Danish Ministry of the Environment
Environmental Protection Agency

Strontium, inorganic and soluble salts

Evaluation of health hazards and proposal of health based quality criteria for drinking water

Environmental Project No. 1525, 2013

Title:

Strontium, inorganic and soluble salts.
Evaluation of health hazards and proposal of health based quality criteria for drinking water

Author:

Elsa Nielsen
Krestine Greve
Ole Ladefoged
Division of Toxicology and Risk Assessment
National Food Institute, Technical University of Denmark

Published by:

The Danish Environmental Protection Agency
Strandgade 29
1401 Copenhagen K
Denmark
www.mst.dk/english

Year:

Authored in 2008
Published in 2013

ISBN no.

978-87-93026-79-7

Content

Preface

The Danish Environmental Protection Agency has requested an evaluation of health hazards by exposure to inorganic and soluble salts of strontium and a proposal of health based quality criteria for drinking water. This resulted in 2008 in the present report, which was prepared by Elsa Nielsen, Krestine Greve and Ole Ladefoged, Department of Toxicology and Risk Assessment, Danish Institute for Food and Veterinary Research, i.e. the present Division of Toxicology and Risk Assessment, National Food Institute, Technical University of Denmark.

The report has been subjected to review and discussion and has been endorsed by a steering committee consisting of representatives from the following Danish authorities:

The Danish Nature Agency,
The Danish Ministry of Food, Agriculture and Fisheries (The Faculty of Agricultural Sciences),
The Danish Veterinary and Food Administration,
The National Board of Health, Denmark,
Danish Regions,
The Danish Environmental Protection Agency.

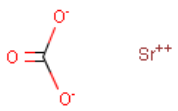
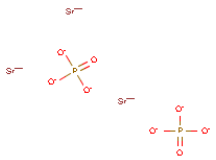
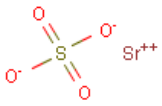
The Danish Environmental Protection Agency
Copenhagen, December 2013.

1 General description

Elemental strontium (Sr) is not radioactive and exists naturally in four stable isotopes (^{84}Sr, ^{86}Sr, ^{87}Sr, ^{88}Sr). Radioactive isotopes of strontium, of which ^{89}Sr and ^{90}Sr are the most important, are formed in nuclear plant reactors and during nuclear weapon explosions and thus not occurring naturally; these isotopes are not covered in this evaluation. Elemental strontium is a commonly occurring alkaline earth metal and can exist in the oxidation states 0 and +2. It belongs to group IIA of the periodic table and behave similar chemically to magnesium and calcium, also belonging to this group. Elemental strontium is highly reactive and exists only under normal environmental conditions associated with other elements. In this evaluation only soluble inorganic strontium salts are considered in relation to an estimation of a health based quality criterion in drinking water. Strontium chromate is not covered by this evaluation as its toxicity is attributed to the hexavalent chromium ion. This document is based on reviews and evaluations prepared by ATSDR (2004) and IRIS (2002). The most common cationic salts of strontium are listed below (Table 1.1 and 1.2).

1.1 Identity

Table 1.1 (ChemFinder, ChemIDplus Advanced, ATSDR 2004, HSDB 2003)

	Strontium carbonate	Strontium chloride	Strontium phosphate	Strontium sulfate
Molecular formula	$SrCO_3$	$SrCl_2$	$Sr_3(PO_4)_2$	$SrSO_4$
Structural formula				
Molecular weight	147.63	158.53	452.8	183.68
CAS-no	1633-05-2	10476-85-4	7446-28-8	7759-02-6
Synonyms	Strontianite; carbonic acid, strontium salt (1:1); CI 77837	Strontium dechloride	Phosphoric acid, strontium salt (2:3); Tristrontium bis(orthophosphate)	Sulfuric acid, strontium salt (1:1); celestite; celestine

1.2 Physico-chemical properties

Table 1.2 (ChemFinder, ChemIDplus Advanced, ATSDR 2004, HSDB 2003)

	Strontium carbonate	Strontium chloride	Strontium phosphate	Strontium sulfate
Description	White Solid	White Solid	White Solid	Colorless Solid
Melting point °C	1494	875	-	1605
Boiling point °C	-	1250	-	-
Density (g/ml)	3.5	3.05	-	3.96

	Strontium carbonate	Strontium chloride	Strontium phosphate	Strontium sulfate
Solubility (Water: g/l)	0.011 (at 18°C)	538 (at 20°C)	Insoluble	0.14 (at 30°C)

1.3 Production and use

The principal strontium minerals of commercial interest, extracted from strontium ore, are celestite ($SrSO_4$) and strontianite ($SrCO_3$) (ATSDR 2004).

Strontium compounds are used in making ceramics and glass products, pyrotechnics (strontium nitrate), paint pigments (strontium chromate), fluorescent lights (strontium phosphate), medicines used to treat osteoporosis (strontium chloride, strontium ranelate), getters (a material added in small amounts during a chemical or metallurgical process to absorb impurities) in zinc production (strontium carbonate), alloy (strontium metal), in toothpaste for temperature-sensitive teeth (strontium chloride) and phosphate fertilizers.

Phosphate fertilizers are known to contain between 20 and 4000 mg Sr/kg solid by weight (Lee and von Lehmden 1973, Raven and Loeppert 1997 – quoted from ATSDR 2004).

Pyrotechnic displays (fireworks) release low levels of strontium of about 9 ng/m^3 in the immediate environment of the display (Perry 1999 – quoted from ATSDR 2004).

Television faceplate glass and other devices containing cathode-ray tubes (CRT) contain strontium in the faceplate glass of the picture tube to block x-ray emissions. Major manufacturers of television picture tube glass incorporate about 8% by weight of strontium oxide (SrO) into the glass faceplate material. Most commercial uses of strontium compounds and products use strontium carbonate as the feed material (ATSDR 2004).

The strontium salt of ranelic acid, strontium ranelate, is an orally active drug used for treatment of postmenopausal osteoporosis. The recommended dose is 2 g/day for 3-5 years (Mosekilde et al. 2005).

According to the Danish Product Register, strontium is used in paints, laquers, dyes, enamels, binding agents and products for corrosion protection (Dansk Produkt Register 2006).

The Danish Plant Directorate has no data regarding the concentration of strontium in fertilisers (Plantedirektoratet 2007).

1.4 Environmental occurrence and fate

Strontium is a naturally occurring element that makes up approximately 0.02-0.03% of the earth's crust. Strontium ore is found in nature as the minerals celestite ($SrSO_4$) and strontianite ($SrCO_3$). It is widely distributed throughout the earth and has continuously cycled between the atmosphere, biosphere, hydrosphere, and lithosphere for many millions of years. Rocks, soil, dust, coal, oil, surface and underground water, air, plants, and animals all contain varying amounts of strontium. Typical concentrations in most materials are a few mg/kg (ATSDR 2004).

1.4.1 Air

Strontium compounds in the atmosphere are present as wet or dry aerosols. It is released into the atmosphere primarily as a result of natural sources, such as sea spray, entrainment of dust particles and re-suspension of soil by wind. Emissions from burning coal and oil, land application of phosphate fertilizers and using pyrotechnic devices increase strontium levels in air. Entrainment of soil and dust particles with significant concentrations of strontium is most significant in areas with higher soil strontium concentrations and in coastal regions due to sea spray (ATSDR 2004).

From the atmosphere strontium is transported and re-deposited on the earth by dry or wet deposition. Rain, sleet, snow, or other forms of moisture can wash airborne particles containing strontium from the atmosphere by wet deposition. Wet deposition depends on conditions such as particle solubility, air concentration, rain drop size distribution, and rain fall rate. Dry deposition results from gravitational settling, impact, and sorption on surfaces (NCRP 1984 - quoted from ATSDR 2004).

Strontium is emitted into the atmosphere as strontium oxide (SrO) during thermal processes. SrO is unstable and reacts with moisture or carbon dioxide in the air to form strontium hydroxide ($Sr[OH]_2$) or strontium carbonate ($SrCO_3$), respectively. $Sr[OH]_2$ in contact with water in clouds or during washout by rain will ionize to form Sr^{2+} and $SrOH^+$ ions. There is no evidence in the literature for interaction of SrO with other compounds in the atmosphere (ATSDR 2004).

The average amount of strontium that has been measured in air from different parts of the United States is 20 ng/m^3 (ATSDR 2004). Atmospheric concentrations of strontium emitted from coal fired power plants have been found to range from 17 to 2,7 $\mu g/m^3$ in the western United States and are approximately 9,8 µg/m3 in the eastern United States (Ondov et al. 1989, Que Hee et al. 1982 – quoted from ATSDR 2004).

The atmospheric concentrations of strontium in Denmark are measured daily on 15 different locations. The yearly average amount is in the range 1-5 ng/m^3 with the highest concentration in areas with sea-spray or windborne soil particles (DMU 2006).

1.4.2 Water

Strontium is released to surface water and groundwater by the natural weathering of rocks and soils and from the discharge of wastewater directly into streams and aquifers. Only a very small part of the strontium found in water is from the settling of strontium dust out of the air. Strontium is relatively mobile in water, however, the formation of insoluble complexes or sorption of strontium to soils can reduce its mobility in water (ATSDR 2004).

Strontium is also released to the groundwater by the natural re-crystallizing of rocks. Elevated concentrations of strontium can be found in basins with low groundwater flow. Groundwater basins with a high flow will only contain limited concentrations of strontium due to leaching out (Roskilde Amt report 2005).

Strontium is removed from the oceans, the largest reservoir of dissolved strontium, by deposition in marine carbonate sediment. Some strontium is transported from oceans to the atmosphere in sea spray, returning to the terrestrial environment in the form of precipitation (Capo et al. 1998 - quoted from ATSDR 2004).

