Concise International Chemical Assessment Document 77

STRONTIUM AND STRONTIUM COMPOUNDS

First draft prepared by Mr Peter Watts, Toxicology Advice & Consulting Ltd, Sutton, England; and Mr Paul Howe, Centre for Ecology and Hydrology, Monks Wood, England

Published under the joint sponsorship of the United Nations Environment Programme, the International Labour Organization and the World Health Organization, and produced within the framework of the Inter-Organization Programme for the Sound Management of Chemicals.

The **International Programme on Chemical Safety (IPCS)**, established in 1980, is a joint venture of the United Nations Environment Programme (UNEP), the International Labour Organization (ILO) and the World Health Organization (WHO). The overall objectives of the IPCS are to establish the scientific basis for assessment of the risk to human health and the environment from exposure to chemicals, through international peer review processes, as a prerequisite for the promotion of chemical safety, and to provide technical assistance in strengthening national capacities for the sound management of chemicals.

The **Inter-Organization Programme for the Sound Management of Chemicals (IOMC)** was established in 1995 by UNEP, ILO, the Food and Agriculture Organization of the United Nations, WHO, the United Nations Industrial Development Organization, the United Nations Institute for Training and Research and the Organisation for Economic Co-operation and Development (Participating Organizations), following recommendations made by the 1992 UN Conference on Environment and Development to strengthen cooperation and increase coordination in the field of chemical safety. The purpose of the IOMC is to promote coordination of the policies and activities pursued by the Participating Organizations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

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FOREWORD

Concise International Chemical Assessment Documents (CICADs) are published by the International Programme on Chemical Safety (IPCS)—a cooperative programme of the World Health Organization (WHO), the International Labour Organization (ILO), and the United Nations Environment Programme (UNEP). CICADs have been developed from the Environmental Health Criteria documents (EHCs), more than 200 of which have been published since 1976 as authoritative documents on the risk assessment of chemicals.

International Chemical Safety Cards on the relevant chemical(s) are attached at the end of the CICAD, to provide the reader with concise information on the protection of human health and on emergency action. They are produced in a separate peer-reviewed procedure at IPCS. They may be complemented by information from IPCS Poison Information Monographs (PIM), similarly produced separately from the CICAD process.

CICADs are concise documents that provide summaries of the relevant scientific information concerning the potential effects of chemicals upon human health and/or the environment. They are usually based on selected national or regional evaluation documents or on existing EHCs. Before acceptance for publication as CICADs by IPCS, these documents undergo extensive peer review by internationally selected experts to ensure their completeness, accuracy in the way in which the original data are represented, and the validity of the conclusions drawn.

The primary objective of CICADs is characterization of hazard and dose–response from exposure to a chemical. CICADs are not a summary of all available data on a particular chemical; rather, they include only that information considered critical for characterization of the risk posed by the chemical. The critical studies are, however, presented in sufficient detail to support the conclusions drawn. For additional information, the reader should consult the identified source documents upon which the CICAD has been based.

Risks to human health and the environment will vary considerably depending upon the type and extent of exposure. Responsible authorities are strongly encouraged to characterize risk on the basis of locally measured or predicted exposure scenarios. To assist the reader, examples of exposure estimation and risk characterization are provided in CICADs, whenever possible. These examples cannot be considered as representing all possible exposure situations, but are provided as guidance only. The reader is referred to EHC 170.[1]

While every effort is made to ensure that CICADs represent the current status of knowledge, new information is being developed constantly. Unless otherwise stated, CICADs are based on a search of the scientific literature to the date shown in the executive summary. In the event that a reader becomes aware of new information that would change the conclusions drawn in a CICAD, the reader is requested to contact IPCS to inform it of the new information.

Procedures

The flow chart on page 2 shows the procedures followed to produce a CICAD. These procedures are designed to take advantage of the expertise that exists around the world—expertise that is required to produce the high-quality evaluations of toxicological, exposure, and other data that are necessary for assessing risks to human health and/or the environment. The IPCS Risk Assessment Steering Group advises the Coordinator, IPCS, on the selection of chemicals for an IPCS risk assessment based on the following criteria:

- there is the probability of exposure; and/or
- there is significant toxicity/ecotoxicity.

Thus, it is typical of a priority chemical that:

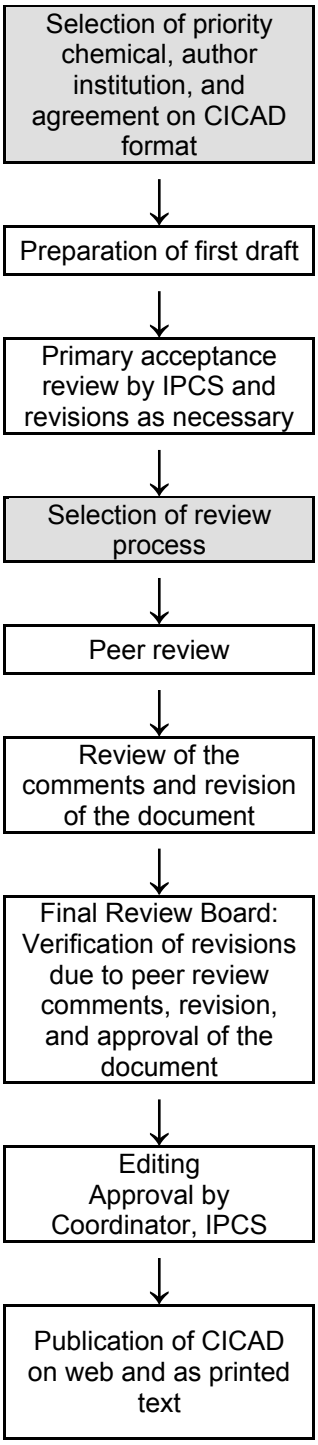
- it is of transboundary concern;
- it is of concern to a range of countries (developed, developing, and those with economies in transition) for possible risk management;
- there is significant international trade;
- it has high production volume;
- it has dispersive use.

The Steering Group will also advise IPCS on the appropriate form of the document (i.e. a standard CICAD or a de novo CICAD) and which institution bears the responsibility for the document production, as well as on the type and extent of the international peer review.

The first draft is usually based on an existing national, regional, or international review. When no appropriate source document is available, a CICAD may be produced de novo. Authors of the first draft are usually, but not necessarily, from the institution that developed the original review. A standard outline has been developed to encourage consistency in form. The

[1] International Programme on Chemical Safety (1994) *Assessing human health risks of chemicals: derivation of guidance values for health-based exposure limits.* Geneva, World Health Organization (Environmental Health Criteria 170) (also available at http://www.who.int/pcs/).

CICAD PREPARATION FLOW CHART



Advice from Risk Assessment Steering Group

Criteria of priority:

- there is the probability of exposure; and/or
- there is significant toxicity/ecotoxicity.

Thus, it is typical of a priority chemical that:

- it is of transboundary concern;
- it is of concern to a range of countries (developed, developing, and those with economies in transition) for possible risk management;
- there is significant international trade;
- the production volume is high;
- the use is dispersive.

Special emphasis is placed on avoiding duplication of effort by WHO and other international organizations.

A usual prerequisite of the production of a CICAD is the availability of a recent high-quality national/regional risk assessment document = source document. The source document and the CICAD may be produced in parallel. If the source document does not contain an environmental section, this may be produced de novo, provided it is not controversial. If no source document is available, IPCS may produce a de novo risk assessment document if the cost is justified.

Depending on the complexity and extent of controversy of the issues involved, the steering group may advise on different levels of peer review:

- standard IPCS Contact Points;
- above + specialized experts;
- above + consultative group.

first draft undergoes primary review by IPCS to ensure that it meets the specified criteria for CICADs.

The second stage involves international peer review by scientists known for their particular expertise and by scientists selected from an international roster compiled by IPCS through recommendations from IPCS national Contact Points and from IPCS Participating Institutions. Adequate time is allowed for the selected experts to undertake a thorough review. Authors are required to take reviewers' comments into account and revise their draft, if necessary. The resulting second draft is submitted to a Final Review Board together with the reviewers' comments. At any stage in the international review process, a consultative group may be necessary to address specific areas of the science. When a CICAD is prepared de novo, a consultative group is normally convened.

The CICAD Final Review Board has several important functions:

- to ensure that each CICAD has been subjected to an appropriate and thorough peer review;
- to verify that the peer reviewers' comments have been addressed appropriately;
- to provide guidance to those responsible for the preparation of CICADs on how to resolve any remaining issues if, in the opinion of the Board, the author has not adequately addressed all comments of the reviewers; and
- to approve CICADs as international assessments.

Board members serve in their personal capacity, not as representatives of any organization, government, or industry. They are selected because of their expertise in human and environmental toxicology or because of their experience in the regulation of chemicals. Boards are chosen according to the range of expertise required for a meeting and the need for balanced geographic representation.

