BERYLLIUM AND BERYLLIUM COMPOUNDS

First Listed in the *Second Annual Report* on Carcinogens as *Reasonably Anticipated to be Human Carcinogens* changed to *Known to be Human Carcinogens* in the *Tenth Report on Carcinogens*

CARCINOGENICITY

Beryllium and beryllium compounds are *known to be human carcinogens* based on sufficient evidence of carcinogenicity 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 an excess 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 relative risks 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 epidemiology studies to indicate a difference in smoking habits between the groups of workers exposed to beryllium or beryllium compounds and the non-exposed workers used as control groups.

These conclusions are supported by data from animal studies (IARC 1994, Finch *et al*. 1996), which have shown consistent increases in lung cancer in rats, mice, and monkeys exposed to beryllium or beryllium compounds (by inhalation or intratracheal instillation). Beryllium metal, beryllium-aluminum alloy, beryl ore, beryllium chloride, beryllium fluoride, beryllium hydroxide, beryllium sulfate (and its tetrahydrate), and beryllium oxide all induce lung tumors in rats exposed by either a single intratracheal instillation or a one-hour inhalation exposure. Beryllium oxide and beryllium sulfate induce lung cancer (anaplastic carcinoma) in monkeys after intrabronchial implantation or inhalation. Osteosarcoma has been induced in rabbits exposed to beryllium metal, beryllium carbonate, beryllium oxide, beryllium phosphate, beryllium silicate, or zinc beryllium silicate by intravenous injection and/or implantation into the bone.

OTHER INFORMATION RELATING TO CARCINOGENESIS OR POSSIBLE MECHANISMS OF CARCINOGENESIS

Beryllium compounds do not cause mutations in a variety of *Salmonella typhimurium* tester strains, but they do induce genetic transformations in a variety of cultured mammalian cells (IARC 1994). These genetic transformations 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 brittle metal with a close-packed hexagonal crystal structure that 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 and soluble in acids and alkalies. 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 (WHO 1990, IARC 1994, HSDB 2000a).

Beryllium chloride occurs as white-to-colorless deliquescent crystals. It is very soluble in cold and hot water, soluble in 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 in a slightly basic pH. It is soluble in acids and alkalies and insoluble in water. Beryllium oxide occurs as a white powder or gel that is insoluble in cold and hot water and soluble in acids, alkalies, and ammonium carbonate. Beryllium metaphosphate is a white porous powder or granular material that is insoluble in water. Beryllium orthophosphate is soluble in cold and hot water and acetic acid. Beryllium sulfate occurs as colorless crystals that are insoluble in cold water and alcohol, but decompose 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. Beryl ore is a colorless, blue-green, yellow, or white transparent hexagonal crystal that is insoluble in acid (IARC 1994, Chemfinder 1998).

Beryllium metal is available in the United States as a technical grade with over 99.5% purity, as a commercial grade with 97% minimum purity, and as an electro-refined metal in various grades. Beryllium chloride and beryllium fluoride are available with 11.2% and 19.0% beryllium content, respectively. Both contain various metallic impurities. Beryllium-aluminum alloy is available as a grade containing 62% beryllium and 38% aluminum. Beryllium hydroxide is available with varying percentages of beryllium content and metallic impurities, depending on the source of ore (beryl-derived or bertrandite-derived). Beryllium oxide is available as technical grade, chemically pure, pure, and ceramic grade and as single crystals. Commercial-grade beryllium oxide available in the United States has an approximate purity of 99.5%. Beryllium sulfate crystals are available with a minimum of 20% beryllium. Beryllium sulfate tetrahydrate is produced commercially in a highly purified state. Beryl ore is available in commercial grades containing 70% to 90% beryl, including 10% to 13% beryllium oxide (IARC 1994).

USE

Beryllium is an extremely light metal with a very high melting point. Because of its unique properties, beryllium has many practical uses in industry. When used in alloys, it increases thermal and electrical conductivity and strength (WHO 1990). Addition of just 2% beryllium to copper forms alloys that are six times stronger than copper alone (IARC 1994). Beryllium alloys find limited use in industry because they are difficult to make or very brittle, because of the low solubility of most other metals in solid beryllium (WHO 1990).

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 (WHO 1990, IARC 1994, ATSDR 2000).

Beryllium alloyed with copper, aluminum, or other metals is used in the electronics, automotive, defense, and aerospace industries. Beryllium alloys are used in electrical connectors and relays, springs, precision instruments, aircraft engine parts, non-sparking 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 (WHO 1990, IARC 1994, USDOE 1998, ATSDR 2000).

