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Report on Carcinogens

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U.S. Department of Health and Human Services
Public Health Service
National Toxicology Program

Pursuant to Section 301 (b) (4) of the Public Health
Service Act as amended by Section 262, PL 95-622

Beryllium and Beryllium Compounds

CAS No. 7440-41-7 (Beryllium)

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

Known to be human carcinogens

First listed in the *Second Annual Report on Carcinogens* (1981)

Also known as Be

Carcinogenicity

Beryllium and beryllium compounds are *known to be human carcinogens* based on sufficient evidence of carcinogenicity from studies in humans. Beryllium and beryllium compounds were first listed in the *Second Annual Report on Carcinogens* as *reasonably anticipated to be human carcinogens* based on sufficient evidence of carcinogenicity from studies in experimental animals. The listing was revised to *known to be human carcinogens* in the *Tenth Report on Carcinogens* in 2002.

Cancer Studies in Humans

Epidemiological studies indicate an increased risk of lung cancer in occupational groups exposed to beryllium or beryllium compounds (Steenland and Ward 1991, Ward *et al.* 1992), supporting the conclusion that beryllium and beryllium compounds are carcinogenic in humans. An association with lung cancer has consistently been observed in several occupational populations exposed to beryllium or beryllium compounds, with a relative risk of 1.2 to 1.6. Groups with greater exposure or longer time since first exposure show higher risks, which supports a cause-and-effect relationship. Acute beryllium pneumonitis, which is a marker for high exposure to beryllium, is associated with higher lung-cancer rates (with a relative risk as high as 2.3) (Steenland and Ward 1991). Although smoking could be a factor in the cancers observed in these studies, no evidence was found in any of the published epidemiological studies to indicate a difference in smoking habits between the groups of workers exposed to beryllium or beryllium compounds and the non-exposed workers in the control groups.

Cancer Studies in Experimental Animals

Beryllium and/or beryllium compounds caused tumors in several species of experimental animals, at two different tissue sites, and by several different routes of exposure. Beryllium metal and several beryllium compounds, including beryllium-aluminum alloy, beryl ore, beryllium chloride, beryllium hydroxide, beryllium sulfate tetrahydrate, and beryllium oxide, caused lung tumors in rats exposed by either inhalation for one hour or a single intratracheal instillation. Inhalation exposure to beryllium metal also caused lung tumors in *p53*^{+/-} transgenic mice (a strain with increased susceptibility to carcinogen-induced cancer). In rhesus monkeys, lung cancer was observed following inhalation exposure to beryllium sulfate (anaplastic carcinoma) or intrabronchial implantation of beryllium oxide. Bone cancer (osteosarcoma) was observed in rabbits exposed to beryllium metal, beryllium carbonate, beryllium oxide, beryllium phosphate, beryllium silicate, or zinc beryllium silicate by intravenous injection or implantation into the bone (IARC 1993, Finch *et al.* 1996, 1998)

Studies on Mechanisms of Carcinogenesis

Beryllium compounds did not cause mutations in *Salmonella typhimurium*, but they did cause genetic damage in various cultured rodent cells (IARC 1993). The genotoxic effects of beryllium compounds

may result from binding of ionic beryllium to nucleic acids, which can cause infidelity of DNA replication (Leonard and Lauwerys 1987).

Properties

Beryllium is a silver-gray to grayish-white group II metallic element with an atomic weight of 9.01, melting point of 1,287°C, boiling point of 2,970°C, and density of 1.85 at 20°C. It has a close-packed hexagonal crystal structure and has several unique chemical properties. It is the lightest of all solid and chemically stable substances and has a very high melting point, specific heat, heat of fusion, and strength-to-weight ratio. Beryllium is lighter than aluminum, but it is over 40% more rigid and approximately one-third more elastic than steel. It is insoluble in water but soluble in acids and alkalis. It has excellent electrical and thermal conductivity and is not magnetic. At ordinary temperatures, beryllium resists oxidation in air; however, a thin film of beryllium oxide forms on the surface, making it highly resistant to corrosion. In alloys, beryllium contributes hardness, strength, and high electrical and thermal conductivity and enhances resistance to corrosion, wear, and fatigue (IPCS 1990, IARC 1993, HSDB 2009).