Strontium has been measured in drinking water in different parts of the United States by the US-EPA to be less than 1 mg/l (ATSDR 2004).

In Denmark reported values of strontium concentrations in groundwater are in the range 0.28 mg/l to 53 mg/l (Roskilde Amt report, 2005).

Strontium was found in all 28 groundwater samples analysed in Denmark in 2003 by GRUMO. The highest concentration was reported to be 1.8 mg/l, and the median value was estimated to be 240 µg/l and the 75 percentile was 380 µg/l (GRUMO 2004).

Strontium was found in 52 of 53 groundwater samples analysed in Denmark in 2000 by GRUMO. The highest concentration was reported to be 34 mg/l, and the median value was estimated to be 329 µg/l and the 75 percentile was 487 µg/l (GRUMO 2000).

1.4.3 Soil

Strontium is found naturally in soil where the sorption is dominated by simple ion exchange. The disposal of coal ash, incinerator ash, industrial wastes and land application of phosphate fertilizers may increase the concentration of strontium in soil. A major portion of strontium in soil dissolves in water and will move downward into the groundwater depending on the mobility of the strontium ion. This mobility increases with increasing concentration of exchangeable ions and with decreasing cation exchange capacity in the soils. Chemical reactions can transform the water-soluble strontium compounds into insoluble forms or opposite (ATSDR 2004).

The principal abiotic processes that transform strontium in soils and sediments are mediated by sorption and desorption reactions between the soil solution and matrix (precipitation, complexation, and ion exchange), and controlled by pH, ionic strength, solution speciation, mineral composition, organic matter, biological organisms, and temperature (Bunker et al. 2000 - quoted from ATSDR 2004).

The amounts of strontium in soil vary over a wide range. The average concentration is 240 mg Sr/kg (Capo et al. 1998; EPA 1995a – quoted from ATSDR 2004).

Plant to soil concentration ratios for strontium are 0.017-1.0 (ratio of strontium in wet vegetation to strontium in dry soil) (NCRP 1984 - quoted from ATSDR 2004), and indicate that strontium can be easily absorbed into plants from soil. The uptake of strontium by plants is greatest in sandy soils having low clay and organic matter content (Baes et al. 1986 - quoted from ATSDR 2004). The concentration of nutritive mineral elements in soil such as calcium lowers the intake of strontium to the aboveground phytomass (Lembrechts 1993 - quoted from ATSDR 2004.

1.4.4 Foodstuffs

The uptake or bioaccumulation of strontium by plants and vertebrates is the mechanism by which strontium in air, water, and soil enters into the food chain of humans. DOE found by measuring the ^{90}Sr content in US food, that grain, leafy vegetables, and dairy products contribute the greatest percentage of dietary strontium to humans (ATSDR 2004).

The highest concentrations of strontium in foodstuffs are observed in leafy vegetables, such as cabbage (64.2 mg Sr/kg dry weight) (USGS 1980 – quoted from ATSDR 2004).

In fermented milk products the concentration of strontium ranged from 0.21 to 0.79 mg/kg of the edible form (mean 0.44 mg/kg). In marine smoked fish the concentration of strontium ranged from 0.02 to 4.63 mg/kg of the edible form (mean 1.16 mg/kg) (Nabrzyski and Gajewska 2002).

In general, strontium is present in foodstuffs that are rich in calcium. Concentrations of strontium in biological material tend to be about one thousand times less than the concentrations of calcium (Davidson et al. 1979)

1.5 Bioaccumulation

The uptake or bioaccumulation of strontium by plants and vertebrates is the mechanism by which strontium in air, water, and soil enters into the food chain of humans.

Bioconcentration factors (BCFs) for ^{90}Sr, have been measured by several investigators in both aquatic and terrestrial organisms. In a study by Friday (1996) BCF values for ^{90}Sr in aquatic, terrestrial, and wetland ecosystems were reported and illustrate that the organisms with the highest uptake are aquatic organisms such as fish, macroinvertebrates, macrophytes, and zooplankton. Because of the similarity of strontium to calcium, boney fish had a very high BCF, with a value >50,000 measured in the bony tissue. In the muscle tissue of boney fish, BCF values for ^{90}Sr ranged from 610 (benthic invertebrate and fish feeders) to 3400 (piscivores). Organisms such as fish bio-accumulate strontium with an inverse correlation to levels of calcium in water, however, this correlation is not universal and does not apply to other organisms such as algae and plants. BCFs for ^{90}Sr in corn grains and soybeans were 0.15 and 2.51 respectively (Friday 1996 and NCRP 1984 - quoted from ATSDR 2004).

1.6 Human exposure

Human exposure to strontium can result from inhalation, consumption of food, drinking water, or incidental ingestion of soil or dust contaminated with strontium. Food and drinking water are the largest sources of exposure to strontium (ATSDR 2004).

Using the average atmospheric concentration in Denmark of 5 ng Sr/m^3 (DMU 2006), and assuming the inhalation rate as 0.5 m^3/kg bw/day (for children 1-5 years old), the inhalation exposure of strontium will be 2.5 ng Sr/kg bw/day. For an adult (body weight of 70 kg), the daily exposure of strontium from air would be 175 ng.

Using the concentration of strontium in U.S. drinking water of 1 mg/l (ATSDR 2004), and the consumption rate of 0.08 l/kg bw/day (for children 1-10 years old), the intake from drinking water would be 0.08 mg Sr/kg bw/day. For an adult (body weight of 70 kg), the daily exposure of strontium from drinking water would be 5.6 mg.

Using the highest reported concentrations of strontium in Danish ground water of 53 mg/l (Roskilde Amt report 2005), and the consumption rate of 0.08 l/kg bw/day (for children 1-10 years old), the intake from drinking water would be 4.2 mg Sr/kg bw/day (assuming no dilution of groundwater). For an adult (body weight of 70 kg), the daily exposure of strontium from drinking water would be 297 mg.

Several estimates of dietary intake of strontium have been reported. In a total diet study in the United Kingdom, the total dietary exposure to strontium was estimated at 1.3 mg/day. The exposure given does not include the contribution from drinking water (Ysart et al. 1999 - quoted from ATSDR 2004).

As part of an Australian Market Basket Survey in 1994, the estimated daily intakes of strontium for female adults ranged from 0.89 to 1.2 mg/day. In the same study the estimated daily intakes of strontium for 6-month-old infants fed exclusively breast milk or infant formula were 47 and 254 µg/day, respectively (Gulson et al. 2001 - quoted from ATSDR 2004).

Combining air, water, and diet exposures estimates, the total daily exposure to strontium for adults is ~3.3 mg/day (ATSDR 2004).

2 Toxicokinetics

2.1 Absorption, distribution and excretion

2.1.1 Inhalation

The deposition of strontium particulates in the respiratory tract is affected by the size of the inhaled particles, age-related factors, airway geometry and airstream velocity within the respiratory tract. Larger particles that are deposited in the ciliated airways can be transferred by mucociliary transport into the oesophagus and swallowed. Particles deposited in the alveolar region can be absorbed after extracellular dissolution or ingestion by phagocytic cells (ATSDR 2004).

A worker accidentally inspired an unknown quantity of $^{90}SrCl_2$ (physical form unknown) and over the subsequent 800 days, ^{90}Sr was excreted in the urine with half-times of 3.3 (52%), 17 (7%), and 347 days (18%). The urinary:faecal excretion ratio was 3:1 (Petkau and Pleskach 1972 – quoted from ATSDR 2004).

Two workers accidentally inhaled $^{90}SrTiO_3$ (physical form unknown), and ^{90}Sr was detected in urine over a period of 225 days (Navarro and López 1998 – quoted from ATSDR 2004).

In rats exposed to aerosols of $^{85}SrCO_3$, $^{85}Sr_3(PO_4)_2$, $^{85}SrF_2$, ^{85}SrO, or $^{85}SrTiO_3$ (particle sizes and doses not specified) greater than 99% of the initial lung burden of ^{85}Sr was cleared from the lung 5 days after inhalation of the carbonate, phosphate, fluoride, or oxide, whereas 60% of the ^{85}Sr remained in the lung after inhalation of the more insoluble strontium titanate. Four to 6 days after inhalation >99% of the body burden of ^{85}Sr was in the skeleton (Willard and Snyder 1966 – quoted from ATSDR 2004).

In rats, which received an intratracheal dose of ^{89}Sr-enriched fly ash (sieved to have a particle diameter of distribution of 90% less than 20 μm) the tissue:plasma concentration ratios were >1 (1.5-2) in the liver, kidney, stomach, and small intestine, and <1 (0.7-0.9) in the spleen, heart, and brain. The relatively high concentrations of strontium in the gastrointestinal tract may reflect the mechanical clearance of strontium from the airways to the oesophagus. (Srivastava et al. 1984a – quoted from ATSDR 2004).

In rats which received an intratracheal dose of 360-760 μg strontium as $SrTiO_3$, strontium was eliminated from the lung with half-times of 0.4 days (85%) and 130 days (15%). The long retention phase reflects the slow absorption of the insoluble $SrTiO_3$ deposited in the lung, whereas the rapid phase reflects the mechanical clearance from the tracheobronchial region (Anderson et al. 1999b – quoted from ATSDR 2004).

In rats which received an intratracheal dose of $SrCl_2$, strontium was cleared from the lung with a half-time <1 day and was eliminated from the body in the urine (4-6% of the initial body burden) and in the faeces (10-18%) (Naményi et al. 1986 – quoted from ATSDR 2004).