Beryllium oxide is the most important high-purity commercial beryllium chemical produced (Kirk-Othmer 1978). It is used in high-technology ceramics, electronic heat sinks, electrical insulators, microwave oven components, gyroscopes, military vehicle armor, rocket nozzle 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 1994, ATSDR 2000). 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 for the manufacture of phosphors for fluorescent lamps.

Beryl ore is processed to make beryllium and its compounds. Industry is increasing the use of beryllium in fiber optics and cellular network communication systems (USDOI 1990). Because it is expensive, applications will be limited to those that require light weight, high strength, and high thermal conductivity. In 1989, an estimated 23% of beryllium was used as alloy and metal in aerospace and defense applications, 17% as alloy and oxide in electrical equipment, 35% as alloy and oxide in electronic components, and 25% as alloy, metal, and oxide in other applications (USDOI 1990). In 1987, 22% of the beryllium produced was used as alloy and metal in aerospace and defense applications, 36% as alloy and oxide in electrical equipment, 20% as alloy and oxide in electronic components, and 22% as metal, alloy, and compounds in other applications (USDOI 1988). Beryllium–aluminum alloy is not known to be produced for commercial use (IARC 1980). It has been used in light aircraft construction (Merian 1984). It also has potential use in casting alloys, where it refines the grain size, resulting in better surface polishing, reduces melt losses, and improves casting fluidity (Kirk-Othmer 1978, IARC 1980). 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. Beryllium fluoride also is used in the manufacture of glass and nuclear reactors (Sax 1987). Beryllium metaphosphate has limited use as a raw material in special ceramic compositions and as a catalyst carrier. The primary use of beryllium sulfate tetrahydrate is as a chemical intermediate in the processing of beryl and bertrandite ores (Sax 1987). A former use of beryllium zinc sulfate was as an oxygen-dominated phosphor in luminescent materials (IARC 1980, Sax 1987).

PRODUCTION

Beryllium was discovered in 1798, but it did not become commercially important until the 1930s. Demand fluctuates with changes in government defense programs, nuclear energy demand, and the aerospace industry (IARC 1994). Only one U.S. company produces and processes beryllium and beryllium ores (ATSDR 2000).

Although more than 40 beryllium-bearing minerals are known, only two (beryl and bertrandite) currently are commercially important. Beryl ($3BeO{\cdot}Al_2O_3{\cdot}6SiO_2$), which contains approximately 11% beryllium oxide (up to 4% beryllium), is the predominant beryllium-containing mineral mined in the world. 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 1994).

Bertrandite ($4BeO{\cdot}2SiO_2{\cdot}H_2O$) is the principal beryllium-containing mineral mined in the United States, accounting for approximately 85% of U.S. consumption. Bertrandite contains less than 1% beryllium, but it can be efficiently processed into beryllium hydroxide (IARC 1994).

The United States is the world's largest producer of beryllium raw materials (WHO 1990). Annual U.S. production of beryllium minerals (reported as beryl equivalents) ranged from approximately 4,300 to more than 6,700 metric tons between 1980 and 1991 (IARC 1994). Beryllium content of U.S. production ranged from 173 to 255 metric tons between 1991 and 2000 (USGS 2001).

In 1987, two U.S. companies produced beryllium alloys and beryllium oxide (U.S. DOI 1988). In 1985, approximately 3.3 million lb of beryllium ore, less than 2,532 lb of beryllium oxide, and 7,332 lb of unspecified beryllium compounds were imported (USDOC 1986). In 1984, the United States imported 2.7 million lb of beryllium ore, less than 179 lb of beryllium oxide and 43,059 lb of unspecified beryllium compounds (USDOC 1985). The 1979 Toxic Substances Control Act Inventory reported that in 1977, three companies produced 605,000 lb of beryllium oxide, and one company imported 500 lb; two companies produced 550,000 lb of beryllium sulfate, with some site limitations; and one company produced 5.5 million lb of beryl ore. No data were reported for beryllium phosphate or beryllium zinc sulfate (TSCA 1979). U.S. companies have produced beryllium and some beryllium compounds commercially since the 1940s and beryllium oxide since 1958 (IARC 1972).

EXPOSURE

The primary route of human exposure to beryllium is inhalation of dusts and fumes. Over time, beryllium slowly enters the bloodstream and is eventually excreted by the kidneys. It takes months or years for the body to remove inhaled beryllium. Beryllium may also be ingested in drinking water or contaminated foodstuffs, but only 1% of ingested beryllium enters the bloodstream, so this is not considered an important mode of exposure. Beryllium also is inhaled and ingested from cigarette smoke and can enter the body through cuts in the skin (ATSDR 2000).