Beryllium chloride occurs as white-to-colorless deliquescent crystals. It is highly soluble in water, alcohol, benzene, ether, chloroform, and carbon disulfide, and insoluble in ammonia and acetone. Beryllium fluoride occurs as a colorless amorphous mass that is readily soluble in water but only slightly soluble in alcohol. Beryllium hydroxide exists in three forms: a metastable tetragonal crystalline solid, a stable orthorhombic crystalline solid, and a slimy, gelatinous substance with a slightly basic pH. It is insoluble in water but soluble in acids and alkalis. Beryllium oxide occurs as a white powder or gel that is insoluble in hot water and soluble in acids, alkalis, and ammonium carbonate. Beryllium metaphosphate is a white porous powder or granular material that is insoluble in water. Beryllium orthophosphate is soluble in water and acetic acid. Beryllium sulfate occurs as colorless crystals; it is insoluble in cold water and alcohol but decomposes in hot water. Beryllium sulfate tetrahydrate occurs as colorless crystals that are soluble in water, practically insoluble in ethanol, and slightly soluble in concentrated sulfuric acid (IARC 1993, ATSDR 2002).

Beryl ore occurs as colorless, blue-green, yellow, or white transparent hexagonal crystals that are insoluble in acid. Beryllium-copper alloy usually contains 4.0% to 4.25% beryllium by weight. It has a melting point of 870°C to 980°C and produces toxic fumes of beryllium oxide upon heating. Beryllium-aluminum alloy may contain 20% to 60% beryllium (IARC 1993, ATSDR 2002).

Use

Beryllium's unique properties (as a light metal with a very high melting point) make it very useful in industry. In alloys, it increases thermal and electrical conductivity and strength; addition of just 2% beryllium to copper forms alloys that are six times stronger than copper alone (IARC 1993). A 2010 U.S. Geological Survey Mineral Commodities Survey reported that based on sales revenues, nearly half of beryllium use was in computer and telecommunications products, and the remainder was in aerospace and defense applications, appliances, automotive electronics, industrial components, and other applications (Jaskula 2010).

Pure beryllium metal is used in aircraft disc brakes, X-ray transmission windows, space vehicle optics and instruments, aircraft and satellite structures, missile parts, nuclear reactor neutron reflectors, nuclear weapons, fuel containers, precision instruments, rocket propellants, navigational systems, heat shields, mirrors, high-speed computers, and audio components. Beryllium alloyed with copper, aluminum, or other metals is used in the electronics, automotive, defense, and aerospace industries. More specifically, beryllium alloys

are used in electrical connectors and relays, springs, precision instruments, aircraft engine parts, nonsparking tools, submarine cable housings and pivots, wheels, pinions, automotive electronics, molds for injection-molded plastics, telecommunications devices, computers, home appliances, dental applications, golf clubs, bicycle frames, and many other applications (IPCS 1990, IARC 1993, ATSDR 2002, HSS 2009). Beryllium-copper alloy is used in a wide variety of applications, including electrical connectors and relays, wheels and pinions, nonsparking tools, and switches in automobiles (ATSDR 2002). Beryllium-aluminum alloy has been used in light aircraft construction (Merian 1984). It also may be used in casting alloys, where it refines the grain size, resulting in better surface polishing, reduces melt losses, and improves casting fluidity (IARC 1980, Kaczynski 2002).

Beryllium oxide is the most important high-purity commercial beryllium chemical produced (Kaczynski 2000). It is used in high-technology ceramics, electronic heat sinks, electrical insulators, microwave oven components, gyroscopes, military vehicle armor, rocket nozzles, crucibles, nuclear reactor fuels, thermocouple tubing, laser structural components, substrates for high-density electrical circuits, and automotive ignition systems, and as an additive to glass, ceramics, and plastics (IARC 1993, ATSDR 2002). Beryllium oxide also is used in the preparation of beryllium compounds, as a catalyst for organic reactions, and in high-temperature reactor systems. Beryllium oxide was used in the past in the manufacture of phosphors for fluorescent lamps.

