THORIUM DIOXIDE
CAS No. 1314-20-1
First Listed in the *Second Annual Report on Carcinogens*

CARCINOGENICITY

Thorium dioxide is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity in humans (Grampa 1971, CHIP 1981, Kojiro *et al.* 1985, IARC 2001). Several large cohort studies and numerous case reports of individuals injected with thorium-232 dioxide (Thorotrast) as a radiographic contrast agent indicate that both the risk of cancer and death from cancer are increased by three to four fold. Liver neoplasms, including cholangiocarcinoma, hemangiosarcoma, and hepatocellular carcinoma are the most common with greater than 100-fold increased risk and a latency period of 15 to 25 years. Hemangiosarcoma, typically a very rare tumor, accounted for approximately one-third of the tumors. These studies show a consistent relationship between the amount of Thorotrast administered and risk of liver cancer. The risk of acute lymphoid leukemia, but not chronic lymphoid leukemia, was increased 5- to 20-fold in Thorotrast-treated patients with an average latency of five years. The risk of extrahepatic bile duct, gallbladder, and pancreatic cancers and mesothelioma were increased in some studies, but were not consistently significantly increased (IARC 2001).

There is sufficient evidence of carcinogenicity of thorium dioxide in experimental animals (Wegener 1979, CHIP 1981, IARC 2001). When administered by intravenous injection, thorium dioxide induced hemangioendotheliosarcomas or reticuloendotheliosarcomas of the liver, spleen, and lung in rabbits, cholangiocellular carcinomas in hamsters, and liver cell adenomas in rats. Subcutaneous injection of thorium dioxide induced local fibrosarcomas in rats and mice; intraperitoneal injection induced sarcomas in rats, mice, hamsters, rabbits, and guinea pigs.

PROPERTIES

Thorium dioxide is a radioactive, heavy, white crystalline powder. It is insoluble in water and alkalies, and slightly soluble in acids and biological fluids. Thorium dioxide is incandescent when heated. Thorium dioxide has the highest melting point (nearly 3000°C) of any metal oxide. It is available in the United States in stocks of different particle sizes with purities ranging from 99.5% to 99.99%. The X-ray contrast medium, Thorotrast, is a 25% colloidal thorium dioxide suspension in aqueous dextrin. Thorium-232 emits α-particles with a half-life of 1.4×10^{10} years (Kirk-Othmer 1997, HSDB 2001, IARC 2001).

USE

Thorium was discovered in 1828 and its radioactivity was discovered in 1898. In the early 1900s, the only commercial use for thorium was in gas lamp mantles. Although demand for gas mantles declined with the advent of electric lights, mantle manufacturing still accounted for 92% of thorium's nonfuel use as late as 1950 (Hedrick 2000). Major uses for thorium dioxide are in high temperature ceramics, gas mantles, nuclear fuel, flame spraying, crucibles, medicines, nonsilica optical glass, in thoriated tungsten filaments, and as a catalyst. It has also been used as a diagnostic aid (radiopaque medium) in feline medication (HSDB 2001). Use of thorium dioxide as a radiopaque medium for X-ray imaging in certain medical diagnostic

procedures began in the 1930s, but was practically discarded in the 1950s when harmful latent effects from its use were noted (Grampa 1971, IARC 2001).

PRODUCTION

Thorium occurs in several minerals including monazite, thorite, huttonite, and thorogummite. The 1979 TSCA inventory identified three domestic producers with a combined annual production of 555,500 lb (TSCA 1979). Between 1987 and 1994, only one U.S. company produced monazite as a by-product from mineral sands mined for titanium and zirconium minerals. All monazite produced in the U.S. was exported. Thorium-bearing monazite was last produced domestically in 1994. Current U.S. consumption of thorium products is met entirely from imports and existing industry and government stocks. Several domestic companies continue to process or fabricate various forms of thorium for nonenergy uses such as described above (ATSDR 1990, Hedrick 2000). Twelve current U.S. suppliers of thorium dioxide were identified (Chem Sources 2001).

Imports of thorium dioxide-equivalents ranged from approximately 43,000 to more than 150,000 lb/year between 1983 and 1987 (ATSDR 1990). Between 1990 and 2000, annual imports of thorium ore and thorium compounds, expressed as thorium dioxide equivalents, were 3,100 to 451,000 lb and 6,900 to 93,700 lb, respectively. Imports of thorium ore showed significant declines after 1992, while imports of thorium compounds fluctuated from year to year. In 2000, 24,400 lb of thorium compounds were imported (Hedrick 2000).

Exports of thorium dioxide equivalents ranged from approximately 2,200 to 45,000 lb between 1983 and 1987 (ATSDR 1990). Between 1990 and 2000, exports fluctuated between a low of 15 lb in 1994 to a high of 10,208 lb in 2000 (Hedrick 2000).

EXPOSURE

The primary routes of potential human exposure to thorium dioxide are inhalation, intravenous injection, ingestion, and dermal contact. Occupational exposures may occur in the uranium, tin, rare-earth metal, and phosphate mining, milling, and processing industries, gas mantle manufacturing, and other thorium processing industries (ATSDR 1990, IARC 2001). Potential exposure may also have occurred during the formulation, packaging, preparation, or administration of the compound as a pharmaceutical. Based on the amount of Thorotrast produced, more than 2.5 million people worldwide were exposed to thorium dioxide between 1930 and 1950 (IARC 2001). The injection dosages ranged from 2 to 70 mL of Thorotrast solution, depending on the area to be X-rayed (Saragoca *et al.* 1972).

Although thorium is widespread in the environment from both natural and anthropogenic sources, concentrations in air, soil, drinking water, and foods are very low. Very few studies have investigated daily intakes of thorium in the general population. Estimated total daily intakes of thorium-230 and thorium-232 in air, food, and water ranged from approximately 0.02 to 0.17 pCi (ATSDR 1990).

EPA's Toxic Chemical Release Inventory (TRI) reported industrial releases of thorium dioxide from 1988 to the present (TRI99 2001). Between 1988 and 1993, industrial releases ranged from 42,000 lb (1993) to 679,129 lb (1988). After 1993, one pound of thorium dioxide was released in 1995 and 1996, and no releases were reported from 1997 to 1999.

REGULATIONS

Under the Food, Drug, and Cosmetic Act (FD&CA), FDA has approved thorium dioxide for use as a radiopaque medium for X-ray imaging in cases where there is limited life expectancy. In March of 1980, the Nuclear Regulatory Commission withdrew authorizations for use and transfer of thorium dioxide for internal or external medicinal use in humans. Authorizations were issued; however, for research, development, educational, commercial, or operational purposes under conditions specified by the Commission, the use and transfer of the material for these purposes may not exceed 15 lb at any one time or a total of 150 lb in any one calendar year. FDA has determined that thorium dioxide for drug use is a new drug, and therefore, subjects it to the requirements of a new drug application for marketing.

OSHA regulates thorium dioxide under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 175.

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