In hamsters administered $^{85}SrCl_2$ (in saline solution) directly into the nasal tract, 67% of the ^{85}Sr was absorbed in 4 hours and 63% was estimated to have been absorbed directly from the nasopharynx region of the respiratory tract (Cuddihy and Ozog 1973 – quoted from ATSDR 2004).

In dogs, which received a 2-22-minute nose-only exposure to aerosols of $^{85}SrCl_2$ (AMAD (activity median aerodynamic diameter) 1.4-2.7 μm, GSD (geometric standard deviation) 2.0), 37% of the body burden was distributed to the skeleton twelve hours after the exposure and after 4 days 84% was in the skeleton. Less than 1% of the initial lung burden remained in the lung 12 hours after the exposure. The whole body elimination half-times were 0.6 days (59%), 9 days (12%), and 300 days (29%). An initially large faecal component of excretion was followed by urinary:faecal excretion ratios of 1.0-1.4 (Fission Product Inhalation Project 1967a – quoted from ATSDR 2004).

2.1.2 Oral intake

A study compared the area under the plasma strontium concentration-time curves in adult human males and females and found no significant difference (10.6 and 9.3 mmol/l-min, respectively). Although the fraction absorbed could not be estimated in this study because the area under the curve for an intravenous dose was not measured, the results suggest that there were no substantive differences in absorption between males and females (Vezzoli et al. 1998 – quoted from ATSDR).

Studies conducted in infants and children indicate that approximately 15-30% of dietary strontium is absorbed (Alexander et al. 1974; Harrison et al. 1965; Kahn et al. 1969a, Sutton et al. 1971a – quoted from ATSDR).

From published data on ^{90}Sr and calcium concentrations in human bone tissues and diets of people in the United Kingdom during the period from 1955 to 1970, it was concluded that approximately 4.75% of the dietary intake of ^{90}Sr was taken up by the adult skeleton. The skeletal uptakes of strontium varied with age, being highest, approximately 10%, in infants and during adolescence, ages in which bone growth rates are high relative to other. Approximately 7.5% of the cortical bone ^{90}Sr burden was eliminated from bone each year (equivalent to elimination halftimes of approximately 9.2 years). The rate of elimination from trabecular bone was approximately 4 times this value (Papworth and Vennart 1984 – quoted from ATSDR 2004).

Whole body elimination of a tracer dose of ^{85}Sr in nine human subjects was measured for periods of 42-108 days. The mean elimination halftime was estimated to be 91 days (±32, SD) (Likhtarev et al. 1975 – quoted from ATSDR 2004).

Three healthy human subjects received a single oral dose of $SrCl_2$. The estimated average whole-body elimination half-times, estimated over 13 days, were 2 (30%) and 59 days (70%) (Uchiyama et al. 1973 – quoted from ATSDR 2004).

Adult male rats that received a single oral dose of 1.4 mg strontium as $SrCl_2$ absorbed 19% of the dose (Sips et al. 1997 – quoted from ATSDR 2004); which is similar to values reported for humans (Sips et al. 1995, 1996 – quoted from ATSDR 2004).

In rats during lactation, fractional absorption of strontium appears to increase. Rats administered a tracer dose of ^{85}Sr as $SrCl_2$ in drinking water between 14 and 16 days after the start of lactation absorbed twice as much strontium as control rats that were not lactating and received the same oral dose of strontium; 11% of the dose was absorbed in lactating rats compared to 5% in controls. Absorption was estimated in this study as the fraction of the dose in the skeleton, urine, and pups 3 days after the start of exposure (Kostial et al. 1969b – quoted from ATSDR 2004).

In rats, age-related changes in absorption of strontium have been observed, suggesting the possibility of increased absorption of strontium during the neonatal period in humans. Absorption was found to decrease

from 85% of the dose at 15 days of age to 8% of the dose at ages older than 89 days (Forbes and Reina 1972 – quoted from ATSDR 2004).

In rats, the strontium:calcium absorption ratio was 0.75 over a fairly wide range of absorbed fractions of calcium. This suggests that strontium and calcium may be absorbed by similar mechanisms (Marcus and Wasserman 1965 – quoted from ATSDR 2004).

Several studies indicate that active vitamin D (calcitriol or $1,25(OH)_2D_3$) affect the gastrointestinal absorption of strontium by inducing the synthesis of proteins that are important in the absorption of calcium in the intestine (Bianchi et al. 1999, Bronner et al. 1986, Gross and Kumar 1990 – quoted from ATSDR 2004). A group of 18 women (66 years old) were treated with calcitriol at a daily dose of 0.5 µg for two years. The intestinal absorption of strontium was 13.7% compared to 10.4% for the untreated controls. The basal absorption percentages before treatment were 8.7 and 9.2%, respectively (Sairanen et al. 2000 – quoted from ATSDR 2004).

In rats exposed to 1.9 mg Sr/l (as $SrCl_2$) in drinking water for 3 months, the strontium concentrations (per mg protein) in the mitochondrial, lysosomal, and microsomal fractions of liver were approximately 5 times that of cytosol. The serum concentration of strontium in rats exposed to 3.4 mg Sr/l (as $SrCl_2$) in drinking water for 3 months was 8.7 mg/l and tissue:serum strontium concentration ratios (based on the latter mean serum concentration) were as follows: liver, 0.7; heart, 1.2; muscle, 1.1; adrenal, 1.3; brain, 1.2; and bone, 1300. Strontium:calcium ratios in these tissues were approximately 0.05–0.1 (Skoryna 1981b – quoted from ATSDR 2004).

2.1.3 Dermal contact

Human subjects were exposed to strontium through intact or abraded skin after topical applications of $^{85}SrCl_2$ in aqueous solution. The absorption of ^{85}Sr through intact skin over 6 hours was 0.26% (range, 0.14- 0.37%) of the applied dose, indicating that undamaged skin is a relatively effective barrier to penetration by strontium. Strontium absorption through abraded skin was 38% (range, 25.5-45.8%) of the applied dose after 30 minutes and 57.4% (range of coefficients, 55.7-65.3%) after 6 hours. External counting of the patella and right forearm, suggested that the absorbed strontium had been taken up by bone. The ^{85}Sr was excreted in urine (faecal excretion was not measured in this study) (Ilyin et al. 1975 – quoted from ATSDR 2004).

An *in vitro* study evaluated penetration of ^{90}Sr through abdominal skin removed from 5- or 9-day-old Wistar rats and arranged in vertical penetration cells. The radionuclide in a chloride carrier solution (0.01-1.0% strontium chloride w/v) was applied to the epidermal surface; radioactivity of the permeated ^{90}Sr in the receptor chamber solution was measured by liquid scintillation spectrometry. Penetration was inversely related to concentration of the carrier solution. At a carrier concentration of 0.1%, penetration was 0.5% for hairless skin of 5-day old rats compared to 2% for hairy skin of 9-day old rats. The authors attributed this difference to the barrier provided by the intact stratum corneum in 5-day skin, indicating that hair follicles in skin of 9-day-old rats increase the permeability of skin to strontium. In experiments in which epidermal layers were stripped (by the 20x repeated application of adhesive tape) or entirely removed from skin of 5-dayold rats, penetration was approximately 25% over 24 hours (Bauerová et al. 2001 – quoted from ATSDR 2004).

2.2 Transfer through placenta and breast milk

In rats, the uptake of strontium by the foetus was highest (1-2% of an injected maternal dose) after a maternal dose was given on or after the 16th day of gestation when ossification of the foetal skeleton begins (Hartsook and Hershberger 1973, Wykoff 1971 – quoted from ATSDR 2004).

Lactating rats were orally exposed to tracer concentrations of ^{85}Sr in drinking water during the 14th through 16th days of lactation. Approximately 5% of the ingested dose was recovered in the nursing pups 24 hours after the end of the 2-day exposure (Kostial et al. 1969b – quoted from ATSDR 2004).

Pregnant mice received an intravenous injection of strontium at different stages of pregnancy. Foetal strontium burden after maternal exposure was 4.5% of dose administered on the 18th day of pregnancy compared to 0.7% of dose administered on the 14th day of pregnancy. In mice, ossification of the foetal skeleton begins on approximately the 14th day of gestation, at which point, the foetal strontium burden begins to increase. Thus, foetal transfer was highest when the maternal dose occurred at the time of greatest skeletal growth (Rönnbäck 1986, Olsen and Jonsen 1979 – quoted from ATSDR 2004).

In mice, the skeletal (long bones): soft tissue concentration ratio at the end of gestation was approximately 40 in both the foetuses and dams. Thus, the distribution of strontium in the foetus is similar to that of the mother with most of the strontium burden in the skeleton (Jacobsen et al. 1978 – quoted from ATSDR 2004).

In lactating mice and their offspring, the tissue distribution of strontium was found to be similar after an intraperitoneal dose to the dams during lactation; concentrations in bone were approximately 1000 times higher than in the liver and kidney. The strontium concentration in calvaria of the lactating pups, after 5 days of lactation, was approximately 3 times that of the dams, whereas the concentration in long bones of pups and dams were similar. The difference in the bone concentrations in the dams and pups may reflect the relatively higher rate of bone formation in the pups and associated incorporation of strontium into the new bone (Jacobsen et al. 1978 – quoted from ATSDR 2004).

2.3 Species differences

Incorporation of strontium into the skeleton is likely to be relatively higher in adult rats compared to other mammals due to differences in bone physiology. Unlike most mammals (including humans), the epiphyseal growth plate of the long bones of rats never entirely transforms into bone after sexual maturity. Thus, although reduced after the age of 12 months, bone growth in rats continues throughout life. (Leininger and Riley 1990 – quoted from ATSDR 2004).

2.4 Mode of action

Strontium is a molecular surrogate for calcium and thus the toxicity of strontium is related to its interference in biological processes that normally involve calcium. Approximately 99% of the total body burden of strontium is distributed to the skeleton (ICRP 1993 – quoted from ATSDR 2004).