The entire U.S. population is exposed to small amounts of beryllium by consuming contaminated food or water or inhaling dust or fumes. The U.S. Environmental Protection Agency (EPA) have estimated the daily beryllium intake from background environmental exposure to be 420 ng for the general population. EPA has estimated the total annual release of beryllium to the atmosphere from point sources to be 5,500 lb, principally from beryllium–copper alloy production. EPA's Toxic Chemical Release Inventory estimated that the nine facilities that produced, processed, or used beryllium or beryllium compounds in the United States released a total of 48,714 lb of beryllium and beryllium compounds to the environment in 1996. Of that total, 97.4% was released to land, less than 1% (32 lb) to water, and 2.6% (1,254 lb) to air. A facility in Elmore, Ohio, reporting under industrial classifications for manufacture of primary nonferrous metals (Standard Industry Classification [SIC] code 3339) and copper rolling and drawing (SIC 3351), released more than 10,000 lb of the substances, accounting for 57.6% of the release (TRI96 1998). In 1999, 74,178 lb of beryllium was released from all U.S. industries, approximately 72% to land (TRI99 2001). Approximately 721,000 persons living within 12.5 miles of point sources potentially are exposed to small amounts of beryllium (median concentration, 0.005 $\mu g/m^3$) (Merian 1984). In the eastern United States, urban atmospheric concentrations of beryllium have been measured at 0.3 to 3.0 ng/m^3. Concentrations measured in rural areas were one-twelfth those in urban areas. Beryllium occurs naturally in rocks and minerals at concentrations ranging from 0.038 to 11.4 mg/kg. The beryllium content of mineral oils has been estimated to be less than 100 µg/L. People who work in beryllium manufacturing, fabricating, and reclaiming industries are exposed to higher levels of beryllium than is the general public. Smokers also may be exposed to higher levels of beryllium, because cigarette smoke contains beryllium (ATSDR 2000). Beryllium was found in three brands of German cigarettes (0.47, 0.68, and 0.74 µg/cigarette) (WHO 1990). An estimated 4.5% to 10% of the beryllium in a cigarette passes to the smoker in the tobacco smoke (HSDB 2000b).

The highest levels of human exposure to beryllium are through occupational exposure, which may occur via 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 also may lead to at-home exposure to beryllium on work garments. Studies in the workplace found that air concentrations from personal monitors mounted on clothing increased when the amount of beryllium dust on the fabric increased (HSDB 2000a).

As industrial uses of beryllium and beryllium compounds increase, more workers are exposed, from miners to workers at processing plants and factories that convert beryllium into alloys and chemicals. The National Occupational Exposure Survey conducted by the National Institute for Occupational Safety and Health between 1981 and 1983 estimated that 13,935 workers, including 740 women, potentially were exposed to beryllium (NIOSH 1990). The Occupational Safety and Health Administration (OSHA) estimated that approximately 25,000 U.S. workers have been exposed to beryllium (HSDB 2000a).

REGULATIONS

In 1973, EPA issued a National Emissions Standard for Hazardous Air Pollutants for beryllium and beryllium oxide extraction and production sites and for beryllium rocket motor firing. In 1980, EPA published a water quality criteria document on beryllium for the protection of human health under the Clean Water Act and established regulations under the Resource Conservation and Recovery Act (RCRA) and the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) for releases of beryllium and beryllium compounds. These regulations were based on the inclusion of beryllium and its compounds on the EPA Carcinogen Assessment Group’s list of potential carcinogens. The CERCLA adjusted reportable quantity is 10 lb for beryllium and beryllium powder and 1 lb for beryllium chloride and beryllium fluoride. RCRA established handling, reporting, and record-keeping requirements for wastes known to contain beryllium or beryllium compounds. EPA regulates beryllium in drinking water under the Safe Drinking Water Act. Beryllium and its compounds are regulated under the Superfund Amendments and Reauthorization Act, which subjects them to reporting requirements.

The U.S. Food and Drug Administration regulates beryllium in bottled water under the Federal Food, Drug and Cosmetics Act.

The National Institute for Occupational Safety and Health recommends that exposure to beryllium and beryllium compounds should not exceed 0.5 $\mu g/m^3$. OSHA currently recommends 2 $\mu g/m^3$ as an 8-hour permissible exposure limit (PEL) for beryllium, 5 $\mu g/m^3$ as a ceiling concentration not to be exceeded for more than 30 minutes at a time, and 25 $\mu g/m^3$ as a maximum peak never to be exceeded. For construction and shipyard employment, the PEL is 2 $\mu g/m^3$ as an 8-hour time-weighted average, with no provisions for ceiling or peak exposures. OSHA regulates beryllium and certain beryllium compounds under the Hazard Communication Standard and as chemical hazards in laboratories. Regulations are summarized in Volume II, Table 22.

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