Board members, authors, reviewers, consultants, and advisers who participate in the preparation of a CICAD are required to declare any real or potential conflict of interest in relation to the subjects under discussion at any stage of the process. Representatives of nongovernmental organizations may be invited to observe the proceedings of the Final Review Board. Observers may participate in Board discussions only at the invitation of the Chairperson, and they may not participate in the final decision-making process.

1. EXECUTIVE SUMMARY

This Concise International Chemical Assessment Document (CICAD)[1] on natural strontium and strontium compounds (stable isotopes) was prepared jointly by Toxicology Advice & Consulting Ltd[2] and the Centre for Ecology and Hydrology in the United Kingdom. The physicochemical and mammalian toxicology sections were based on the 2004 toxicological profile produced by the United States of America's (USA) Agency for Toxic Substances and Disease Registry (ATSDR, 2004). A draft version of this toxicological profile had been made available in 2001, and certain key literature published in the intervening period was included in the 2004 final version. In May 2006, Toxicology Advice & Consulting Ltd carried out a comprehensive literature search of relevant databases for the period 2000–2006 to identify any critical references published subsequent to those incorporated in the ATSDR source document.[3] The Centre for Ecology and Hydrology carried out comprehensive literature searches to identify relevant information on environmental aspects in June 2006. Information on the nature of the peer review and the availability of the source document is presented in Appendix 2. Information on the peer review of this CICAD is presented in Appendix 3. The International Chemical Safety Cards (ICSCs) for strontium (ICSC 1534), strontium carbonate (ICSC 1695), strontium sulfate (ICSC 1696) and strontium chromate (ICSC 0957), produced by the International Programme on Chemical Safety (IPCS), have also been reproduced in this CICAD (IPCS, 2004a, 2004b, 2006a, 2006b).

Strontium metal reacts rapidly with water and oxygen and is thus found in nature only in the 2+ oxidation state. Natural strontium is not radioactive and exists in four stable isotopic forms: ^{88}Sr (82.6%), ^{86}Sr (9.9%), ^{87}Sr (7.0%) and ^{84}Sr (0.6%). Strontium accounts for 0.02–0.03% of Earth's crust, where it is found mainly as celestite (strontium sulfate) or strontianite (strontium carbonate). Radioactive isotopes of strontium are not reviewed in this CICAD.

In recent years, imports of strontium into the USA have been relatively steady at about 31 000–39 000 tonnes per year. In 2001, more than 85% of strontium consumed in the USA was used in the manufacture of ceramics and glass products, primarily in television faceplate glass. Strontium compounds are also used in ceramic ferrite magnets (strontium ferrite) and other ceramic and glass applications, pyrotechnics (strontium nitrate), paint pigments (strontium chromate), fluorescent lights (strontium phosphate), getters in zinc production (strontium carbonate), alloys for aluminium casting (strontium metal) and medicines (strontium chloride, strontium peroxide). The total amount of strontium compounds placed on the Canadian market annually is currently about 5400 tonnes.

Strontium can be released into the air (mainly as strontium oxide) by natural processes (e.g. weathering of rocks, particle entrainment, wind resuspension and sea spray) or as a result of human activities (e.g. milling, processing, coal burning and phosphate fertilizer use). In air, the oxide rapidly forms the hydroxide or carbonate. Atmospheric strontium is returned to the ground by deposition. Strontium is released to surface water and groundwater by natural weathering of rocks and soils. In water, it exists as a hydrated cation. Aqueous strontium can sorb to the surface of certain minerals. Like calcium, strontium has moderate mobility in soils and sediments and sorbs moderately to metal oxides and clays. Plants readily absorb strontium via their normal calcium uptake pathway. Earthworms do not accumulate strontium in soils high in calcium; however, strontium accumulation may occur in acidic, calcium-poor soils. Strontium is readily accumulated in otoliths, vertebrae and opercula of fish. In fact, strontium chloride solutions have been used to deliberately mark salmon fry for later identification in the wild. In higher organisms, bioaccumulation occurs in bone due to strontium's similarity to calcium.

Average strontium concentrations in air are generally below 0.1 $\mu g/m^3$, although higher concentrations may occur near coal-burning plants. The average concentration of strontium in seawater is approximately 8 mg/l. Strontium was present in nearly all fresh surface waters across the USA; average concentrations were between 0.3 and 1.5 mg/l. Strontium concentrations in European stream waters range over 4 orders of magnitude, from 0.001 to 13.6 mg/l, with a median value of 0.11 mg/l. Mean strontium levels of up to 2 mg/l have been reported for river water contaminated by old mine workings. The median strontium concentration in European stream sediments was 126 mg/kg. Mean strontium levels of up to 225 mg/kg dry weight have been reported for river sediments contaminated by old mine workings. The average concentration of strontium in soils worldwide is approximately 240 mg/kg. The median strontium concentrations in European soils were 95 mg/kg in subsoil and 89 mg/kg in topsoil. Average concentrations in drinking-water in Germany and the USA were reported to be about 0.34 mg/l and 1.1 mg/l, respectively. In food plants, the highest concentrations were measured in leafy vegetables (e.g. 64 mg/kg dry weight in cabbages).

[1] For a complete list of acronyms and abbreviations used in this report, the reader should refer to Appendix 1.

[2] Now called bibra – toxicology advice & consulting.

[3] One of the authors searched for new critical papers in November 2009 and concluded that there were none (see Appendix 2).

For adult humans, the total daily intake of strontium in many parts of the world is estimated to be up to about 4 mg/day. Drinking-water contributes about 0.7–2 mg/day, and food (mainly leafy vegetables, grains and dairy products) another 1.2–2.3 mg/day. The contribution from air is insignificant by comparison. Intakes might be substantially higher in areas where strontium concentrations in the drinking-water are at the high end of the measured range. In regions where concentrations in soil are high, food plants may also make a substantially higher contribution to daily intake, particularly if predominantly locally produced plant foods are consumed.

The typical adult body burden of strontium is about 0.3–0.4 g, with 99% found in the skeleton. Humans absorb some 11–30% of ingested strontium. The gastrointestinal absorption of strontium was higher in 15-day-old rats than in 89-day-old rats; age dependence of gastrointestinal absorption has not been observed in humans. Absorption from the lungs is rapid for soluble strontium compounds but slow for insoluble strontium compounds. Dermal absorption of strontium compounds is slow. Strontium can act as an imperfect surrogate for calcium; the distribution of absorbed strontium mimics that of calcium, and strontium can exchange with calcium in the bone. Strontium uptake from the gastrointestinal tract and skeletal retention of strontium are reduced by co-administration with calcium, phosphates or sulfates. Maternal strontium can be transferred to the fetus during pregnancy and to the infant via the breast milk. In humans, the strontium to calcium ratio in bone is 3×10^{-4} at birth and increases to about 5×10^{-4} in adults. In the body, strontium probably forms complexes with hydroxyapatite, carbonate, phosphate, citrate and lactate and can interact with various calcium-binding and calcium transport proteins. Absorbed strontium is excreted mainly in the urine and faeces. Following ingestion or inhalation, there is an early rapid phase of excretion, reflecting excretion of unabsorbed material. This is followed by a slow phase (estimates of biological half-lives range from several weeks up to 28 years), presumably reflecting slower elimination from the skeleton.

Strontium chloride, strontium carbonate, strontium sulfate and strontium nitrate showed a low acute oral toxicity in rats and/or mice. The acute dermal toxicity of strontium sulfate in rats was low. Local damage to the oesophagus and duodenum occurred in monkeys given strontium chloride by capsule daily for 1 week.

Strontium can interfere with bone mineralization in the developing skeleton. Indeed, numerous studies have shown that a key target tissue following repeated oral exposure to strontium is the bone. The most informative study identified (based on extent of examination, use of lowest doses and longest duration) found no treatment-related adverse effects in young rats fed strontium at about 40 mg/kg body weight per day for 90 days in the diet, with changes in thyroid structure and weight, liver glycogen content and pituitary weight at 160 mg/kg body weight per day. Bone histology was normal in young rats fed strontium at 190 mg/kg body weight per day for 20 days in the diet. Minor effects on the bone were seen in young rats fed strontium at about 380 mg/kg body weight per day in the same study and in mice given drinking-water supplying 350 mg/kg body weight per day for 29 days. Longer-term studies did not identify a lower no-effect level. In several studies, repeated exposure to higher oral doses caused numerous bone and cartilage abnormalities, including impaired calcification, reduced mineral content, increased complexed acidic phospholipids, non-mineralized (osteoid) regions, spongiosa, wider epiphyseal plates, lower bone densities, disorganized trabeculae, smaller bones and rickets. Markers of bone effects included changes in serum levels of activated vitamin D and calbindin-D proteins and changes in acid and alkaline phosphatase activities in certain organs.

No carcinogenicity studies meeting current guidelines were identified for strontium compounds. Strontium chromate induced local tumours when implanted into the respiratory tract of rats. However, chromium(VI) compounds are mammalian carcinogens, and the chromate ion was considered to be responsible for the activity of strontium chromate.

