MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Strontium (CAS # 7440-24-6) and Inorganic Compounds

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SUBJECT: Screening Level for Strontium (CAS # 7440-24-6) and Inorganic Compounds

The initial threshold screening level (ITSL) for strontium is 2,000 ug/m^3 based on a 24-hour averaging time.

Strontium (CAS # 7440-24-6) is a chemical element with the symbol Sr with an atomic weight of 87.62. Strontium has a melting temperature of 777°C and boiling point at 1382°C. It has four stable isotopes: ^{84}Sr (0.6%), ^{86}Sr (9.9%), ^{87}Sr (7.0%), and ^{88}Sr (83%) with ^{87}Sr being radiogenic (^{87}Sr is formed either from stellar reactions or from radioactive decay of ^{87}Rb). Strontium also has twelve unstable isotopes of which ^{90}Sr (half-life of 29 years) and ^{89}Sr (half-life of 50.5 days) are considered the most important as they are by-products of nuclear reactors and nuclear weapons (EPA, 2011a). An alkaline earth metal, strontium is silver-white or yellowish metallic element that is highly reactive chemically and will react with air or water. It is most likely found as strontium oxide, strontium hydroxide, or less frequently as strontium nitride in emissions. Strontium is the 15th most abundant element on earth averaging 0.025% of the earth's crust is found mainly as sulfate mineral celestite ($SrSO_4$) and carbonate strontianite ($SrCO_3$). Strontium is used in aluminium-silicon casting alloys; in magnesium alloys used in car and motorcycle engines; in science as a calcium replacement when studying cellular neurotransmission; for red coloration in fireworks and signal flares; in glass for color television cathode ray tubes; in ferrite magnets; in refining zinc; in phosphoring compounds; in toothpaste for sensitive teeth; in pottery glazes; in 3D screens; as laboratory reagents in the manufacture of chemical reactive devises; and in the treatment of osteoporosis (Wikipedia, 2011).

A literature review was conducted to determine an initial threshold screening level (ITSL) for strontium. The following references and databases were searched to derive the above screening level: Environmental Protection Benchmark Chemical Criteria Database (EPBCCD), United States Environmental Protection Agency (US EPA) Integrated Risk Information System (IRIS), National Institute for Occupational Safety and Health (NIOSH), American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values and Biological Exposure Indices (TLV/BEI) 2010 guide, National Toxicology Program (NTP) Study Database, International Agency for Research on Cancer (IARC), Acute Database, Chemical Abstract Service (CAS) Online (searched 12/15/10), National Library of Medicine (NLM)-online, EPA Aggregated Computational Toxicology Resource (ACToR) Database, US EPA TSCATS database, and Hazardous Substances Data Bank (HSDB).

There is an oral reference dose (RfD) of 0.6 mg/kg-day based on a 20-day oral study of strontium in young and adult rats performed by Storey E. in 1961. Groups of five young (40-60 g) and three adult (200-250 g) female rats were fed a diet containing 1.6% calcium, 0.9% phosphorus, and 0, 0.19, 0.38, 0.75, 1.0 (young only), 1.5, or 3% strontium as strontium carbonate for 20 days. Assuming young rats consume 10% and adult rats consume 5% of their body weight in food per day, these doses correspond to 190, 380, 750, 1000, 1500, and 3000 mg/kg/day for young rats and 95, 190, 375, 750, and 1500 mg/kg/day for adult rats (EPA, 2011b). Rats were examined for changes in bone mineralization and defects in cartilage. Initial and final body weights were recorded. Terminal levels of calcium and strontium were measured in serum and in five selected ashed bones for each dose level. Both tibia from each animal were examined histologically, and the proximal epiphyseal cartilages were measured. As dietary levels of strontium increased, young rats and adult rats gained less weight than controls. In young rats, at 0.38% dietary strontium the epiphyseal plate was irregular and slightly widened, however for dietary strontium levels above 0.75%, the cartilage plate became so irregular that measurements were not reliable. Changes observed with the dose of 0.38% and higher were inhibition of calcification, as evidenced by increasing width of epiphyseal cartilage, presence of uncalcified bone matrix and decreased ash weight of bone. In adult rats the epiphyseal cartilage is slightly wider than normal at 1.5% dietary strontium, and metaphyseal osteoid seams are irregularly increased in width. For young rats, the dietary level of 0.19% strontium showed no adverse effects (NOAEL) and 0.38% strontium was the lowest observed adverse effect level (LOAEL). In adult rats, the dietary level of 0.75% strontium was a NOAEL and 1.5% strontium was a LOAEL.