Beryllium chloride is used primarily to manufacture beryllium metal by electrolysis in the laboratory. It also is used as an acid catalyst in organic reactions. Beryllium fluoride and beryllium hydroxide are used commercially in the production of beryllium metal and beryllium alloys, and beryllium fluoride is used in the manufacture of glass and nuclear reactors (Sax and Lewis 1987). Beryllium sulfate is used primarily for the production of beryllium oxide powder for ceramics, and beryllium nitrate is used as a chemical reagent and for stiffening mantles in gas and acetylene lamps (HSDB 2009). The primary use of beryllium sulfate tetrahydrate is as a chemical intermediate in the processing of beryl and bertrandite ores (Sax and Lewis 1987). Beryllium metaphosphate has limited use as a raw material in special ceramic compositions and as a catalyst carrier. Beryllium zinc sulfate was formerly used as an oxygen-dominated phosphor in luminescent materials (IARC 1980, Sax and Lewis 1987).

Production

Beryllium was discovered in 1798, but it did not become commercially important until the 1930s. Although more than 40 beryllium-bearing minerals are known, only two (beryl and bertrandite) currently are commercially important. Beryl ($3\text{BeO}\cdot\text{Al}_2\text{O}_3\cdot 6\text{SiO}_2$), which contains approximately 11% beryllium oxide (up to 4% beryllium), is the predominant beryllium-containing mineral mined. Beryl is found largely in Brazil and the former Soviet Union. Impurities in beryl include alkali metals, alkaline-earth metals, iron, manganese, and phosphorus. Emeralds (beryl containing chromium), aquamarine (beryl containing iron), and other semiprecious gems are examples of beryl at its purest gem quality (IARC 1993, Jaskula 2009).

U.S. companies have produced beryllium and some beryllium compounds commercially since the 1940s and beryllium oxide since 1958 (IARC 1972). Bertrandite ($4\text{BeO}\cdot 2\text{SiO}_2\cdot \text{H}_2\text{O}$) is the principal beryllium-containing mineral mined in the United States; it contains less than 1% beryllium, but it can be efficiently processed into beryllium hydroxide (IARC 1993). The Topaz-Spor Mountain area of Utah is currently being mined for beryllium; it contains a large reserve of bertrandite, totaling about 15,800 metric tons (35 million pounds) of beryllium (Jaskula 2009). The United States is the world's largest

producer of beryllium, accounting for roughly 86% of world production in 2009; total U.S. production was 120 metric tons (265,000 lb), down from 176 metric tons (388,000 lb) in 2008. Other countries producing beryllium (in order of amount produced in 2007) are China, Mozambique, Portugal, Madagascar, and Brazil (Jaskula 2009, 2010).

In 2009, U.S. beryllium consumption, imports, exports, and government stockpile releases were considerably lower than in each of the previous four years (Jaskula 2010). Consumption was 140 metric tons (309,000 lb), down from 220 metric tons (485,000 lb) in 2008; imports for production were 20 metric tons (44,000 lb), down from 70 metric tons (154,000 lb); exports were 30 metric tons (66,000 lb), down from 112 metric tons (247,000 lb); and government stockpile releases were 11 metric tons (24,000 lb), down from 39 metric tons (86,000 lb). In 2009, one U.S. producer of beryllium oxide and one U.S. producer of beryllium sulfate were identified, but no U.S. producers of beryllium nitrate (SRI 2009). U.S. suppliers identified in 2009 included 2 for beryllium, 16 for beryllium oxide, 1 for beryllium hydroxide, 4 for beryllium sulfate, 9 for beryllium sulfate tetrahydrate, 4 for beryllium chloride, 5 for beryllium fluoride, and 2 for beryllium copper alloy (ChemSources 2009).

Natural sources of beryllium and beryllium compounds in the atmosphere (annual amounts) are windblown dust (5 metric tons, or 11,000 lb) and volcanic particles (0.2 metric tons, or 441 lb). Anthropogenic sources include electric utilities (3.5 metric tons, or 7,716 lb), industry (0.6 metric tons, or 1,323 lb), metal mining (0.2 metric tons, or 441 lb), and waste and solvent recovery (0.007 metric tons, or 15 lb) (ATSDR 2002).