Genotoxicity data on strontium compounds are few. A limited study reported that a single oral dose of strontium chloride induced chromosomal aberrations in the bone marrow of mice. However, strontium compounds showed no activity in vitro. Strontium chloride did not induce chromosome damage in hamster oocytes in culture, deoxyribonucleic acid (DNA) damage in bacteria or hamster embryo cells or cell transformation in hamster embryo cells. Strontium sulfate did not induce chromosome damage in hamster lung cells in culture or mutation in an Ames bacterial test. Strontium carbonate was also not mutagenic in an Ames test. The only strontium compound with identified genotoxic activity in vitro was strontium chromate. This chromium(VI) compound induced bacterial mutations in an Ames test, sister chromatid exchanges in hamster fibroblast cells in culture and cell transformation in hamster embryo cells. The chromate moiety is believed to be responsible for the observed activity.

No effects on reproduction/fertility or fetal development were seen in a screening study in which rats (both sexes) were given strontium sulfate by gavage for about 6–8 weeks starting 2 weeks before mating. According to a review, no effects on fertility were seen when rats were given strontium chloride in the drinking-water over three generations. Following repeated oral dosing of pregnant mice with strontium carbonate, adverse effects on bone

were seen in the offspring. Repeated oral dose studies in weanling and adult rats indicated that the younger animals were more sensitive than adults to the effects of strontium on bone.

Very little information is available on the toxicity of stable strontium to humans. A study in Turkey suggested a relationship between strontium exposure and childhood rickets. Soil strontium concentration was the sole indicator of likely exposure. The diet in the endemic area was largely dependent on grains grown in the area.

From a study in which no adverse effects (the examination included a microscopic evaluation of the bone) were seen in young rats ingesting strontium at a dose of 40 mg/kg body weight per day for 90 days, a tolerable daily intake (TDI) of 0.13 mg/kg body weight per day can be derived. Although estimated intakes in many parts of the world are below this figure, intakes may exceed this value for certain populations living in regions where strontium concentrations in the drinking-water or food plants are high. The available data are inadequate for the derivation of a tolerable inhalation concentration.

Strontium is required for the normal development of some unicellular microorganisms, calcerous algae, corals, gastropods, bivalves and cephalopods. Strontium has low acute toxicity to aquatic organisms in the laboratory. For freshwater organisms, most tests are based on strontium chloride, and 48 h and 96 h median lethal concentrations (LC_{50}s) of strontium range from 75 to 910 mg/l; a 21-day median effective concentration (EC_{50}) for strontium, based on reproductive impairment in daphnids, was 60 mg/l. Acute LC_{50}s in marine organisms suggest that they are less sensitive than freshwater organisms to strontium.

The overlap of the range of natural levels of strontium in surface waters with the concentrations of strontium that cause toxicity in aquatic organisms indicates that many of the test organisms in the freshwater studies must have been acclimatized not to natural waters but to strontium-deficient ones or derived from populations in low-strontium areas. Furthermore, marine toxicity values represent strontium "added" beyond the normal concentration in seawater (around 8 mg/l), and in some of the marine studies, the "background" strontium concentration was not measured. Therefore, realistic exposure/effect ratios cannot be derived for strontium from the available information.

2. IDENTITY AND PHYSICAL/CHEMICAL PROPERTIES

Strontium is an alkaline earth metal. Although in theory it can exist in the 0 or 2+ oxidation states, elemental strontium reacts rapidly with water and oxygen, and so strontium is found in nature only as Sr^{2+} compounds (Cotton & Wilkinson, 1980; Hibbins, 1997). Natural strontium is not radioactive. There are four stable isotopes: ^{84}Sr, ^{86}Sr, ^{87}Sr and ^{88}Sr, sometimes collectively referred to as stable strontium, with natural abundances of 0.56%, 9.86%, 7.00% and 82.58%, respectively (Lide, 1995). In addition, 22 radioactive isotopes of strontium are known. The most important, ^{89}Sr and ^{90}Sr, are formed during nuclear reactor operations and nuclear explosions (ATSDR, 2004). The radioactive isotopes are not reviewed in this CICAD.

Details of the chemical identification of strontium compounds covered in this CICAD are given in Table 1. Important physicochemical data are presented in Table 2.

Additional physicochemical properties for strontium metal, strontium carbonate, strontium sulfate and strontium chromate are given in the ICSCs reproduced in this CICAD.

3. ANALYTICAL METHODS

Some of the more well-established methods for quantifying strontium in biological samples are summarized in Table 3. Following sample workup, graphite furnace atomic absorption spectroscopy has been used to measure strontium in blood, bone and urine (Burguera et al., 1999) and in soft tissues (D'Haese et al., 1996). Strontium can be measured using inductively coupled plasma atomic emission spectroscopy following acid digestion of blood or tissue samples (NIOSH, 1994; Piette et al., 1994) and by inductively coupled plasma mass spectrometry following acid treatment of serum (Muňiz et al., 1999) or bone (Outridge et al., 1996). Total reflection X-ray fluorescence (blood) (Prange et al., 1989), thermal neutron activation and radiometric measurement (serum) (Teree & Cohn, 1966) and proton-induced X-ray emission (hair) (Clayton & Wooller, 1985) have also been used. Inductively coupled plasma mass spectrometry was able to detect strontium in amniotic fluid and maternal plasma at levels of 0.03 µg/l and 0.06 µg/l, respectively, in humans exposed only to environmental strontium (Silberstein et al., 2001). The elemental distribution of strontium in cartilage and bone has been analysed using high-resolution synchrotron radiation-induced micro X-ray fluorescence (Zoeger et

Table 1: Chemical identification of strontium and strontium compounds reviewed in this CICAD (adapted from ATSDR, 2004).

Chemical name	Synonyms	Chemical formula	Relative molecular mass	CAS no.
Strontium	—	Sr	87.6	7440-24-6
Strontium acetate	Strontium diacetate	$Sr(O_2CCH_3)_2$	205.7	543-94-2
Strontium carbonate	Carbonic acid, strontium salt (1:1); strontianite	$SrCO_3$	147.6	1633-05-2
Strontium chloride	Strontium dichloride	$SrCl_2$	158.5	10476-85-4
Strontium chromate	Chromic acid, strontium salt	$SrCrO_4$	203.6	7789-06-2
Strontium fluoride	Strontium difluoride	SrF_2	125.6	7783-48-4
Strontium hydroxide	Strontium hydrate	$Sr(OH_2)_2$	121.6	18480-07-4
Strontium nitrate	Nitric acid, strontium salt; strontium dinitrate; strontium(II) nitrate (1:2)	$Sr(NO_3)_2$	211.6	10042-76-9
Strontium oxide	Strontia; strontium monoxide	SrO	103.6	1314-11-0
Strontium peroxide	Strontium dioxide	SrO_2	119.6	1314-18-7
Strontium phosphate	—	$Sr_3(PO_4)_2$	452.8	7446-28-8
Strontium sulfate	Celestine; celestite	$SrSO_4$	183.7	7759-02-6
Strontium sulfide	Strontium monosulfide	SrS	119.7	1314-96-1
Strontium titanate	—	$SrTiO_3$	183.5	12060-59-2

CAS, Chemical Abstracts Service

Table 2: Selected physicochemical properties of strontium and strontium compounds reviewed in this CICAD (adapted from ATSDR, 2004).

Chemical name	Melting point (°C)	Boiling point (°C)	Solubility in water (g/l)
Strontium	777	1382	Decomposes
Strontium acetate	Decomposes	Not applicable	369 (cold)
Strontium carbonate	No data	Decomposes at 1100	0.11 at 18 °C
Strontium chloride	875	1250	538 at 20 °C
Strontium chromate	No data	No data	1.2 at 15 °C[a]; 30 at 100 °C
Strontium fluoride	Decomposes at >100	2489	0.12 at 18 °C
Strontium hydroxide	375	No data	470 at 100 °C
Strontium nitrate	570	645	790 at 18 °C
Strontium oxide	2430	3000	229 at 100 °C
Strontium peroxide	Decomposes at 215	Not applicable	Decomposes
Strontium phosphate	No data	No data	Insoluble
Strontium sulfate	1605	No data	0.14 at 30 °C
Strontium sulfide	>2000	No data	Decomposes
Strontium titanate	No data	No data	Insoluble

[a] From IARC (1990).

al., 2006). Strontium in bone can be measured in vivo using source-excited X-ray fluorescence, with a minimum detection limit of 0.25 mg of strontium per gram of calcium (Pejovic-Milic et al., 2004).

Table 4 summarizes some well-established methods for quantifying strontium in environmental samples. Strontium in air and water can be measured by filtration, acid digestion and flame atomic absorption spectroscopy (OSW, 1992; ASTM, 1999). Aqueous strontium can also be quantified by acid digestion and spectrophotometry (AOAC, 1990) or inductively coupled plasma atomic emission spectroscopy (USEPA, 2000).

Table 3: Analytical methods for determining strontium in biological samples (adapted from ATSDR, 2004).

