8% to 1%. In contrast, cadmium's use in batteries grew from 8% in 1970 to 75% in 2000 (IARC 1993, Plachy 2000). In 2009, NiCd battery production was the leading end use of cadmium, followed by pigments, coatings and plating, stabilizers for plastics, nonferrous alloys, and other specialized uses (Tolcin 2009a).

Cadmium chloride is used in electroplating, photocopying, calico printing, dyeing, mirrors, analytical chemistry, vacuum tubes, and lubricants and as a chemical intermediate in production of cadmium-containing stabilizers and pigments (IARC 1993, HSDB 2009). However, its uses are declining. Cadmium chloride was used as a fungicide for golf courses and home lawn turf, but these uses were banned by the U.S. Environmental Protection Agency in the late 1980s (ATSDR 1999). Cadmium sulfate is used in electroplating, fluorescent screens, vacuum tubes, and analytical chemistry; as a chemical intermediate to produce pigments, stabilizers, and other cadmium compounds; as a fungicide or nematocide; and as an electrolyte in Weston cells (portable voltage standards). Cadmium nitrate is used in photographic emulsions, to color glass and porcelain, in nuclear reactors, and to produce cadmium hydroxide for use in alkaline batteries (IARC 1993, HSDB 2009).

Cadmium sulfide is used primarily in pigments for paints, glass, ceramics, plastics, textiles, paper, and fireworks. It is also used in solar cells, fluorescent screens, radiation detectors, smoke detectors, electron-beam-pumped lasers, thin-film transistors and diodes, phosphors, and photomultipliers. Cadmium oxide is used primarily in NiCd batteries, but also as a catalyst and in electroplating, electrical contacts, resistant enamels, heat-resistant plastics, and manufacture of plastics (such as Teflon) and nitrile rubbers. Cadmium oxide has been used as a nematocide and ascaricide in swine (IARC 1993, HSDB 2009).

Production

Cadmium is a rare element, not found in its pure state in nature. It occurs mainly as cadmium sulfide (CdS, or greenockite) in zinc deposits. Cadmium is chiefly recovered as a by-product of zinc concentrates, and its production depends on the demand for zinc (Llewellyn 1994). The United States began commercial production of cadmium in 1907 and was the world's leading producer from 1917 to the late 1960s. U.S. cadmium production peaked in 1969, at 5,740 metric tons (12.7 million pounds) (USGS 2009). Average annual production levels fell to 2,758 metric tons (6 million pounds) for the 1970s, 1,498 metric tons (3.3 million pounds) for the 1980s, 1,437 metric tons (3.2 million pounds) for the 1990s, and 1,196 metric tons (2.6 million pounds) for the 2000s (Tolcin 2009a, USGS 2009). In 2009, the United States and India each produced 700 metric tons (1.54 million pounds) of cadmium, tying them as the ninth-largest producers of cadmium globally (Tolcin 2009a). U.S. production accounted for almost 4% of 2009 world cadmium production. U.S. production of cadmium compounds was 670 metric tons (1.5 million pounds) in 1999, 460 metric tons (1 million pounds) in 2000, 31 metric tons (68,000 lb) in 2001, and 33 metric tons (73,000 lb) in 2002 (Plachy 2000, 2002). No more recent data on production of cadmium compounds were found.

Eight U.S. companies were identified as major producers of cadmium compounds in the 1990s (ATSDR 1999). Only three U.S. companies were reported to have produced refined cadmium in 2009 (Tolcin 2009a). One company recovered cadmium as a by-product of zinc leaching from roasted sulfide concentrates, and the other two companies thermally recovered cadmium metal from spent NiCd batteries and other cadmium-bearing scrap. In 2010, 15 U.S. suppliers of cadmium metal, 13 suppliers of cadmium metal powder, and numerous suppliers of various cadmium compounds were identified (ChemSources 2010).

U.S. imports of cadmium fell over the late 20th century and early 2000s. Annual cadmium imports averaged 694 metric tons (1.5 million pounds) in the 1960s, 2,088 metric tons (4.6 million pounds) in the 1970s, 2,524 metric tons (5.6 million pounds) in the 1980s, 1,156 metric tons (2.5 million pounds) in the 1990s, and 216 metric tons (476,000 lb) in the 2000s. For 2009, U.S. imports of cadmium were estimated to be 194 metric tons (428,000 pounds). Annual U.S. exports averaged 425 metric tons (937,000 lb) in the 1960s, 188 metric tons (414,000 lb) in the 1970s, 211 metric tons (465,000 lb) in the 1980s, 454 metric tons (1 million pounds) in the 1990s, and 425 metric tons (937,000 lb) in the 2000s. For 2009, U.S. exports were estimated to be 676 metric tons (1.5 million pounds) (Tolcin 2009a, USGS 2009).

Exposure

The general population may be exposed to cadmium through consumption of food and drinking water, inhalation of cadmium-containing particles from ambient air or cigarette smoke, or ingestion of contaminated soil and dust. Tobacco smokers are exposed to an estimated 1.7 μg of cadmium per cigarette. Food is the major source

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of cadmium exposure for nonsmokers; average cadmium levels in the U.S. food supply range from 2 to 40 ppb. The daily adult intake of cadmium is estimated to be approximately 30 µg, with the largest contribution from grain cereal products, potatoes, and other vegetables. Exposures through drinking water or ambient air typically are very low (ATSDR 1999).