Exposure

The primary route of human exposure to beryllium is through inhalation of dusts and fumes (ATSDR 2002). Beryllium may also be ingested in drinking water or food. Beryllium was measured in fruit and fruit juices at concentrations ranging from less than 0.1 $\mu\text{g}/\text{L}$ in a pineapple to 74.9 $\mu\text{g}/\text{L}$ in a papaya. Cigarettes contain beryllium at concentrations of up to 0.0005 μg per cigarette. According to the U.S. Environmental Protection Agency's Toxics Release Inventory, 2007 environmental releases totaled 14,185 lb of beryllium from 12 facilities and 862,894 lb of beryllium compounds from 61 facilities (TRI 2009). In measurements at 100 U.S. locations, the average daily beryllium concentration in air was less than 0.0005 $\mu\text{g}/\text{m}^3$. Beryllium was detected at 2,760 of 50,000 U.S. surface-water sites, at an average concentration of 1.9 $\mu\text{g}/\text{L}$, and at 30 of 334 groundwater sites, at an average concentration of 1.7 $\mu\text{g}/\text{L}$. Beryllium occurs naturally in soils at concentrations ranging from less than 1 to 15 mg/kg. The average daily inhalation exposure to beryllium for a U.S. adult was estimated at less than 0.0006 μg , and the average daily exposure from food was estimated at 0.12 μg (ATSDR 2002).

The highest levels of human exposure to beryllium are through occupational exposure, which may occur through inhalation of beryllium dust or dermal contact with products containing beryllium. Workers with the highest potential for exposure include beryllium miners, beryllium alloy makers and fabricators, phosphorus manufacturers, ceramics workers, missile technicians, nuclear reactor workers, electric and electronic equipment workers, and jewelers. Occupational exposure may also lead to at-home exposure to beryllium on work garments. In studies in the workplace, air concentrations from personal monitors mounted on clothing increased when the amount of beryllium dust on the fabric increased (HSDB 2009). The National Occupational Hazard Survey (conducted from 1972 to 1974) estimated that 10,510 workers potentially were exposed to beryllium (NIOSH 1976). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 13,938,000 workers,

Report on Carcinogens, Thirteenth Edition

including 739 women, potentially were exposed to beryllium; 4,305 workers, including 849 women, to beryllium oxide; 1,822 workers, including 230 women, to beryllium sulfate tetrahydrate; and 1,740 workers, including 37 women, to beryllium-copper alloy (NIOSH 1990).

Regulations

Department of Energy (DOE)

DOE has established the Chronic Beryllium Disease Prevention Program to protect workers from excessive beryllium exposure and beryllium disease.

Department of Transportation (DOT)

Numerous beryllium compounds and beryllium compounds not otherwise specified are considered hazardous materials, and special requirements have been set for marking, labeling, and transporting these materials.

Environmental Protection Agency (EPA)

Clean Air Act

National Emission Standards for Hazardous Air Pollutants: Beryllium compounds are listed as hazardous air pollutants.

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

Clean Water Act

Effluent Guidelines: Beryllium and beryllium compounds are listed as a toxic pollutants. Limits have been established for beryllium in biosolids (sewage sludge) when disposed of via incineration.

Beryllium chloride, beryllium fluoride, and beryllium nitrate are designated as hazardous substances.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 10 lb for beryllium; = 1 lb for beryllium chloride, beryllium fluoride, beryllium nitrate.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Beryllium and beryllium compounds are listed substances subject to reporting requirements.

Resource Conservation and Recovery Act

Listed Hazardous Waste: Waste code for which the listing is based wholly or partly on the presence of beryllium powder = P015.

Beryllium powder and beryllium compounds are listed as hazardous constituents of waste.

Safe Drinking Water Act

Maximum contaminant level (MCL) = 0.004 mg/L for beryllium.

Food and Drug Administration (FDA)

Maximum permissible level of beryllium in bottled water = 0.004 mg/L.

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. Acceptable peak exposure = 0.025 mg/m³ (30-min maximum duration per 8-h shift) for beryllium and beryllium compounds (as Be).

Ceiling concentration = 0.005 mg/m³ for beryllium and beryllium compounds (as Be).

Permissible exposure limit (PEL) = 0.002 mg/m³ for beryllium and beryllium compounds (as Be).

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted average (TLV-TWA) = 0.00005 mg/m³ for beryllium and beryllium compounds (as Be).

Potential for dermal absorption.

National Institute for Occupational Safety and Health (NIOSH)

Immediately dangerous to life and health (IDLH) limit = 4 mg/m³ for beryllium and beryllium compounds (as Be).

Beryllium and beryllium compounds are listed as potential occupational carcinogens.

Ceiling recommended exposure limit = 0.0005 mg/m³ for beryllium and beryllium compounds (as Be).

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