Sample matrix	Sample preparation	Analytical method	Detection limit	% recovery	Reference
Blood	Acidification with nitric acid; dilution; addition of lanthanum matrix modifier	GFAAS	0.13 mg/l	94.5–102.5	Burguera et al. (1999)
Blood	Acid digestion; iron extraction; cleanup by ion exchange; thin film deposition	TRXF	0.04 mg/l	No data	Prange et al. (1989)
Blood	Acid digestion; dilution	ICP-AES	0.3 mg/l	113	NIOSH (1994); Piette et al. (1994)
Blood serum	Dry ashing; neutron activation; chemical separation	TNA	0.02 mg/l	75–90	Teree & Cohn (1966)
Blood serum	Acidification and dilution	ICP-MS	No data	99	Muñiz et al. (1999)
Bone	Acidification with nitric acid; dilution; addition of lanthanum matrix modifier	GFAAS	0.13 mg/l	96.5–102.9	Burguera et al. (1999)
Bone	Acid digestion	ICP-MS	6 µg/g dry weight	No data	Outridge et al. (1996)
Hair	Ashing	PIXE	1 µg/g	No data	Clayton & Wooller (1985)
Tissues	Acid digestion; dilution	ICP-AES	No data	113	NIOSH (1994)
Tissues	Complexometric digestion in TMAH/EDTA matrix with heat	GFAAS	0.0022 µg/g	99 ± 4.2	D'Haese et al. (1996)
Urine	Acidification with nitric acid; dilution; addition of lanthanum matrix modifier	GFAAS	0.13 mg/l	98.8–101.5	Burguera et al. (1999)

EDTA, ethylenediaminetetraacetic acid; GFAAS (total strontium), graphite furnace atomic absorption spectroscopy; ICP-AES (total strontium), inductively coupled plasma atomic emission spectroscopy; ICP-MS (isotopic strontium composition), inductively coupled plasma mass spectrometry; PIXE (total strontium), proton-induced X-ray emission; TMAH, tetramethylammonium hydroxide; TNA (total strontium), thermal neutron activation and radiometric measurement; TRXF (total strontium), total reflection X-ray fluorescence

Table 4: Analytical methods for determining strontium in environmental samples (adapted from ATSDR, 2004).

Sample matrix	Sample preparation	Analytical method	Reference
Air	Particulate collection on cellulose filter; acid digestion	FAAS (ASTM Method D4185)	ASTM (1999)
Water	Acid digestion	Spectrophotometric measurement (total strontium) (AOAC Method 911.03)	AOAC (1990)
Water	Filtration; acid digestion; addition of matrix modifier	FAAS (ASTM Method D3920; OSW Method 7780)	OSW (1992); ASTM (1999)
Water	Wet acid digestion	ICP-AES (USEPA Method 200.15)	USEPA (2000)
Saline water	Dilution	FAAS (ASTM Method D3352)	ASTM (1999)

AOAC, Association of Official Analytical Chemists; ASTM, American Society for Testing and Materials; FAAS (total strontium), flame atomic absorption spectroscopy; ICP-AES (total strontium), inductively coupled plasma atomic emission spectroscopy; OSW, Office of Solid Waste, United States Environmental Protection Agency; USEPA, United States Environmental Protection Agency

4. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE

4.1 Natural and anthropogenic sources

Strontium occurs naturally in Earth's crust (at approximately 0.02–0.03%) in the form of minerals such as celestite (strontium sulfate) and strontianite (strontium carbonate). Minor amounts occur in other mineral deposits and in, or near, sedimentary rocks associated with gypsum, anhydrite, rock salt, limestone and dolomite. Strontium can also occur in shales, marls and sandstones (ATSDR, 2004). It is released into the air by natural processes, such as weathering of rocks by wind, entrainment of dust particles, resuspension of soil by wind and sea spray. Air in coastal regions has higher concentrations of strontium as a result of sea spray (Capo et al., 1998). Releases to surface water and groundwater result from the natural weathering of rocks and soils (ATSDR, 2004).

Strontium can be released into the air as a result of human activities, such as milling and processing of

strontium compounds, coal burning and the use of phosphate fertilizers and pyrotechnic devices (Lee & von Lehmden, 1973; Que Hee et al., 1982; Ondov et al., 1989; Raven & Loeppert, 1997; Perry, 1999). Strontium deposition in peat cores in Indiana, USA, has increased 7-fold from 8.1 mg/m^2 per year in early times (1339–1656) to 57.0 mg/m^2 per year in 1970–1973, presumably due to human activities (Cole et al., 1990). The amount of strontium discharged into the air by coal-fired power plants depends on the strontium concentration in coal, the amount of coal burned and the efficiency of fly ash recovery. Approximately 90% of coal mass is consumed during the combustion process, leaving 10% as residual, non-volatile material (fly ash) containing strontium at 100–4000 mg/kg (Furr et al., 1977). Atmospheric emissions from coal-fired power plants contained strontium at concentrations of 17–2718 μg/m^3 and approximately 9800 μg/m^3 in the western and eastern USA, respectively (Que Hee et al., 1982; Ondov et al., 1989). Phosphate fertilizers may contain strontium at concentrations between 20 and 4000 μg/g (Lee & von Lehmden, 1973; Raven & Loeppert, 1997). Strontium can be released into the atmosphere in windblown soil to which phosphate fertilizers have been applied. Low levels of strontium (about 9 ng/m^3 air) were found in the immediate environment of pyrotechnic displays (Perry, 1999).

4.2 Production and use

The principal strontium minerals of commercial interest are celestite (strontium sulfate) and strontianite (strontium carbonate). Celestite is usually converted to strontium carbonate for commercial purposes. The black ash method (alternatively known as the calcining method) and the soda ash method (also known as direct conversion) are the two most common recovery techniques for strontium. The black ash method produces chemical-grade strontium carbonate, containing about 98% strontium carbonate and 2% by-products and impurities. The soda ash method produces technical-grade strontium carbonate containing at least 97% strontium carbonate (Ober, 1998).

From 1994 to 2001, imports of strontium minerals and compounds into the USA for consumption have remained relatively steady at approximately 31 000–38 500 tonnes per year. Exports of strontium compounds from the USA were much lower during this period (e.g. 1120 tonnes in 1994, 929 tonnes in 2001 and 340 tonnes in 2002) (Ober, 1998, 2002). In recent years, about 5400 tonnes of strontium compounds have been put on the market in Canada annually. The major contributors to this total (in tonnes) are strontium nitrate (2000), strontium carbonate (1200), strontium oxide (1000), strontium metal (1000), strontium chloride (100), strontium sulfate (20), strontium titanate (10) and strontium phosphate (10) (Health Canada, personal communication, 2007).

In 2001, more than 85% of all strontium consumed in the USA was used in the manufacture of ceramics and glass products, primarily in television faceplate glass. In the USA, all colour televisions and other devices containing cathode-ray tubes are legally required to 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% of strontium oxide into the faceplate glass. Strontium is added to the glass melt in the form of strontium carbonate. Upon heating and solidification, it is transformed to strontium oxide. Strontium compounds are also used in ceramic ferrite magnets (strontium ferrite) and other ceramic and glass applications, pyrotechnics (strontium nitrate), paint pigments (strontium chromate), fluorescent lights (strontium phosphate), getters in zinc production (strontium carbonate), alloys (strontium metal) and medicines (strontium chloride, strontium peroxide). Strontium metal has limited commercial use. One minor use of strontium is as an alloy material for the production of aluminium castings. Most commercial processes use strontium carbonate as the feed material (Hibbins, 1997; Ober, 2002).

5. ENVIRONMENTAL TRANSPORT, DISTRIBUTION AND TRANSFORMATION

5.1 Environmental transport and distribution

5.1.1 Air

Some strontium is transported from oceans, the largest reservoir of dissolved strontium, to the air in sea spray (Capo et al., 1998). Strontium released into the air from natural and anthropogenic activities is transported and redeposited on Earth by dry or wet deposition. Analysis of the aerial deposition of ^{90}Sr following the 1986 Chernobyl accident in Ukraine found that 96% of atmospheric ^{90}Sr returned to Earth as wet deposition (Hirose et al., 1993).

5.1.2 Water

Oceanic strontium can leave the oceans by sea spray and by deposition in marine carbonate sediment (Capo et al., 1998). Strontium in water can sorb as hydrated ions on the surface of kaolinite clay minerals, weathered minerals (e.g. amorphous silica) and iron oxides (Hayes & Traina, 1998; O'Day et al., 2000; Sahai et al., 2000).

5.1.3 Soils and sediments

Strontium has moderate mobility in soils and sediments and sorbs moderately to metal oxides and to the surface of clays and other minerals (Hayes & Traina, 1998; O'Day et al., 2000; Sahai et al., 2000). On calcite (calcium carbonate), low concentrations of the Sr^{2+} cation may sorb by electrostatic attraction as hydrated ions, or higher concentrations may precipitate as strontianite (strontium carbonate), thus reducing mobility (Parkman et al., 1998).