In bones, strontium affects bone development, which may lead to rachitic changes. This adverse effect is caused by strontiums ability to substitute the binding of calcium to the hydroxyapatite crystals during bone calcification, inhibiting the calcification of eiphyseal cartilage, or by displacing calcium from existing calcified matrix. Strontium may also prevent the normal maturation of chondrocytes in the epophyseal plates of long bones (ATSDR 2004).

Children are more susceptible to the effects of stable strontium than adults because they absorb strontium through the gastrointestinal tract at slightly higher amount and because they have actively growing bones that incorporate more strontium than mature bones (ATSDR 2004).

The adequacy of calcium nutrition is a critical factor regarding strontium toxicity and inadequate calcium levels can exacerbate rachitic changes (El Solh and Rousselet 1981 – quoted from IRIS 2002). The effect of dietary calcium on strontium toxicity was demonstrated in weanling Sprague-Dawley rats. Rachitic changes were observed when the rats were feed a diet for 4 weeks containing 950 mg Sr/kg bw/day and 0.69% calcium but not when the dietary calcium was raised to 1.6% (Engfeldt and Hjerquist 1969 – quoted from IRIS 2002).

Studies indicate that excess strontium indirectly suppresses the activation of vitamin D3 in the kidney, which severely reduces the expression of calbindin D mRNA and the translation of calbindin D protein (a calcium-binding protein involved in absorption) in the duodenum. As a result, duodenal absorption of calcium is reduced (Armbrecht et al. 1979,1998, Omdahl and DeLuca 1972 – quoted from ATSDR 2004).
Several in vitro experiments have demonstrated that strontium, although less efficient than calcium, is able to stimulate histamine release from rat mast cells (Alm and Bloom 1981a,1981b, Atkinson et al. 1979, Foreman 1977, Foreman and Mongar 1972a,1972b, Foreman et al. 1977 – quoted from ATSDR 2004). This is probably relevant to humans, since strontium has been shown to degranulate human lymphocytes (Neighbor et al. 1982 – quoted from ATSDR 2004) and stimulate the release of 5-hydroxytryptamine by human platelets (Best et al. 1981 – quoted from ATSDR 2004).

3 Human toxicity

3.1 Single dose toxicity

No data have been found

3.2 Irritation

No data have been found

3.3 Sensitisation

In a case report a 35-year-old female developed an anaphylactic reaction upon inhaling fumes from a flare that contained approximately 31% strontium as strontium nitrate. The ingredients of the flare included potassium perchlorate, sulphur and sawdust/oil binder and thus the exact contribution of strontium to the development of anaphylaxis in this case is uncertain.

3.4 Repeated dose toxicity

An epidemiological study was carried out in the Ulaş Health Region of Sivas, Turkey, to determine whether higher levels of strontium in the soil might be a contributing factor to the high prevalence of childhood rickets, 32% compared to 4.4% nationally among children aged up to 5 years. Soils surrounding 55 villages were characterized as to strontium concentration (Group 1, >350 ppm; Group 2, <350 ppm). A total of 2140 children (ages 6-60 months) from these localities (613 in Group 1 and 1527 in Group 2) were examined for one or more signs of rickets: craniotabes (localized craniomalacia or thinning of cranium), rachitic rosary (beadlike growths at the ends of ribs where they join cartilage), conspicuous bulging at the wrist, bony deformities of the legs (bowleg, knock-knee), and delayed closure of the fontanelles. A significantly higher proportion of Group 1 children had one or more rachitic signs than those in Group 2: 31.5% vs. 19.5%. In addition, the severity of disease (number of rachitic signs per child) was higher in Group 1 compared to Group 2. The children were divided into subgroups in order to investigate the effect of other variables. The proportion of children with any signs of rickets was shown to be significantly higher in Group 1 than in Group 2 for the all subgroups, except three subgroups: aged 6-12, 13-18, 25-36 and 37-48 month (not 19-24 and 49-60 subgroup); those breast fed for less than four, 4-6, 7-12 and 13-24 month (not 24+ subgroup); those evaluated as above the 3rd centile or below the 3rd centile in height; and those evaluated as above the 3rd centile or below the 3rd centile in weight ($p<0.01$-0.05).The authors attributed the higher incidence of rickets in Group 1 children to their diet, which, after weaning, is mainly based on grains grown in strontium-rich soil (Özgür et al. 1996).

An epidemiological study examined the relationship between trace metals, including strontium, in drinking water and the rates of various kinds of vascular disease in 24 communities in the lowest quartile of the economic scale in Texas. The concentration of strontium was measured in samples of drinking water and 2,187 urine samples from subjects (aged 5-97 years) in families that had resided within their respective

communities for at least 10 years. There was a significant correlation between mean strontium levels in drinking water and in the urine. However, the only statistically significant correlation observed was between strontium (in urine and in drinking water) and a decreased community mortality rate (in people over 45 years old) for hypertension with heart disease (Dawson et al. 1978 – quoted from ATSDR 2004).

3.5 Toxicityto reproduction

No *in vivo* data have been found.

Results of one *in vitro* study suggest that stable strontium is not directly harmful to human spermatozoa. In developing an improved method to be used by fertility clinics for testing the functional capacity of human spermatozoa, it was found that inclusion of strontium chloride in the testing medium improved the rate of penetration compared to calcium chloride (Mortimer 1986, Mortimer et al. 1986 – quoted from ATSDR 2004).

3.6 Mutagenic and genotoxic effects

No data have been found

3.7 Carcinogenic effects

In one case-control study, no association was found between the incidence of liver cancer in 1984 on Chongming Island in China and the levels of stable strontium detected in hair (Wang et al. 1990 – quoted from ATSDR 2004).

4 Animal toxicity

4.1 Single dose toxicity

For strontium nitrate, the oral LD_{50} for mice was reported to be 2350 mg Sr/kg bw in males (Llobet et al. 1991a – quoted from ATSDR 2004).

For strontium chloride administered by gavage, the oral LD_{50} for albino mice was reported to be 2900 mg Sr/kg bw for males and 2700 mg strontium/kg bw for females (Ghosh et al. 1990 – quoted from ATSDR 2004).

4.2 Irritation

No data have been found

4.3 Sensitisation

No data have been found

4.4 Repeated dose toxicity

The oral studies on strontium compounds included in ATSDR (2004) and IRIS (2002) are summarised in Table 4.4 and supplementary information on the studies is given in the text. The NOAELs and LOAELs presented in this section are those stated in the reviews and criteria documents.

Rats, 6 days (Armbrecht et al. 1998 quoted from ATSDR 2004):
The dose was sufficient to suppress the serum levels of activated vitamin D and the concentrations of calbindin D protein (two calcium-binding proteins induced by vitamin D).

Rats, 2 weeks (Kroes et al. 1977 – quoted from ATSDR 2004):
Strontium was detected in bone following ingestion of 11 or 110 mg/kg bw/day, but not at lower doses (0.1 or 1.0 mg/kg bw/day).

Rats, 2 weeks (Kshirsagar 1976 – quoted from ATSDR 2004):
Giving the rats a normal low-strontium diet for 2 weeks reversed the decreases in body weight gain, the decreases in acid and alkaline phosphatase activities in the small intestine and the decreases in acid phosphatase activity (8%) in the livers.

Rats, 3 weeks (Neufeld and Boskey 1994 – quoted from ATSDR 2004):
The ash weight (mineral content) of metaphyseal bone was reduced and the complexed acidic phospholipid content (lipid nucleator of bone mineral) was significantly higher than in controls. Large areas of non-mineralised bone (osteoid) were observed in epiphyseal bone and secondary spongiosa. The epiphyseal plates

were abnormally wide and the metaphyses were abnormally long and dense. The diaphyses contained localized areas of decreased bone density. The primary

Table 4.4. Animal repeated dose toxicity studies on strontium, oral administration