A study by Skoryna, (1981) investigated the oral toxicity of stable strontium in male adult RVH hooded rats. The rats (12/group) were divided into four groups and fed ad libitum a standard laboratory diet and administered 0.002, 900, 1900, or 3400 ppm strontium chloride in their drinking water for 3 years. Assuming that an adult rat consumes water at a rate of 49ml/day, the experimental doses correspond to 70, 147, and 263 mg/kg Sr/day (EPA, 2011b). Control and experimental groups received adequate amounts of calcium (0.35 ppm) and magnesium (0.0682 ppm) in their drinking water. The animals were weighed and examined weekly. Histologic examinations of bone and observation of body weight changes in rats receiving strontium in drinking water revealed no abnormalities. The following tissues were examined on gross and histologic levels: brain, lung, heart, skeletal muscle, liver, spleen, adrenal and kidney tissue. No evidence of morphologic changes were observed and the organs were not weighed. The concentration of strontium in tissues as well as strontium:calcium ratios were determined by graphite furnace atomic absorbtion. Except for bone, no significant levels of strontium were detected in the organs at any dosage levels. A chronic NOAEL of 3400 ppm was identified from this study.

A study by Marie et al., (1985) administered stable strontium to weanling male Sprague-Dawley rats. The purpose of the study was to determine the effect of low doses of strontium on mineral homeostasis and bone histology. Eight rats per group received 0, 0.19, 0.27, 0.34, and 0.40% strontium chloride in distilled water for 9 weeks (EPA, 2011b). The diet contained 0.5% calcium. Based on body weight and water consumption data, the authors estimated average strontium intakes of 0, 316, 425, 524, and 633 mg/kg-day. The authors concluded that an oral dose lower than 0.40% (633 mg/kg-day) dose group showed signs of increased mineralization lag time; excessive osteoid thickness associated with a decline in the rate of calcification, which resulted in slow growth rate; and a decreased double-labeled osteoid surface, which frequently resulted in defective long bone growth. This study identified a NOAEL of 525 mg/kg and a LOAEL of 633 mg/kg-day.

Table 1: Summary of Principle and Supporting Studies for Oral RfD

Study	Species	Duration/Route	NOAEL	LOAEL
Marie et al. 1985	Rat (Sprague-Dawley)	9 wks ad lib in water	524 mg/kg/day	633 mg/kg/day
*Storey 1961	Rat (young and adult)	20 d ad lib in food	190 mg/kg/day (young) 750 mg/kg/day (adult)	380 mg/kg/day (young) 1500 mg/kg/day (adult)
Skoryna 1981	Rat (male RVH hooded)	3 years ad lib in water	263 mg/kg/day	NOAEL at highest dose given

* study used to determine the oral RfD.

Osteoporosis treatments have used strontium in patients Skoryna (1981) reported subjective improvement in patients with osteoporosis receiving 274 – 1,750 mg Sr/day as the gluconate, carbonate, or lactate. No adverse effects were reported. Strontium is not recognized as a standard therapy for osteoporosis. The toxic effect of excessive strontium intake is inhibition of calcification of epiphyseal cartilage and deformities of long bones at high doses. Strontium causes adverse effects on bone by substituting for calcium in the hydroxyapatite crystal during bone calcification or by displacing calcium from existing calcified matrix (Skoryna, 1984).

"Because of active bone growth, young animals are more sensitive than adult animals to excessive strontium intakes. In addition to the information presented in the critical study (Storey, 1961), the greater sensitivity of young animals was also determined by Storey (1962). Both young (50-70 g) and adult (200-250 g) rats of both sexes were provided a diet containing 1.8% strontium as strontium carbonate. The exposure continued for up to 7 months with several interim sacrifices. After only 3 weeks of exposure, the young rats exhibited a 'rachitic gait' with the most obvious changes occurring in the distal end of the femur and the proximal end of the tibia. The epiphyseal plate was reported to be 'grossly widened' and the 'metaphysic was a mass of soft white tissue.' Conversely, it was 3 months before any change was observed in the adult rats, this being the appearance of fine traverse lines in the upper tibial metaphysic. The author goes on to portray significant differences in the effects seen in young animals vs. adults provided the same dietary concentration of strontium" (EPA, 2011b).

Development of a Screening Level

The oral RfD is based on the Storey, 1961 study. Based on Rule 232(1)(b) an ITSL can be determined from an oral RfD using the following equation:

$$ITSL = Oral\ldots RfD \times \frac{70kg}{20m^3}$$

Where 70 kg is the value of the default body weight for the human and 20 m^3 is used to define the minute volume (default ventilation rate) for the human. Taking the oral RfD, which was determined to be 0.6 mg/kg-day above gives:

$$ITSL = 0.6\,{}^{mg}\!/_{kg/day} \times \frac{70kg}{20m^3} = 2.1\,{}^{mg}\!/_{m^3} = 2{,}100\,{}^{\mu g}\!/_{m^3}$$

ITSL = 2,000 µg/m^3.

Based on Rule 232(2)(b) the averaging time is 24 hours.

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