Distribution coefficient (K_d) values for Sr^{2+} sorption vary widely, reflecting differences in soil and sediment conditions as well as the analytical techniques used (NCRP, 1984; Bunde et al., 1997). The in situ K_d values for stable strontium and ^{90}Sr determined in soil cores taken from the fallout area of the 1945 blast in Nagasaki, Japan, were 496 and 300 l/kg, respectively. Migration rates for ^{90}Sr in soils from this area were estimated to be 4.2 mm per year when the percolation rate of soil water was 2500 mm per year. Most ^{90}Sr remained close to the soil surface in these soils (Mahara, 1993). In 1996, at most sites in the contaminated zone near Chernobyl, Ukraine, more than 95% of ^{90}Sr was located in the upper 30 cm layer (Kashparov et al., 2001). Organic matter in soils has a substantial effect on strontium transport through soils into groundwater. K_d values decreased down the soil profile in podzol forest soil with an organic-rich topsoil and lower clay layers, from 140 to 44 l/kg (Bunzl & Schimmack, 1989). The Sr^{2+} cation chemically complexes with organic matter, and the resulting complexes precipitate (Helal et al., 1998a). Complex formation is enhanced by calcium cations, increasing the removal of strontium cations from solution and reducing strontium ion mobility (Helal et al., 1998a). Nitrate fertilizers inhibit complex formation and increase strontium ion mobility (Helal et al., 1998b). K_d values of 15–40 l/kg were measured for ^{90}Sr (Sr^{2+}) in aquifer sediments near liquid waste disposal facilities at the Hanford site in the state of Washington, USA, where rapid ion exchange dominates (Monetti, 1996). K_d values were measured for ^{90}Sr (Sr^{2+}) in aquifer sediments beneath wastewater ponds that contained high salt concentrations at the National Environmental and Engineering Laboratory in Idaho, USA (Bunde et al., 1998); values ranged from 56 to 62 l/kg at initial sodium and potassium concentrations of 300 mg/l and 150 mg/l, respectively. For initial aqueous sodium concentrations of 1 g/l and 5 g/l, K_d values were 4.7 l/kg and 19 l/kg, respectively. At the Chalk River Nuclear Laboratory in Ontario, Canada, a ^{90}Sr waste plume in groundwater initially advanced rapidly as ^{90}Sr was outcompeted by high concentrations of calcium and magnesium cations for sorption sites in sediments; as the concentrations of calcium and magnesium cations declined, the migration of the ^{90}Sr plume slowed (Toran, 1994). High salt concentrations (marine water, brines or high-salinity water) can increase the mobility of ^{90}Sr (Sr^{2+}) by decreasing strontium sorption to sediments and increase the transport of strontium with the environmental cycling of water (Bunde et al., 1997, 1998).

5.1.4 Biota

Plants do not need strontium but readily absorb it from soil via their normal calcium uptake pathway (NCRP, 1984). The ratio of the strontium concentration in wet vegetation to that in dry soil ranges from 0.017 to 1.0 (NCRP, 1984). Plant uptake of strontium is greatest in sandy soils with low clay and organic matter content (Baes et al., 1986) and is reduced by soil calcium and potassium (Lembrechts, 1993). Strontium deposited on plant surfaces from the atmosphere may remain on the plant, be washed off or be absorbed directly into the plant through the leaves. Contamination by direct deposition on foliage surfaces is relatively brief, with a weathering half-life of approximately 14 days (Lassey, 1979). In three species of fruit-bearing plants exposed to strontium (as ^{85}Sr) by aerial deposition, translocation was localized to the deposition site (Carini et al., 1999). Uptake of strontium through the leaves is minor compared with root uptake. Once absorbed into the plant, strontium translocates to other parts of the plant, such as the leaves or fruit. Translocation in plants depends on species and growth stage, and accumulation is highest in the growing parts (Kodaira et al., 1973). Leaf fall results in release of strontium to the soil surface. Downward migration of ^{90}Sr is slowed by recycling of the contaminated litter by vegetation (Cooper & Rahman, 1994). Subsurface strontium can be transported to topsoil by burrowing animals and is spread to the surrounding environment via animal tissues and faecal deposits (Arthur & Janke, 1986).

5.2 Environmental transformation

Strontium is emitted into the atmosphere principally as strontium oxide, which reacts rapidly in the presence of moisture or carbon dioxide to form strontium hydroxide or strontium carbonate. The former ionizes to form Sr^{2+} and $SrOH^+$ cations (ATSDR, 2004). In water, strontium exists primarily as a strongly hydrated Sr^{2+} cation, which is firmly coordinated with six or more water molecules in aqueous solution (Cotton & Wilkinson, 1980; ATSDR, 2004). These Sr^{2+} ions retain the hydration sphere (O'Day et al., 2000) when sorbing on the surface of kaolinite clay minerals, weathered minerals (e.g. amorphous silica) and iron oxides (Sahai et al., 2000). Sorbed carbonate on iron oxides enhances the sorption of Sr^{2+} and permits the nucleation of Sr^{2+} as strontium carbonate (Sahai et al., 2000). On calcite (calcium carbonate), Sr^{2+} sorption occurs by electrostatic attraction as hydrated ions, but precipitation of strontianite (strontium carbonate) may occur at higher concentrations (Parkman et al., 1998).

5.3 Bioaccumulation

Bioconcentration factors (BCFs) for ^{90}Sr in aquatic, terrestrial and wetland ecosystems at the United States Department of Energy Savannah River Site in South Carolina have been reported. The highest values were found for bony fish. BCF values exceeded 50 000 for the bony tissue, because the uptake and distribution of strontium and calcium are very similar. In the muscle tissue of bony fish, BCF values for ^{90}Sr ranged from high (610; benthic invertebrate and fish feeders) to very high (3400; piscivores). Strontium is readily accumulated in otoliths, vertebrae and opercula of fish. In fact, strontium chloride solutions have been used to deliberately mark salmon fry for later identification in the wild (Schroder et al., 1995). High values were also found for other aquatic species, such as macroinvertebrates (insects), macrophytes (white water lilies and bladderwort) and zooplankton (Friday, 1996). Bioaccumulation of strontium (Sr^{2+}) by fish is inversely correlated to the concentrations of Ca^{2+} and H^{+} in water (Chowdhury et al., 2000; Chowdhury & Blust, 2001). Chowdhury & Blust (2001) observed that calcium and strontium act as competitive inhibitors in fish. In most aquatic environments, strontium is a trace element, whereas calcium is a major element, so strontium is unlikely to inhibit calcium uptake. Thus, it is the concentration of strontium relative to that of calcium in the water, and not the absolute concentration of strontium, that should determine uptake of strontium. The uptake of strontium showed an increase at low levels of the complexing species ethylenediaminetetraacetic acid (EDTA) and nitrilotriacetic acid (NTA) because the higher affinity of EDTA and NTA for Ca^{2+} than for Sr^{2+} results in decreased competition between Sr^{2+} and Ca^{2+} at the gill uptake sites (Chowdhury & Blust, 2002). However, the correlation with calcium is not universal and does not apply to other organisms, such as algae and plants (NCRP, 1984). Earthworms do not accumulate strontium in soils high in calcium; however, strontium accumulation may occur in acidic, calcium-poor soils (Morgan et al., 2001).

6. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

6.1 Environmental levels

The average concentration of strontium in Earth's crust is about 200–300 mg/kg (ATSDR, 2004) or 340–370 mg/kg (Capo et al., 1998). Reported concentrations range from 20 mg/kg in sandstone up to 465 mg/kg in basalt. Wood may contain strontium at 8–2500 mg/kg (Capo et al., 1998). The anthropogenic activities of an industrialized human society have led to increased local concentrations of strontium (ATSDR, 2004).

6.1.1 Air

Two surveys reported the strontium content in urban air to range from 4 to 100 ng/m^3 and to average 20 ng/m^3 (Dzubay & Stevens, 1975). An average concentration of 29.1 ng/m^3 was measured in urban air in the Los Angeles basin in California, USA, during 1985 (Witz et al., 1986). Strontium concentrations in urban air in Illinois, USA, between 1985 and 1988 averaged 0.9–4.8 ng/m^3 (Sweet et al., 1993). Concentrations may be higher near coal-burning plants, where strontium can be released with stack emissions (ATSDR, 2004).