Species/strain	Duration/ Dose levels/ Chemical form	Effects (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Reference
Rats Young, adult, old	6 days 0, 0.8% strontium in diet low in calcium	↓ Activation of vitamin D3 ↓ Concentration of calcium binding protein ↓ Absorption of calcium			Armbrecht et al. (1998–– in ATSDR 2004)
Rats/♂♀) Adult SPF Wistar	2 weeks 0, 0.1, 1.0, 11, 110 mg Sr/kg bw/day Strontium chloride in diet adequate in calcium and vitamin D	110: No effect on bones, no histological changes, no renal effects, no effect on body weight, no effects on serum levels of calcium, phosphorus, or magnesium, no behavioural effects ↑ Total number of erythrocytes (FM) ↑ Leucocyte count (M)	110 (Hemato, Skel, hepatic, renal, bd wt) (ATSDR)		Kroes et al. (1977 - in ATSDR 2004)
Rats/♂ Weanling 3 weeks Wistar	2 weeks 0, 3000 mg Sr/kg bw/day Strontium phosphate in diet	↓ Acid and alkaline phosphatase activities in small intestine and liver ↑ Phosphatase activities in bone ↓ Body weight gain (62%)		3000 (gastro, skel, hepatic, bd wt) (ATSDR)	Kshirsagar (1976 - in ATSDR 2004)
Rats/♂ Weanling SD 100-125 g	3 weeks 0, 500 mg Sr/kg bw/day Strontium carbonate in diet adequate in calcium, phosphorus, and vitamin	No effect on body weight, no effects on serum levels of calcium, phosphorus, or magnesium Abnormalities of bone structure and bone mineralisation	500 (bd wt, metab) (ATSDR)	500 (skel) (ATSDR)	Neufeld and Boskey (1994 - in ATSDR 2004)
Rats/♂ Weanling 21 days England Wright Y	20 days 0, 1850 mg/kg bw/day Form unspecified in diet adequate in calcium, phosphorus and vitamin D	No effects on serum levels of calcium, phosphorus, or magnesium Abnormalities of bone organization	1850 (metab) (ATSDR)	1850 (skel, bd wt) (ATSDR)	Reinholt et al. (1984 - in ATSDR 2004)
Rats Weanling 21 days England Wright Y	20 days 0, 1850 mg/kg bw/day Form unspecified in diet adequate in calcium, phosphorus and vitamin D	Alterations in cartilage matrix ↓ Body weight gain (28%)			Reinholt et al. (1985 - in ATSDR 2004)
Rats/♀ Young 40-60 g, adults 200-250 g 3/group	20 days Young: 0, 0.19, 0.38, 0.75, 1, 1.5, 3% Sr in diet. Adult: 0, 0.19, 0.38, 0.75, 1.5, 3% Sr in diet. The Sr intakes were calculated to be: 0, 190, 380, 750, 1000, 1500 and 3000 mg/kg-day for young rats and 0, 95, 190, 375, 750 and 1500 mg/kg-day for adult rats.	Young: 380: Cartilage plate irregular and slightly widened 750: Cartilage plate still wider 1000: Cartilage extension in the metaphysic 1500: Cartilage plate almost double width, no regular proceeding of calcification 3000: More extensive changes in cartilage	Young: 190 (IRIS) Adults: 375 (IRIS) Young: 140 (skel, bd wt) 4975 (metab) (ATDSR) Adults: 690 (skel) 2750 (bd wt, metab) (ATDSR)	Young: 380 (IRIS) Adults: 750 (IRIS) Young: 550 (skel) (ATDSR) Adults: 1370 (skel) (ATDSR)	Storey (1961)

Species/strain	Duration/ Dose levels/ Chemical form	Effects (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Reference
	ATSDR: Young: 0, 140, 550, 1080, 1460, 2220, 4975 mg/kg bw/day. Adults: 0, 170, 350, 690, 1370, 2750 mg/kg bw/day. Strontium carbonate in diet containing 1.6 % calcium and 0.9% phosphorus.	Adult: 750: Cartilage plate slightly widened, metaphyseal osteoid irregularly increased 1500: Cartilage plate appreciably wider			
Rats/M♂ SD	26 days 0, 1520 mg Sr/kg bw/day Ingested, adequate dietary calcium, phosphorus, and vitamin D	No histological changes in the parathyroid gland or alterations in parathyroid hormone levels, no effects on serum levels of calcium, phosphorus, or magnesium Abnormally thick hypertrophic zones in epiphyseal growth plates Impaired calcification and resorption at the metaphyseal side ↓ Terminal body weight (16%)	1520 (endocr, metab) (ATSDR)	1520 (skel, bd wt) (ATSDR)	Svensson et al. (1985, 1987 - in ATSDR 2004)
Rats/♀ 36 days Wistar	27 days 0, 50, 100, 510 mg Sr/kg bw/day Strontium carbonate in diet	No effect on body weight, no change in ash weight 510: Rats hypocalcemic ↓ Bone formation rate (24%) ↓ Bone resorption rate (28%) ↓ Intestinal absorption of calcium (20%) ↓ Calcium content in ashed femurs, hypocalcemic effect ↓ Serum calcium concentration (13%) 50: ↑ Calcium content of bone	100 (gastro, skel, metab) 510 (bd wt). (ATSDR)	510 (gastro, skel, metab) (ATSDR)	Morohashi et al. (1994 - in ATSDR 2004)
Rats/♂ Weanling 3 weeks Wistar	4–6 weeks 0, 580, 1270, 2820 mg Sr/kg bw/day Strontium phosphate in diet	2820: Haemorrhage ↑ Mortality rate (30%) ↓ Alkaline phosphatase activity in liver (>26%) ↓ Body weight gain (62%) 1270: Abnormally thickened epiphyseal cartilage plates in the long bones ↓ Alkaline phosphatase activity in small intestine ↓ Body weight gain (15%)	580 (gastro, skel, bd wt) 1270 (hepatic) (ATSDR)	1270 (gastro, skel, bd wt) 2820 (cardio, hepatic, 30% mortality) (ATSDR)	Kshirsagar (1976 - in ATSDR 2004)
Rats/♂ Young SD	43 days 0, 565 mg Sr/kg bw/day	Rachitic effect Osteomalacic effect		565 (skel, resp, 40% mortality, paralysis of	Johnson et al. (1968 - in ATSDR 2004)

Species/strain	Duration/ Dose levels/ Chemical form	Effects (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Reference
	Form not specified (ingestion???)	Paralysis of hind limbs Respiratory difficulties Bone abnormalities ↑ Premature death rate (40%) ↓ Sodium in bone ↑ Potassium in bone ↓ Index of bone mineralisation (percent bone ash)		hindlimbs) (ATSDR)	
Rats/♂ 28 days SD	8 weeks 0, 168 mg Sr/kg bw/day Form not specified, ingested, adequate dietary calcium, phosphorus and vitamin D	No effect on body weight, no effects on serum levels of calcium, phosphorus, or magnesium ↑ Mineral bone volume (17%) ↑ Number of bone forming sites (70%)	168 (skel, bd wt, metab) (ATSDR)		Grunpas et al. (1996 - in ATSDR 2004)
Rats/♂ Weanling SD	9 weeks 0, 316, 425, 524, 633 mg Sr/kg bw/day Strontium chloride, ingested, adequate dietary calcium (0.5%), phosphorus and vitamin D	No effect on body weight, no effects on serum levels of calcium, phosphorus, or magnesium 633: ↓ Bone calcification 316, 524: ↑ Calcified bone growth	524 (skel) 633 (bd wt, metab) (ATSDR)	633 (skel) (ATSDR)	Marie et al. (1985 – ATSDR 2004)
Rats Weanling Wistar	90 days 0, 10, 36, 146, 166 mg Sr/kg bw/day Strontium chloride in diet adequate in calcium (0.85%) and vitamin D	166: No haematological changes, no renal effects, no effects on serum levels of calcium, phosphorus, or magnesium, no behavioural effects ↑ Peripheral glycogen (F) Slight histological changes in liver	166 (Hemato, Skel, hepatic, renal, bd wt, metab) (ATSDR)		Kroes et al. (1977 - in ATSDR 2004)
Rats Young 50-70 g, adult	7 months young: 0, 2160 mg Sr/kg bw/day adult: 0, 1570 mg Sr/kg bw/day Strontium carbonate, ingested	At three weeks: Rachitic gait Spinal kyphosis Bent tibiae Irregular discoloured enamel on anterior teeth Reduced calcification Excess growth of epiphyseal cartilage Abnormal deposition of osteoid in the metaphysis Fragmentation of the epiphyseal plates (not in adults) and isolated nodules of cartilage Osteoid accumulation in skull		> 7 month:1570 (skel) 2160 (skel, bd wt) (ATSDR)	Storey (1962 - in ATSDR 2004)
Rats/♂ 4 weeks old, 50-60 g Wistar	0, 1970 mg Sr/kg bw/day Strontium carbonate in diet low in calcium (0, 0.04%)	Affected bone miniralisation (Tibial length was reduced by 33% and the tibial proximal and distal epiphyseal plates were both about 5 times wider than normal) ↓ Body weight gain (60%)		1970 (skel, bd wt) (ATSDR)	Matsumoto (1976 - in ATSDR 2004)

Species/strain	Duration/ Dose levels/ Chemical form	Effects (mg/kg bw/day)	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Reference
Rats Adult 250 g RVH hooded, 4 groups of 12 rats	3 years 0, 70, 147 and 263 mg Sr/kg bw/day Strontium chloride in drinking water with adequate amounts of calcium (0.35 ppm) and magnesium (0.0682 ppm)	No histological abnormalities in bone No evidence for changes in organ morphology	263 (IRIS)		Skoryna (1981a - in IRIS 2002)
Mice/♂ 21 days C57BL/6J	29 days 0, 350 mg Sr/kg bw/day Strontium chloride in drinking water. Adequate dietary calcium, phosphorus and vitamin D	No effect on tibial length or bone mineral content, no effect on body weight, no effects on serum levels of calcium, phosphorus, or magnesium ↑ Osteoid surface (10%) ↓ Number of active osteoclasts (11%)	350 (bd wt, metab)	350 (skel) (ATSDR)	Marie and Hott (1986 - in ATSDR 2004)

↓: Reduced
↑: Increased
Bd wt = body weight
Cardio = cardiovascular
Endocr = endocrine
Gastro = gastrointestinal
♀: Female
♂: Male
Hemato = haematological
Metab = metabolic
Skel = musculoskeletal

spongiosa of the proximal tibia was longer and the trabeculae was disorganized and apparently disconnected from the overlying calcified cartilage.

Rats, 20 days (Reinholt et al. 1984 – quoted from ATSDR 2004):
The mean thickness of the epiphyseal growth plate was 70% larger than normal. In the epiphyseal regions of long bones, the volume of each zone was larger than its normal counterpart, and in addition, the relative sizes were altered; the proportional volumes of the resting, proliferative, and calcifying zones were significantly smaller and that of the hypertrophic zone was significantly larger than normal. There was an increase in the volume of extracellular matrix in bone, suggested to be associated with a reduced rate of extracellular matrix vesicle degradation.

Rats, 20 days (Reinholt et al. 1985 – quoted from ATSDR 2004):
In the epiphyseal cartilage in the rats, alterations were observed in the proteoglycan composition (slightly higher galactosamine content), chondroitin sulfate chain lengths (larger), regional distributions of large and small chondroitin sulfate peptides, and regional distributions of both non-sulfated chondroitin sulfate disaccharides and hyaluronic aciddisaccharides.