The U.S. Environmental Protection Agency's Toxics Release Inventory (TRI) collects cadmium data in two categories, "cadmium" and "cadmium compounds," and individual facilities may report releases in both categories. From 1988 to 1997, reported releases of cadmium to the environment ranged from about 106,000 to 635,000 lb and releases of cadmium compounds from about 825,000 to 4.1 million pounds. Since 1998 (when the number of industries covered by the TRI was increased), cadmium releases have ranged from a low of about 740,000 lb in 2000 to a high of about 2.8 million pounds in 1998. In 2007, 34 facilities reported releasing about 940,000 lb of cadmium, most of which was released to land on site. Reported releases of cadmium compounds since 1998 have ranged from a low of nearly 8.9 million pounds in 2000 to 3.15 million pounds in 2007, reported by 73 facilities, most of which was released to land on site (TRI 2009).

Workers in a wide variety of occupations potentially are exposed to cadmium and cadmium compounds (IARC 1993). Occupations with the highest potential levels of exposure include smelting zinc and lead ores, welding or remelting cadmium-coated steel, working with solders that contain cadmium, and producing, processing, and handling cadmium powders. The major routes of occupational exposure are inhalation of dust and fumes and incidental ingestion of dust from contaminated hands, cigarettes, or food (ATSDR 1999). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that about 250,000 workers potentially were exposed to cadmium and selected inorganic cadmium compounds. These included workers potentially exposed to unknown cadmium compounds (88,968), cadmium sulfide (42,562), cadmium mercury sulfide (19,707), cadmium selenide (17,939), cadmium oxide (15,727), cadmium chloride (4,748), cadmium nitrate (1,878), and cadmium sulfate (1,313) (NIOSH 1990). The Occupational Safety and Health Administration estimated in 1990 that about 512,000 U.S. workers were exposed to cadmium; however, 70% to over 80% were exposed to cadmium at concentrations below the limits set by occupational standards or guidelines (ATSDR 1999).

Regulations

Department of Transportation (DOT)

Cadmium is considered a hazardous material, and cadmium compounds are considered both hazardous materials and marine pollutants, and requirements have been set for marking, labeling, and transporting these materials.

Environmental Protection Agency (EPA)

Clean Air Act

National Emissions Standards for Hazardous Air Pollutants: Cadmium compounds are listed as a hazardous air pollutant.

New Source Performance Standards: Regulations have been developed to limit cadmium emissions from new municipal waste combustion units.

Urban Air Toxics Strategy: Cadmium compounds have been identified as one of 33 hazardous air pollutants that present the greatest threat to public health in urban areas.

Clean Water Act

Cadmium acetate, cadmium bromide, and cadmium chloride are designated as hazardous substances. Limits have been established for cadmium in biosolids (sewage sludge) when used or disposed of via land application or incineration.

Effluent Guidelines: Cadmium and cadmium compounds are listed as toxic pollutants.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 10 lb for cadmium, cadmium acetate, cadmium bromide, cadmium chloride.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Cadmium and cadmium compounds are listed substances subject to reporting requirements.

Reportable quantity (RQ) = 100 lb for cadmium oxide; = 1,000 lb for cadmium stearate.

Threshold planning quantity (TPQ) = 100 lb for cadmium oxide solids in powder form particle size < 100 µm or solution or molten form; = 1,000 lb for cadmium stearate in powder form particle size < 100 µm or solution or molten form; = 10,000 lb for cadmium oxide and cadmium stearate in all other forms.

Federal Insecticide, Fungicide, and Rodenticide Act

All registrations for cadmium chloride have been cancelled.

Resource Conservation and Recovery Act

Characteristic Hazardous Waste: Toxicity characteristic leaching procedure (TCLP) threshold = 1.0 mg/L for cadmium.

Listed Hazardous Waste: Waste codes for which the listing is based wholly or partly on the presence of cadmium = F006, K061, K064, K069, K100.

Cadmium and cadmium compounds are listed as hazardous constituents of waste.

Safe Drinking Water Act

Maximum contaminant level (MCL) = 0.005 mg/L (cadmium).

Food and Drug Administration (FDA)

Maximum permissible level of cadmium in bottled water = 0.005 mg/L.

Various specified color additives may contain cadmium at levels no greater than 15 ppm.

Specified food additives may contain cadmium at maximum levels that range from 0.05 to 0.13 ppm.

Action levels for cadmium in pottery (ceramics) range from 0.25 to 0.5 µg/mL leaching solution.

Occupational Safety and Health Administration (OSHA)

While this section accurately identifies OSHA's legally enforceable PELs for this substance in 2010,

specific PELs may not reflect the more current studies and may not adequately protect workers.

Ceiling concentration = 0.3 mg/m³ for cadmium fume; = 0.6 mg/m³ for cadmium dust.

Permissible exposure limit (PEL) = 0.005 mg/m³ for cadmium dust and fume.

Comprehensive standards for occupational exposure to cadmium and cadmium compounds have been developed.

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted average (TLV-TWA) = 0.01 mg/m³; = 0.002 mg/m³ for respirable fraction.

National Institute for Occupational Safety and Health (NIOSH)

Immediately dangerous to life and health (IDLH) limit = 9 mg/m³ for cadmium dust and fume.

Cadmium dust and fume are listed as potential occupational carcinogens.

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Report on Carcinogens, Twelfth Edition (2011)

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