6.1.2 Water

In the USA, the National Drinking Water Contaminant Occurrence Database contains data on contaminant concentrations at many points in the public water supply system, including entry, various points in the treatment and distribution systems, and "finished" drinking water. According to the source document (ATSDR, 2004), the average concentrations of strontium in public water supplies that were derived from surface water and groundwater were 1.10 mg/l (range 0.2–3.68 mg/l) and 0.81 mg/l (range 0.010–3.5 mg/l), respectively (USEPA, 2002). In earlier surveys, strontium was present at concentrations below 1 mg/l in nearly all municipal water supplies across the USA (USGS, 1963). The concentration of dissolved strontium in influents from publicly owned treatment works was between 0.025 and 0.45 mg/l (USEPA, 1981). In seven towns in Wisconsin, USA, average strontium concentrations in the drinking-water in 1975 were 0.02, 0.28, 5.4, 8.3, 10.4, 15.1 and 33.9 mg/l, respectively (Curzon & Spector, 1977). In the summer of 1968, mean strontium concentrations in the drinking-water of 24 counties in Texas, USA, ranged from 0.4 to 37.8 mg/l. Only in four counties did the mean concentration exceed 5 mg/l (Dawson et al., 1978).

In Germany, the mean strontium concentration in nearly 4000 drinking-water samples was 0.34 mg/l during 1990–1992. The 10th and 95th percentile values were 0.06 and 0.93 mg/l. All values were above the detection limit (0.5 µg/l), and the maximum recorded concentration was 4.82 mg/l (Anon, 1998).

In a survey in 1995–1996 of 100 samples of consumable bottled water in Canada, strontium concentrations ranged from 1.3 µg/l in water subjected to distillation or reverse osmosis up to 1.44 mg/l in mineral water (Dabeka et al., 2002).

The average concentration of strontium in seawater is approximately 8 mg/l (Demayo, 1986). At several locations around the USA (data from the National Drinking Water Contaminant Occurrence Database), average concentrations of dissolved strontium in lakes/reservoirs and springs were 1.09 mg/l (97.6% of

sites; range 0.002–170 mg/l) and 0.64 mg/l (100% of sites; range 0.028–3.2 mg/l), respectively. In other surface waters, dissolved strontium was detected at 1572 of 1595 sites (98.6% of sites), with an average concentration of 0.36 mg/l (range 0.0005–30 mg/l) (USEPA, 2002). Earlier surveys (USGS, 1963) found strontium to be present at concentrations below 1 mg/l in nearly all fresh surface waters across the USA, and average concentrations in streams were between 0.5 and 1.5 mg/l. Strontium concentrations above 1 mg/l were found in streams of the south-west USA, where the total dissolved solids content is the highest of any area of the continental USA. Streams of most of the Atlantic slope basins, southern USA, upper Great Lakes region and Pacific North-west region generally contain strontium at concentrations below 0.5 mg/l (USGS, 1963). Strontium concentrations in European stream waters range over 4 orders of magnitude, from 0.001 to 13.6 mg/l, with a median value of 0.11 mg/l. Low strontium concentrations were associated with granitic, metamorphic and felsic volcanic rocks; high concentrations were associated principally with limestone, evaporite, dolomite and, in Italy, alkaline volcanic rocks (Salminen et al., 2005). Mean strontium levels of up to 2 mg/l have been reported for river water contaminated by old mine workings in Scotland (Davidson et al., 2005). Neal et al. (1997) reported mean strontium concentrations ranging from 0.04 to 0.1 mg/l for three other Scottish rivers.

Dissolved strontium was detected in groundwater at 4353 of 4383 (99.3%) sites in the USA, with an average concentration of 1.6 mg/l (range 0.0009–200 mg/l) (USEPA, 2002). Earlier surveys reported average concentrations in groundwater to be below 0.5 mg/l, although concentrations above 1 mg/l were seen in the south-western USA. Unusually high concentrations (>20 mg/l) were found in some wells in Wisconsin, USA (USGS, 1963).

Average concentrations of strontium in rain and snow were 0.7–380 µg/l and 0.01–0.76 µg/l, respectively (Capo et al., 1998).

6.1.3 Sediment and soil

The average concentrations of strontium in Earth's crust, exposed upper crust and soils are approximately 370 mg/kg, 340 mg/kg and 240 mg/kg, respectively (USEPA, 1995; Capo et al., 1998; ATSDR, 2004). The median strontium concentrations in European soils were 95 mg/kg (range 6–2010 mg/kg) in subsoil and 89 mg/kg (range 8–3120 mg/kg) in topsoil (Salminen et al., 2005). Typical concentrations of strontium in soil amendments (which are routinely applied to agricultural land) are 250 ± 192 mg/kg dry weight for sewage sludges from publicly owned treatment works, 610 mg/kg for phosphate fertilizers and for limestone, and 80 mg/kg dry weight for manure (Mumma et al., 1984; USEPA, 1995a). Mean strontium levels of up to 225 mg/kg dry weight have been reported for river sediments contaminated by old mine workings in Scotland; mean strontium concentrations below 40 mg/kg were reported upstream and downstream of the mine workings (Davidson et al., 2005). The median strontium concentration in European stream sediments was 126 mg/kg, with a range from 31 to 1352 mg/kg (Salminen et al., 2005).

6.1.4 Biota, including food

Mean strontium concentrations of up to 3.6 g/kg have been reported for shells of freshwater shellfish sampled from rivers contaminated by old mine workings in Scotland. Flesh from mussels contained a mean strontium concentration of 180 mg/kg (Davidson et al., 2005). Mussel shells and flesh sampled from uncontaminated areas contained strontium concentrations of 14 mg/kg and 24 mg/kg, respectively (Segar et al., 1971).

Strontium concentrations in fruits and vegetables are summarized in Table 5. The highest measured concentrations were found in leafy vegetables (e.g. 64 mg/kg dry weight in cabbage) (USGS, 1980; Barnes, 1997). Concentrations (fresh weight) in a wide range of foods—including cereal and bakery products (0.2–18 mg/kg), vegetables, fruits, nuts and berries (0.2–19 mg/kg), meat and meat products (0.03–1.4 mg/kg), fish and other seafood (0.4–12 mg/kg), dairy products and eggs (0.04–7.6 mg/kg), beverages (0.01–1 mg/kg), confectionery (0.1–5.7 mg/kg), condiments (0.7–24 mg/kg), convenience foods (0.4–2.1 mg/kg) and baby foods (0.5–2.8 mg/kg)—have been reported in Finland (Varo et al., 1982).

Wood may contain strontium at 8–2500 mg/kg (Capo et al., 1998). Strontium was measured at 141 mg/kg in tobacco leaves (Sato et al., 1977), and the average concentration in the ash of 12 brands of cigarettes was 373 mg/kg (Iskander, 1986). Strontium was found in waste materials, including municipal solid waste (11–35 mg/kg) and incineration fly ash (110–220 mg/kg) (Lisk, 1988), coal fly ash (30–7600 mg/kg), coal bottom ash (170–6400 mg/kg), flue gas desulfurization by-products (70–3000 mg/kg) and oil ash (50–920 mg/kg) (Eary et al., 1990), and compost (260–420 mg/kg) (Evans & Tan, 1998).

6.2 Human exposure

6.2.1 Environmental

For humans without occupational strontium exposure, the primary exposure sources are drinking-water and food, especially grains, leafy vegetables and dairy products. Concentrations of strontium in these

Table 5: Concentrations of strontium in fruits and vegetables, including juices (adapted from ATSDR, 2004).

Fruit/vegetable produce or juice	Average liquid concentration (µg/l)[a]	Average solid concentration (mg/kg dry weight)[b]
Apple		13.58
Apple juice	0.1271	
Banana	0.1297	
Bean:		
Dry		6.63
Snap		21.7
Blackberry	0.2619	
Boysenberry	0.9523	
Cabbage		64.17
Corn:		
Sweet		0.416
Cucumber		24.0
Currant:		
Red	1.251	
Grape:		
American		25.6
Concord	0.3661	
European		38.4
Red	0.1086	
White	0.6318	
Kiwi	1.744	
Lemon products:		
Lemon	0.0986	
Bottled	0.5334	
Lemonade	0.1653	
Lettuce		22.26
Lime	0.3464	
Mango	0.5121	
Orange		25.56
Orange juice:		
Brazilian	0.0417	
California	0.5368	
Florida	0.0933	
Navel	0.5209	
Pineapple	0.1612	
Papaya	1.690	
Peach		3.082
Pear	0.5912	
Pineapple	0.0604	
Potato		2.562
Raspberry	2.232	
Strawberry	0.3001	
Tangerine	0.0828	
Tomato		9.96
Tomato sauce	0.8894	

[a] From Barnes (1997).
[b] From USGS (1980).

media may vary widely (ATSDR, 2004). Assuming concentrations of 0.34 or 1.1 mg/l in drinking-water (see section 6.1.2), an adult consuming 2 litres of water per day would ingest 0.68 or 2.2 mg of strontium per day from this source. A 2001 total diet study in the United Kingdom estimated an average strontium intake of 1.2 mg/day from food (UKCOT, 2008; UKFSA, 2009), a figure that was similar to that (1.3 mg/day) reported in the equivalent survey carried out in 1994 (Ysart et al., 1999). Similar estimates were obtained in an Australian market basket survey in 1994 for adult females (0.89–1.2 mg/day) (Gulson et al., 2001) and from duplicate diet and market basket studies in Viet Nam (1.2 mg/day) (Giang et al., 2001). Based on analysis of a wide range of foods and national food consumption statistics, Finnish scientists estimated an average dietary strontium intake of 1.9 mg/day. The items contributing to this total were dairy products and eggs (35%), vegetables and fruits (32%), "others" (13%), cereal products (11%), fish (8%) and meat (1%) (Varo et al., 1982). In a study of 31 regions in Japan in 1981, the mean daily strontium intake from the diet (meals) was 2.3 mg per person (regional means ranged from 0.9 to 4.3 mg per person per day) (Shiraishi et al., 1989).