Rats, 20 days (Storey 1961):
The strontium intakes were calculated, by using the approach recommended in an OECD guidance note (OECD 2002), an approach which is used by several international bodies including OECD, the Joint FAO/WHO Expert Committee on Food Additives (JECFA), the Joint FAO/WHO Expert Committee on pesticide Residues (JMPR), the European Food Safety Authority (EFSA) as well as by the National Food Institute in Denmark. The intakes were calculated, in accordance with IRIS (2002), to be 0, 190, 380, 750, 1000, 1500 and 3000 mg/kg/day for young rats and 0, 95, 190, 375, 750 and 1500 mg/kg/day for adult rats, assuming young rats consume 10% and adult rats consume 5% of their body weight (young rat = 100 g og adult rat = 400 g) in food per day. In this study by Storey, the actually weights of the young and adult rats were 40-60 g and 200-250 g, respectively. The intakes in ATSDR (1999) were calculated using an approach that was not further specified. According to the authors histological examinations can be used as a sensitive indicator of the degree of bone calcification by measuring the width of the epiphyseal cartilage plate. Young rats were affected more severely at lower dietary strontium levels than were adult rats. In young rats, at dose levels above 1080 mg/kg bw/day the cartilage plate was so irregular that measurements were unreliable.

Rats, 4-6 weeks (Kshirsagar 1976 – quoted from ATSDR 2004):
The decrease in alkaline phosphatase activity in the small intestine at 1270 mg Sr/kg bw/day was partly reversed by feeding the rats a normal low-strontium diet for 2 weeks. There was radiographic evidence of abnormally thickened epiphyseal cartilage plates in the long bones of the rats exposed to a dose level of 2820 mg Sr/kg bw/day, but no effect was observed at 580 mg Sr/kg bw/day and little effect at 1270 mg Sr/kg bw/day.

Rats, 43 days (Johnson et al. 1968 – quoted from ATSDR 2004):
Unmineralized osteoid was visible in histological sections of vertebrae.

Rats, 9 weeks (Marie et al. 1985 – quoted from ATSDR 2004 and IRIS 2002):
The purpose of this study was to determine the effect of low doses of stable strontium on mineral homeostasis and bone histology. Reduced bone calcification observed at 633 mg Sr/kg bw/day, resulted in slow growth rate; and a decreased double-labelled osteoid surface, which frequently resulted in defective long bone growth.

Rats, 90 days (Kroes et al. 1977 – quoted from ATSDR 2004):
The relative thyroid weight was significantly increased in males at 36 and 146 mg Sr/kg bw/day and the relative pituitary weight was significantly decreased in females at 10 and 166 mg Sr/kg bw/day, but in neither case was there a clear dose-response. Slight histological changes in the thyroid were reported. No hepatic effects were observed in either sex ≤146 mg Sr/kg bw/day.

Rats, 7 months (Storey 1962 – quoted from ATSDR 2004)
The study demonstrated that ingestion of strontium resulted in more severe skeletal effects in young animals than in adults. Adult rats were affected by strontium ingestion in the same way, but to a lesser degree than young animals. Abnormal depositions of osteoid in long bones and skull were not as extensive as in young rats. The epiphyseal plate did not become fragmented. Tooth enamel was abnormally white and pitted. Body weight gain was about a third lower than controls in the young rats. No quantitative body weight data were reported for young or adult animals.

Rats (Matsumoto 1976 – quoted in ATSDR 2004)
Microradiographic and histological analyses of tibial proximal heads revealed that no mineralisation was detectable; that the organization of chondroblasts was irregular, and that osteoid rather than mineralised bone was deposited.

Rats, 3 years (Skoryna 1981, Skoryna and Fuskova, 1981 – quoted from IRIS 2002):
The dose levels estimated in IRIS (2002) are based on the assumption that an adult rat consumes water at a rate of 49 mL/day. The animals were weighed and examined weekly. The animal tissues from different organs (kidney, lungs, adrenal, brain, heart and muscle) were examined on gross and histological levels. No evidence of changes in morphology was observed; organs were not weighed. The concentration of strontium in tissues was determined by heated graphite atomization. In addition, strontium levels in the animals' serum were analysed by standard atomic absorption spectrophotometry. Except for bone, no organ predilection for strontium was observed in either group.

Mice, 29 days (Marie and Hott 1986 – quoted from ATSDR):
In vertebrae, strontium had no effect on the osteoblastic surface (percent endosteal surface showing plump osteoblasts), bone matrix apposition rate, osteoid seam thickness (average width of all endosteal osteoid seams), or calcified bone volume. However, exposure to strontium resulted in a 10% increase in osteoid surface (percent endosteal surface covered by an osteoid seam) and an 11% reduction in the number of active osteoclasts.

4.5 Toxicityto reproduction

Pregnant female Wistar rats (3/group) were administered subcutaneous doses of 10.3, 20.7, 41.4 or 82.8 mg Sr/kg bw/day as strontium nitrate during gestational days 9-19. No effects were seen on the size or body weight of foetuses, litter sizes or the number of resorption sites. Skeletons and zones of calcification were normal and no histological changes were seen in soft tissues. Although this study reported no teratogenic effects of strontium, the small number of dams exposed and fetuses examined preclude a definite evaluation of the results (Lansdown et al. 1972 – quoted from IRIS 2002 and ATSDR 2004).

4.6 Mutagenic and genotoxic effects

Positive results were reported for strontium chloride in a mice bone marrow clastogenicity study. Oral administration of strontium chloride induced chromosomal aberrations in bone marrow cells in a degree that was directly proportional to the concentrations used (males 260, 8667, 2600 mg/kg bw and females 240, 800, 2400 mg/kg bw). The increase was statistically significant compared to the control (Ghosh et al. 1989).

4.7 Carcinogenic effects

No data have been found.

5 Regulations

5.1 Ambient air

-

5.2 Drinking water

US-EPA (2004): DWEL (Drinking water equivalent level): 20 mg/l
Life time: 4 mg/l.

5.3 Soil

-

5.4 Occupational Exposure Limits

-

5.5 Classification

-

5.6 IARC

-

5.7 US-EPA

Oral reference dose (RfD) of 0.6 mg/kg bw/day, based on a NOAEL of 190 mg Sr/kg bw/day (as $SrCO_3$) for rachitic bone observed in 20 day, 9 week and 3 year oral studies in young and adult rats (Storey, 1961, Marie et al., 1985 and Skoryna, 1981) and a uncertainty factor of 300 consisting of 10 for species-to-species extrapolation and 10 for an incomplete database (including a lack of developmental and reproductive data) and to account for uncertainties in using data for strontium carbonate to derive a risk estimate that may apply to other salts of strontium. An uncertainty factor of 3 was applied for sensitive subpopulations; a factor of 10 was not warranted because the critical study was performed in young animals, a recognized sensitive subpopulation (IRIS 1996).

6 Summary and evaluation

6.1 Description

Elemental strontium is not radioactive and exists in four stable isotopes (^{84}Sr, ^{86}Sr, ^{87}Sr, ^{88}Sr). Radioactive isotopes of strontium, of which ^{89}Sr and ^{90}Sr are the most important, are formed in nuclear plant reactors and during nuclear weapon explosions and thus not occurring naturally. Elemental strontium is a commonly occurring alkaline earth metal and can exist in the oxidation states 0 and +2. It belongs to group IIA of the periodic table and behave similar chemically to magnesium and calcium, also belonging to this group. Elemental strontium is highly reactive and exists only under normal environmental conditions associated with other elements.

6.2 Environment

Strontium is a naturally occurring element that makes up approximately 0.02-0.03% of the earth's crust. Strontium ore is found in nature as the minerals celestite ($SrSO_4$) and strontianite ($SrCO_3$). It is widely distributed throughout the earth with typical concentrations in most materials of a few mg/kg.

Strontium is released to surface water and groundwater by the natural weathering of rocks and soils and from the discharge of wastewater directly into streams and aquifers. Elevated concentrations of strontium can be found in basins with low groundwater flow. Groundwater basins with a high flow will only contain limited concentrations of strontium due to leach out. In Denmark reported values of strontium concentrations in groundwater are in the range 0.28 mg/l to 53 mg/l. US-EPA measured strontium in drinking water in different parts of the United States to be less than 1 mg/l.

Strontium is released into the atmosphere primarily as a result of natural sources, such as sea spray, entrainment of dust particles and re-suspension of soil by wind. Emissions from burning coal and oil, land application of phosphate fertilizers and using pyrotechnic devices increase strontium levels in air. The average amount of strontium that has been measured in air from different parts of the United States is 20 ng/m^3. In Denmark the yearly average amount of strontium in air is in the range 1-5 ng/m^3.

Strontium is found naturally in soil where the disposal of coal ash, incinerator ash, industrial wastes and land application of phosphate fertilizers may increase the concentration of strontium in soil. The amounts of strontium in soil vary over a wide range, but the average concentration is 240 mg/kg. Soil to plant concentration ratios for strontium are 0.017–1.0 (ratio of strontium in wet vegetation to strontium in dry soil) and indicate that strontium can be easily absorbed into plants from soil. The highest concentrations of strontium in foodstuffs are observed in leafy vegetables, such as cabbage containing approximately 64.2 mg Sr/kg dry weight.

6.3 Human exposure

The intake of strontium is primarily from food and drinking water but exposure to strontium can also result from inhalation or incidental ingestion of soil or dust contaminated with strontium

Using the highest reported concentrations of strontium in Danish ground water of 53 mg/l (Roskilde Amt report 2005), and the consumption rate of 0.08 l/kg bw/day (for children 1-10 years old), the intake from drinking water would be 4.2 mg Sr/kg bw/day (assuming no dilution of groundwater). For an adult (body weight of 70 kg), the daily exposure of strontium from drinking water would be 297 mg.

In a total diet study in the United Kingdom, the total dietary exposure to strontium was estimated to be 1.3 mg/day. In an Australian Market Basket Survey, the estimated daily intakes of strontium for female adults ranged from 0.89 to 1.2 mg/day. For 6-month-old infants fed exclusively breast milk or infant formula, the estimated daily intakes of strontium were 47 and 254 µg/day, respectively.

Using the yearly average atmospheric concentration in Denmark of 5 ng Sr/m^3 and assuming the inhalation rate as 0.5 m^3/kg bw/day (for children 1-5 years old), the inhalation exposure of strontium will be 2.5 ng Sr/ kg bw/day. For an adult (body weight of 70 kg), the daily exposure of strontium from air would be 175 ng.

6.4 Toxicokinetics

Strontium compounds are absorbed after oral intake. Studies in infants and children indicate that of the ingested strontium approximately 15-30% is absorbed from the gastrointestinal tract. From data on ^{90}Sr concentration in bone, it was estimated that the adult skeleton took up approximately 4.75% of the dietary intake of strontium and the skeleton of infants and adolescents took up approximately 10 %. In adult rats, the absorption of strontium after a single oral dose of $SrCl_2$ was reported to be 19%. In lactating rats administered $SrCl_2$ in drinking water, 11% of the dose was absorbed compared to 5% non-lactating rats. Age-related changes in absorptions have been reported in rats ranging from an 85% absorption at 15 days of age to an 8% absorption at ages older than 89 days. In addition to age, factors affecting absorption include strontium compound solubility and composition of the diet e.g. phosphorus, vitamin D and calcium levels. Calcium absorption is higher during pregnancy and lactation, and studies in animals suggest that strontium absorption may also be higher. Inhalation studies in animals and accidental exposure of workers demonstrate that inhaled strontium compounds can be absorbed. Strontium compounds are not readily absorbed across the skin of humans.

Following absorption, strontium accumulates in the body with 99% of the total body burden in the skeleton. The remainder of the strontium in the body is found in soft tissues. Several studies provide evidence for the transfer of strontium to the foetus through the placenta and to infants through breast milk of exposed mothers. Strontium is eliminated from the body through urine and faeces, following inhalation and oral exposure.

Exposure to excess strontium can lead to rachitic changes that are due to strontium's ability to substitute the binding of calcium to the hydroxyapatite crystals during bone calcification, inhibiting the calcification of eiphyseal cartilage, or by displacing calcium from existing calcified matrix. Strontium may also prevent the normal maturation of chondrocytes in the epophyseal plates of long bones.

Because children absorb strontium at higher amounts than adult and because they have actively growing bones, they are more susceptible to the effect of strontium than adults. In adult rats, the incorporation of strontium into the skeleton is relatively higher compared to other mammals due to differences in bone physiology. Although reduced after the age of 12 months, bone growth in rats continues throughout life.

6.5 Human toxicity

6.5.1 Single dose toxicity

No human data regarding single dose toxicity of stable strontium compounds have been found.

6.5.2 Irritation and sensitisation

In a case report a 35-year-old female developed an anaphylactic reaction upon inhaling fumes from a flare that contained approximately 31% strontium as strontium nitrate. As the flare included potassium perchlorate, sulfur and sawdust/oil binder, the exact contribution of strontium to the development of anaphylaxis in this case is uncertain.

6.5.3 Repeated dose toxicity

An epidemiological study was carried out in the Ulaş Health Region of Sivas, Turkey. A total of 2140 children (ages 6–60 months) were examined for one or more signs of rickets. A significantly higher proportion of Group 1 children (living in areas with >350 ppm Sr in soil) had one or more rachitic signs than those in Group 2 children (living in areas with <350 ppm Sr in soil): 31.5% vs. 19.5%. In addition, the severity of disease (number of rachitic signs per child) was higher in Group 1 compared to Group 2. The children were divided into subgroup in order to investigate the effect of other variables. The proportion of children with any signs of rickets was shown to be significantly higher in Group 1 than in Group 2 for the all subgroups, except three subgroups: aged 6-12, 13-18, 25-36 and 37-48 month (not 19-24 and 49-60 subgroup); those breast fed for less than four, 4-6, 7-12 and 13-24 month (not 24+ subgroup); those evaluated as above the 3rd centile or below the 3rd centile in height; and those evaluated as above the 3rd centile or below the 3rd centile in weight ($p<0.01$-0.05).The authors attributed the higher incidence of rickets in Group 1 children to their diet, which, after weaning, is mainly based on grains grown in strontium-rich soil

In an epidemiological study the relationship between trace metals, including strontium, in drinking water and the rates of various kinds of vascular disease was examined. The concentration of strontium was measured in samples of drinking water and 2187 urine samples from subjects (aged 5-97 years) in families that had resided within their respective communities for at least 10 years. There was a significant correlation between mean strontium levels in drinking water and in the urine. However, the only statistically significant correlation observed was between strontium (in urine and in drinking water) and a decreased community mortality rate (in people over 45 years old) for hypertension with heart disease.

6.5.4 Toxicity to reproduction

Data from an *in vitro* study suggest that stable strontium is not directly harmful to human spermatozoa. In developing an improved method to be used by fertility clinics for testing the functional capacity of human spermatozoa, it was found that inclusion of strontium chloride in the testing medium improved the rate of penetration compared to calcium chloride.

6.5.5 Mutagenic and genotoxic effects

No human data regarding mutagenic and genotoxic effects following exposure to strontium compounds have been found.

6.5.6 Carcinogenic effects

In one case-control study, no association was found between the incidence of liver cancer and the levels of stable strontium detected in hair.

6.6 Animal toxicity

6.6.1 Single dose toxicity

In mice the oral LD_{50}-value for strontium nitrate was 2350 mg Sr/kg bw in males. For strontium chloride the oral LD_{50}-values were 2900 mg Sr/kg bw in males and 2700 mg Sr/kg bw in females.

6.6.2 Irritation and sensitisation

No animal data regarding irritation or sensitisation following exposure to stable strontium have been found.

6.6.3 Repeated dose toxicity

The toxicity of strontium compounds following repeated exposure have been studied in rats and mice using the oral route, in studies with durations ranging from 6 days to 3 years. Following oral administration (dietary, drinking water) skeletal effects were observed in rats at dose levels from 500 mg Sr/kg bw/day (bone mineralisation and structure affected – strontium carbonate in diet for 3 weeks). In a study in mice skeletal effects were observed at 350 mg Sr/kg bw/day (10% increase in osteoid surface and an 11% reduction in the number of active osteoclasts – strontium chloride in drinking water, adequate dietary calcium, phosphorus and vitamin D for 29 days). For further details see Section 4.4 and Table 4.4.

A number of other effects in rats have been reported following oral exposure to strontium. Effects on body weight were observed in rats from 1520 mg Sr/kg bw/day. Reduced alkaline phosphatase activities in the liver and an increased mortality rate were reported in rats at 2820 mg Sr/kg bw/day. In one study paralysis of hind limbs, respiratory difficulties and increase in premature death rate were reported in rats fed 565 mg Sr/kg bw/day.

6.6.4 Toxicity to reproduction

In pregnant female Wistar rats administered subcutaneous doses of up to 82.8 mg Sr/kg bw/day as strontium nitrate during gestational days 9-19, no effects were seen on the size or body weight of foetuses, litter sizes or the number of resorption sites. Skeletons and zones of calcification were normal and no histological changes were seen in soft tissues.

6.6.5 Mutagenic and genotoxic effects

Strontium chloride orally administrated to mice induced chromosomal aberrations in bone marrow cells in a degree that was directly proportional to the concentrations used. The increase was statistically significant compared to the control.

6.6.6 Carcinogenic effects

No animal data regarding carcinogenic effects following exposure to stable strontium have been found.

6.7 Evaluation

The intake of strontium is primarily from food and drinking. Human data indicate that soluble strontium is absorbed following oral intake and inhalation but are not readily absorbed across the skin. In infants and children the absorption of dietary strontium is approximately 15-30%. The uptake of strontium by the skeleton is approximately 4.75% in adults and 10% in infants and adolescents. In adult rats, the absorption of strontium after a single oral dose of $SrCl_2$ was reported to be 19%. Calcium absorption is higher during pregnancy and lactation, and studies in animals suggest that strontium absorption may also be higher. The distribution of absorbed strontium in the human body is similar to that of calcium, with approximately 99% of the total body burden in the skeleton. Several studies provide evidence for the transfer of strontium to the foetus through the placenta and to infants through breast milk of exposed mothers. Strontium is eliminated from the body through urine and faeces.

The incorporation of strontium into the skeleton may be relatively higher in adult rats compared to humans. The epiphyseal growth plate of the long bones of rats never entirely transforms into bone after sexual maturity and thus bone growth in rats continues throughout life.

Stable strontium is of relatively low acute toxicity. In experimental animals, an oral LD_{50}-value for strontium nitrate in male mice of 2350 mg Sr/kg bw and for strontium chloride in male and female mice of 2900 and 2700 mg Sr/kg bw respectively has been reported.

In one case report anaphylaxis was seen in a 35-year-old female after inhaling of fumes from a flare that contained approximately 31% strontium as strontium nitrate. The flare content included potassium perchlorate, sulphur and sawdust/oil binder, and thus the exact contribution of strontium to the development of anaphylaxis in this case is uncertain. Nevertheless, as supporting data indicate that large concentrations of stable strontium can stimulate the release of histamine from mast cells, it is conceivable that a local high concentration of strontium in the

respiratory tract can elicit histamine release. No data regarding irritation following exposure to stable strontium compounds have been found. The available data are not considered adequate in order to evaluate the irritation and sensitisation potentials of stable strontium compounds.