The air makes only a minor contribution to total strontium intake. Based on an average strontium concentration of 20 ng/m^3 in urban air (Dzubay & Stevens, 1975; Witz et al., 1986), an adult breathing approximately 20 m^3 of air per day might inhale 400 ng of strontium daily. This figure may be somewhat higher for persons living near sources of strontium emission and for smokers.

For adults in the USA, the total daily exposure to strontium has been estimated at approximately 3.3 mg/day, made up of 2 mg/day from drinking-water, 1.3 mg/day from the diet and a negligible 0.4 µg/day from inhaled air (ATSDR, 2004).

As part of an Australian market basket survey in 1994, the estimated daily intakes of strontium for 6-month-old infants fed exclusively breast milk or infant formula were 0.05 mg and 0.25 mg, respectively (Gulson et al., 2001).

6.2.2 Occupational

Workers employed at industrial facilities that produce, process and use strontium and strontium compounds will have higher exposures than persons without occupational exposure. In a study of six art glass factories in Italy, personal air sampling revealed median strontium concentrations of 0.5 µg/m^3 (range 0.1–12.6 µg/m^3) for 24 oven chargers and batch mixers and 0.1 µg/m^3 (range 0.1–0.2 µg/m^3) for 8 art glass makers and formers (Apostoli et al., 1998).

7. COMPARATIVE KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

7.1 Body burden and tissue levels

Strontium is very similar to calcium in its physiological behaviour and can act as an imperfect surrogate for calcium (ATSDR, 2004). As with calcium, approximately 99% of the total body burden of strontium is found in the skeleton (ICRP, 1993). The skeletal burden of stable strontium in Japanese adult males was estimated to be approximately 440 mg, compared with 850 g calcium (Tanaka et al., 1981). A review gives a figure of 320 mg for a man weighing 70 kg (Nielsen, 2004). In humans, the highest concentrations occur in the bones and teeth (means 115–138 mg/kg wet weight), with much lower levels (0.05–0.38 mg/kg) in muscle, brain, kidney, liver and lung; concentrations of about 27–53 µg/l were found in the serum/plasma/blood (Olehy et al., 1966; Iyengar et al., 1978; Skoryna, 1981b; Tsalev, 1984). In a small group of adult males, the mean strontium concentration in plasma was 29 µg/l (Sutton et al., 1971a). Average strontium levels in the cadaver tissues of 168 subjects in the USA (expressed as mg/kg ash) were as follows: rib bone, 110; vertebra, 100; aorta, 33; ileum, 25; duodenum, 11; lung, 8.2; kidney, 5.2; heart, 2.6; and liver, 1.6 (Tipton & Cook, 1963; Tipton, 1981).

7.2 Absorption

Good quantitative data on the absorption of inhaled strontium are lacking, but the excretion of radiostrontium in urine and faeces (for several hundred days) following inhalation of airborne radiostrontium by workers provides some evidence that strontium is absorbed from the lungs (e.g. Rundo & Williams, 1961; Petkau & Pleskach, 1972; Navarro & López, 1998).

Laboratory animal studies indicate that the rate of absorption of strontium compounds from the lungs increases with solubility. When dogs were exposed (nose only) to an aerosol of soluble ^{85}Sr-labelled strontium chloride (activity median aerodynamic diameter [AMAD] 1.4–2.7 µm) for 2–22 min, less than 1% of the initial lung burden remained in the lung 12 h after the exposure (Fission Product Inhalation Project, 1967a). In contrast, when dogs were similarly exposed to ^{90}Sr in fused montmorillonite clay particles (AMAD 2.2 µm), the average half-time of elimination of strontium from the lungs (by absorption) was 490 days (Snipes et al., 1974a, 1974b). When rats were exposed to aerosols of ^{85}Sr as the carbonate, phosphate, fluoride, oxide or titanate (particle sizes and doses not specified), less than 1% of the initial ^{85}Sr lung burden remained 5 days after inhalation of the carbonate, phosphate, fluoride or oxide, compared with 60% of the less soluble strontium titanate (Willard & Snyder, 1966).

In rats, an intratracheal dose of strontium chloride was absorbed with a half-time of <1 day (Naményi et al., 1986). By contrast, in rats that received an intratracheal dose of 360–760 µg of strontium as strontium titanate, strontium was eliminated from the lungs with half-times of 0.4 day (85%) and 130 days (15%). This reflects a rapid initial phase of mechanical clearance from the tracheobronchial region, followed by a slow phase of pulmonary absorption (Anderson et al., 1999). Administration of ^{85}Sr-labelled strontium chloride (in saline) directly into the nasal tract of hamsters led to absorption of 67% of the ^{85}Sr in 4 h; 63% was estimated to have been absorbed directly from the nasopharynx region (Cuddihy & Ozog, 1973).

Studies in healthy adult humans or hospital patients given an oral dose of strontium chloride or ingesting strontium in the diet indicate that approximately 20% (range 11–28%) of ingested strontium is absorbed from the gastrointestinal tract. Absorption was quantified from plasma strontium concentration–time profiles for ingested and intravenously injected strontium (bioavailability study) or from measurements of the difference between the amount ingested and the amount excreted in faeces (balance study). Although balance studies might yield underestimates of absorption (because of faecal excretion of absorbed strontium), the two methods yielded similar absorption estimates (Spencer et al., 1960, 1972; LeRoy et al., 1966; Rundo & Lillegraven, 1966; Hart & Spencer, 1967; Uchiyama et al., 1973; Likhtarev et al., 1975; Warren & Spencer, 1976; Leeuwenkamp et al., 1990; Blumsohn et al., 1994; Sips et al., 1994, 1995, 1996; Bianchi et al., 1999). Studies conducted in infants and children indicate that approximately 15–30% of dietary strontium is absorbed, similar to estimates in adults (Harrison et al., 1965; Kahn et al., 1969; Sutton et al., 1971b; Alexander et al., 1974).

Significant age-related differences in absorption of ingested strontium were not seen in these human studies. However, 15-day-old rats absorbed 85% of an oral dose of strontium chloride, whereas rats that were at least 89 days old absorbed just 8% of the dose (Forbes & Reina, 1972). In another study, adult rats absorbed 19% of an oral dose of 1.4 mg of strontium as strontium chloride (Sips et al., 1997), a value similar to that reported for humans (Sips et al., 1995, 1996). These data suggest the possibility that absorption of strontium is more extensive during the neonatal period in humans.

Rats given a tracer dose of ^{85}Sr as strontium chloride in drinking-water between 14 and 16 days after the start of lactation absorbed twice as much strontium as did non-lactating control rats (11% compared with 5% absorption). Absorption was estimated as the fraction of

the dose in the skeleton, urine and pups (Kostial et al., 1969).

Studies in hamsters suggest that absorption can occur in the stomach and small intestine. Following a gavage tracer dose of ^{85}Sr-labelled strontium chloride, 37% was absorbed; 20% was absorbed when the pyloric sphincter had been ligated (Cuddihy & Ozog, 1973).

Co-ingestion of strontium and calcium reduced strontium uptake and skeletal strontium retention (Palmer et al., 1958; Steinbach, 1968; Roushdy et al., 1980, 1981). Oral administration of phosphate (as aluminium phosphate antacid gel) reduced the gastrointestinal absorption of strontium by increasing its excretion in faeces (Carr & Nolan, 1968; Spencer et al., 1969a, 1969b; Keslev et al., 1972). Oral administration of sulfates at the same time as strontium reduced strontium retention in the skeleton (Volf, 1964).

One human study has indicated that undamaged skin is a relatively effective barrier to penetration by strontium. Following application of ^{85}Sr-labelled strontium chloride solution to the intact forearm skin (average area 8 cm^2) of three volunteers for 6 h, absorption over the next 40 days was estimated to be 0.26% (range 0.14–0.37%) of the applied dose (Ilyin et al., 1975).

When 0.01–1.0% strontium chloride solutions containing ^{90}Sr were applied to the epidermal surface of abdominal skin removed from 5- or 9-day-old rats, penetration of radiostrontium was inversely related to concentration. In the case of a 0.1% solution, penetration was 0.5% for the (hairless) skin of 5-day-old rats compared with 2% for (hairy) skin of 9-day-old rats, suggesting that the hair follicles in skin of the older rats allowed increased permeation (Bauerová et al., 2001).