Strontium causes adverse effects on bones (abnormalities of bone organization and bone mineralization) in experimental animals following repeated exposure to high doses. The association between strontium levels in the diet or drinking water and effects on bone has been investigated in several studies in rats with durations ranging form 6 days and up to 3 years, see table 4.4. A NOAEL for bone effects was found in 12 studies and were in the range 100 to 690 mg Sr/kg bw/day. A LOAEL for bone effects was found in 14 of the studies in rats and were in the range 510 to 3000 mg Sr/kg bw/day. In one study in mice a LOAEL of 350 mg Sr/kg bw/day was found. In general effects on bone were less severe in adult rats compared to young rats. A NOAEL of 190 mg Sr/kg bw/day is considered for skeletal toxicity in young rats, based on the study by Story (1961). This NOEAL might be associated with uncertainties related to the standardised estimation of the dose levels from the concentrations in the feed using the assumption that the weights of young and adult rats are 100 g and 400 g, respectively. In the critical study by Storey, the actually weights of the young and adult rats were 40-60 g and 200-250 g, respectively.

Human data on strontium toxicity are limited. In an epidemiological study carried out in the Ulas Health Region of Sivas, Turkey, it was investigated whether higher levels of strontium in the soil might be a contributing factor to the high prevalence of childhood rickets, 32% compared to 4.4% nationally among children aged up to 5 years. Soils surrounding 55 villages were characterized as to strontium concentration (Group 1, >350 ppm; Group 2, <350 ppm). A total of 2140 children were examined for one or more signs of rickets. A significantly higher proportion of Group 1 children had one or more rachitic signs than those in Group 2 (31.5 vs 19.5%. Another epidemiological study examined the relationship between trace metals, including strontium, in drinking water and the rates of various kinds of vascular disease in 24 communities in the lowest quartile of the economic scale in Texas. The only statistically significant product-moment relationship for strontium (in urine and in drinking water) was for a decreased community mortality rate (in people over 45 years old) for hypertension with heart disease.
No toxic effects of stable strontium have been reported for humans at the exposure levels normally encountered in the environment but the epidemiological study in Turkey indicates that rickets may pertain to humans under special circumstances. Factors that have been shown to be important in the development of rickets from strontium exposure include age and dietary intake of phosphorus, calcium and vitamin D. Insufficiency of vitamin D can also by itself cause rickets.

Data on reproductive and developmental toxicity of stable strontium compounds are limited. Results from an in vitro study suggest that stable strontium is not directly harmful to human spermatozoa and in a study in pregnant rats no effects were seen on foetuses at doses up to 82.8 mg Sr/kg bw/day. However, due to limitations in the studies, the available data are not considered adequate in order to evaluate the reproductive and developmental potentials of stable strontium compounds.

Positive results were reported in a mice bone marrow clastogenicity study after oral administration of strontium chloride in doses from 240-2800 mg/kg bw. However, due to limited reporting of the results in this study as well as the lack of other studies on mutagenicity and genotoxicity, no firm conclusion can be drawn regarding genotoxicity.

There are no data regarding cancer in humans or animals resulting from exposure to stable strontium compounds and thus no conclusion can be drawn regarding this endpoint.

6.7.1 Critical effect and NOAEL

Animal data indicate that skeletal effects are the critical effects following oral exposure to stable strontium compounds. Adverse effects were observed on bone development following ingestion of high doses in experimental animals. Young rats were affected more severely at relatively lower dietary strontium levels than were adult rats. There are no direct dose-response data for adverse effects of exposure to stable strontium in humans, but epidemiological data suggest that the oral toxicity observed at high doses in experimental animals may pertain to humans under special circumstances.

A NOAEL for skeletal effects of 190 mg Sr/kg bw/day is considered for rats exposed to strontium carbonate and will form the basis for the purpose of estimating quality criteria in drinking water.

7 TDI and quality criteria

7.1 TDI

The TDI is calculated based on a NOAEL of 190 mg Sr/kg bw/day observed for skeletal effects in young rats:

$$TDI = \frac{NOAEL}{UF_I * UF_{II} * UF_{III}} = \frac{190\ mg/kg\ bw/day}{10 * 5 * 5} = 0.76\ mg/kg\ bw/day$$

The uncertainty factor UF_I accounting for interspecies variability is set to 10 assuming that humans are more sensitive than animals. The UF_{II} accounting for intraspecies variability is set to 5 reflecting the range in biological sensitivity within the human population. As the critical study was performed in young animals, the most sensitive subgroup regarding skeletal effects of strontium, a UF_{II} of 10 is not warranted. The UF_{III} is set to 5 because of inadequate data on reproductive toxicity, genotoxicity and cancer, and because of the uncertainties in the estimation of the dose levels from the dietary concentrations in the critical study.

7.2 Allocation

The general population is predominantly exposed to strontium from drinking water and food.

In Denmark, the latest reported values of strontium in ground water are in the range of 0.28 to 53 mg/l. Using the highest reported concentrations of 53 mg/l, and the consumption rate of 0.08 l/kg bw/day (for children 1-10 years old), the intake of strontium from drinking water would be 4.2 mg Sr/kg bw/day (assuming no dilution of groundwater). For an adult (body weight of 70 kg), the daily exposure of strontium from drinking water would be 297 mg.

According to reported estimates in the UK (Ysart et al. 1999), the human total dietary exposure to strontium is 1.3 mg/day (contribution from drinking water is not included).

According to USGS (US Geological Survey), the highest concentrations of strontium in foodstuffs are observed in leafy vegetables, such as cabbage containing approximately 64.2 mg Sr/kg dry weight.

According to US-EPA, the average concentration of strontium in soil is 240 mg/kg.

No allocation is suggested in relation to drinking water as the contribution of strontium from food is considered as being low compared to the contribution of strontium from the drinking water.

7.3 Quality criterion in drinking water

The quality criterion in drinking water QC_{dw} is calculated based on the TDI of 0.63 mg/kg bw/day and assuming a daily ingestion of 0.08 l/kg bw of drinking water for children 1-10 years old:

$$QC_{dw} = \frac{TDI * Y}{ingestion_{dw}} = \frac{0.76 \text{ mg/kg day} * 1}{0.08 \text{ l/kg bw/day}}$$

$$= 9.5 \text{ mg/l}$$

7.3.1 Quality criterion in drinking water

10 mg/l

8 References

At (2002). Grænseværdier for stoffer og materialer. Arbejdstilsynets At-vejledning C.0.1, oktober 2002.

ATSDR (2004). Toxicological Profile for strontium. ATSDR/TP-04/Strontium, U.S. Department of Health & Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry.

IRIS (2002). Strontium. In: Integrated Risk Information System. Database quest, last revised: 12/03/2002. US-EPA.

ChemFinder: http://chemfinder.cambridgesoft.com/.

ChemIDplus Advanced: http://chem.sis.nlm.nih.gov/chemidplus/

DMU (2006). Personal communication from the National Environmental Research Institute.

Davidson S, Passmore R, Brock JF and Truswell AS (1979). Human nutrition and dietetics. 7.edition, Churchill Livingstone.

Ghosh S, Talukder G and Sharma A (1990). Clastogenic activity of strontium chloride on bone marrow cells in Vivo. Biol Trace Elem Res 25(1), 51-56.

GRUMO (2000). Grundvandsovervågning i Nordjyllands Amt 2001.

GRUMO (2003). Grundvandsovervågning i Nordjyllands Amt 2003.

HSDB (2003). Strontium, elemental. In: Hazardous Substances Data Bank: http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~FTRrv5:1

IARC (1990). Chromium and chromium compounds. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. International Agency fro Research on Cancer. Lyon, France. Vol.49, pp.49-256.

MM (2002). The Statutory Order from the Ministry of the Environment no. 439 of 3 June 2002, on the List of Chemical Substances.

MM (2001). Bekendtgørelse om vandkvalitet og tilsyn med vandforsyningsanlæg. Miljø- og Energiministeriets bekendtgørelse nr. 871 af 21. september 2001.

Mosekilde L, Nielsen LR and Vestergaard P (2005). Ugeskrift for Læger 167/37, 3485-3487.

Nabrzyski M and Gajewska R (2002). Content of strontium, lithium and calcium in selected milk products and in some marine smoked fish. Nahrung/Food 46 (3) 204-208.

OECD (2002). Guidance notes for analysis and evaluation of chronic toxicity and carcinogenicity studies. OECD environmental, health and safety publications.

Series on testing and assessment no. 35 and series on pesticides no. 14. ENV/JM/MONO(2002)19.

Özgür S,Sümmer H and Kocoglu G (1996). Rickets and soil strontium. Arch Dis Child 75, 524-526.

Roskilde Amt Rapport (2005). Strontium i grundvand og drikkevand, 21. juni 2005.

Storey E (1961). Strontium "richets": Bone, calcium and strontium changes.Austral Ann Med 10, 213-222.

US-EPA (2004). 2004 Edition of the drinking water standards and health advisories.

Strontium, inorganic and soluble salts

The Danish Environmental Protection Agency has requested an evaluation of health hazards by exposure to the inorganic and soluble salts of strontium. This resulted in 2008 in the present report which includes estimation of a quality criterion for the mentioned compounds in drinking water.

Danish Ministry of the Environment
Environmental Protection Agency

Strandgade 29
1401 Copenhagen K, Denmark
Tel.: (+45) 72 54 40 00

www.mst.dk