7.3 Distribution

The distribution of absorbed strontium in the human body is similar to that of calcium, with approximately 99% of the total body burden being in the skeleton (ICRP, 1993). Strontium distributes relatively uniformly within the bone volume, where it exchanges with calcium in hydroxyapatite. The strontium to calcium concentration ratio in bone increases with age from approximately 3×10^{-4} at birth to 5×10^{-4} in adults (Tanaka et al., 1981; Papworth & Vennart, 1984). This ratio is about 10–20% higher in cortical bone than in trabecular bone (Tanaka et al., 1981).

In animals, strontium absorbed from the respiratory tract rapidly distributes, primarily to the skeleton. When dogs were exposed (nose only) to an aerosol of soluble ^{85}Sr-labelled strontium chloride (AMAD 1.4–2.7 μm) for 2–22 min, 37% was found in the skeleton within 12 h. After 4 days, 84% was in the skeleton (Fission Product Inhalation Project, 1967a). Within 4–6 days of exposing rats for 30 min to aerosols of ^{85}Sr as the carbonate, phosphate, fluoride or oxide (particle sizes and doses not specified), more than 99% of the body burden of ^{85}Sr was in the skeleton (Willard & Snyder, 1966). Two days after rats were exposed (head only) for 10 min to tracer levels of ^{85}Sr or a mixture of ^{85}Sr and ^{90}Sr aerosols (AMAD 1.8–2.8 μm), the concentration in bone was 100–2000 times higher than in soft tissues. The rank order of soft tissue concentrations (highest to lowest) was muscle > skin > liver > kidney, and none was detected in the lungs (Fission Product Inhalation Project, 1967b). In rats exposed to ^{89}Sr-enriched airborne fly ash (90% with a particle diameter less than 20 μm) for 6 h, strontium was detected in various tissues. On the day after exposure, the tissue to plasma strontium concentration ratios were 0.3–0.5 in the liver, kidney, small intestine and heart (Srivastava et al., 1984b).

Although intratracheal instillation does not precisely replicate inhalation exposure, the two exposure routes likely lead to similar distribution patterns. In rats given an intratracheal dose of ^{89}Sr-enriched fly ash (90% with a particle diameter below 20 μm), radioactivity was eliminated from the lung and appeared in plasma and other tissues within days of the exposure; tissue to 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 (Srivastava et al., 1984a). The relatively high concentrations of strontium in the gastrointestinal tract probably reflect the mechanical clearance of strontium from the airways to the oesophagus.

In an analysis of published data from the United Kingdom on ^{90}Sr and calcium concentrations in human bone tissues and diets during 1955–1970, scientists concluded that skeletal uptakes of strontium varied with age, being highest (at about 10% of dietary intake) in infants and during adolescence, when bone growth rates are relatively high, and lower (at about 4.75% of intake) in adults. Approximately 7.5% of the cortical bone ^{90}Sr burden was eliminated from bone each year (equivalent to an elimination half-time of approximately 9.2 years). The rate of elimination from trabecular bone was approximately 4 times higher (Papworth & Vennart, 1984).

Administration of strontium chloride hexahydrate to rats in the diet at concentrations up to 1200 mg/kg for 90 days had no effect on strontium levels in blood or muscle. At 30 mg/kg of diet and above for 14 days or at 75 mg/kg of diet and above for 90 days, there were dose-related increases in strontium in the bone. At 3000 mg/kg of diet for 2 weeks, the females had strontium concentrations of 2, 1 and 1451 μg/g in blood, muscle and bone (wet tissue), respectively. At 4800 mg/kg of diet for 90 days, the males had strontium concentrations

of 2, 2 and 5941 µg/g in blood, muscle and bone (wet tissue), respectively (Kroes et al., 1977).

In rats given drinking-water containing strontium (as strontium chloride) at 3.4 mg/l for 3 months, the serum concentration of strontium was 8.7 mg/l, and the tissue to serum strontium concentration ratios were as follows: liver, 0.7; heart, 1.2; muscle, 1.1; adrenal, 1.3; brain, 1.2; and bone, 1300. Strontium to calcium ratios in these tissues were approximately 0.05–0.1 (Skoryna, 1981a). In rats given an intraperitoneal injection of strontium, tissue to plasma strontium concentration ratios 1–5 h later were <1 in the fat, spleen, liver, ovary, testis, skeletal muscle and heart and 1.2–1.7 in the lung, small intestine, salivary gland, kidney and skin (Brues et al., 1969). The tissue to plasma concentration ratio exceeded 2 in the seminal vesicles of mice several days after an intraperitoneal dose of strontium (Brues et al., 1967).

Information on the subcellular location of strontium in soft tissues is extremely limited. In rats drinking water containing strontium (as strontium chloride) at 1.9 mg/l for 3 months, strontium concentrations (per milligram of protein) in the mitochondrial, lysosomal and microsomal fractions of liver were about 5 times higher than the concentration in cytosol (Skoryna, 1981a). As much as 50–80% appeared to be bound to protein (Kshirsagar, 1977).

In human blood obtained from blood banks, strontium concentrations were 7.2 µg/l in the erythrocyte fraction and 44 µg/l in the plasma fraction, suggesting that most of the blood strontium resides in the plasma (Olehy et al., 1966). Strontium binds to (as yet uncharacterized) proteins in human serum. When incubated at 10 mg/l with human serum, some 45% of strontium was ultrafilterable (Alda & Escanero, 1985). Others reported a value of 60% for the ultrafilterable fraction in two subjects with a plasma strontium concentration of 3.5 mg/l after an intravenous dose of 20 or 100 mg of strontium chloride (Harrison et al., 1955). This concentration is 160 times higher than that reported in subjects not receiving strontium supplements (Versieck et al., 1993); in these subjects without supplements, a larger fraction of the serum strontium may be bound, as binding appears to be saturable (Berg et al., 1973; Alda & Escanero, 1985). Values of 30–40% protein binding have been reported for plasma from adult guinea-pigs and 50% for fetal guinea-pig plasma (Twardock et al., 1971).

No placental transfer of strontium was detected when rats were given an intratracheal dose of ^{89}Sr-enriched fly ash on days 14–18 of gestation. Strontium concentrations in whole fetus, liver, lung, heart and kidney were similar to those in sham-treated controls (Srivastava et al., 1990).

Strontium concentrations were similar in amniotic fluid and in the maternal blood when examined in eight healthy women during weeks 16–20 of pregnancy (Silberstein et al., 2001). Transfer coefficients—expressed as the ratio of ^{90}Sr concentrations (per gram of calcium) in the fetal and maternal skeletons—were determined for six residents of the Techa River region of Russia who were exposed to strontium (as a result of releases from a plutonium production plant) prior to pregnancy and their seven stillborn infants. The transfer coefficients (fetal to maternal ratio) varied from 0.012 to 0.24, with the higher values associated with maternal exposures that occurred during adulthood and lower values associated with maternal exposures during childhood or adolescence. The difference was not related to the maternal strontium burden at pregnancy and may reflect a lower availability of strontium deposited in cortical bone during periods of active bone growth. It was concluded that strontium in the maternal skeleton can be transferred to the fetus during pregnancy (Tolstykh et al., 1998, 2001).

The fetus begins to accumulate strontium from the beginning of ossification (Olsen & Jonsen, 1979). For example, when mice were given an injection of strontium on day 14 of pregnancy (about the time ossification starts), the fetal strontium burden was 0.7% of the maternal dose, compared with 4.5% if the maternal dose was given on day 18 of pregnancy. Thus, fetal transfer was higher when the mothers were dosed at the time of greatest skeletal growth (Rönnbäck, 1986). A similar observation has been made in rats; uptake of strontium by the fetus was highest (1–2% of an injected maternal dose) when the mothers were dosed on or after the 16th day of gestation (when ossification of the fetal skeleton begins) (Wykoff, 1971; Hartsook & Hershberger, 1973). The distribution of strontium in the fetus at the end of gestation is similar to that in the mother, with most of the strontium burden in the skeleton. In mice, the skeletal (long bones) to soft tissue concentration ratio was approximately 40 in both the fetuses and dams (Jacobsen et al., 1978).

Strontium enters mammary milk in humans and can be transferred to newborns during breastfeeding (Harrison et al., 1965). The mean concentration of strontium in breast milk of 12 healthy women was 74 µg/l (range 39–93 µg/l), and the strontium to calcium concentration ratio was 2.4×10^{-4} (Harrison et al., 1965). In a study of 29 healthy women, the concentration of strontium in colostrum samples collected during the first 3 days after delivery was comparable with that in serum from venous blood samples taken 20 min before delivery. In contrast, the concentration of calcium in colostrum was significantly higher than that in maternal serum. Whereas calcium transport was active, strontium transfer seemed to be based primarily on a concentration gradient mode of action (Rossipal et al., 2000). Animal studies provide

additional evidence for transfer of strontium from breast milk to newborns during lactation (Hopkins, 1967; Rönnbäck et al., 1968; Kostial et al., 1969; Jacobsen et al., 1978). When rats were given ^{85}Sr at tracer concentrations in drinking-water on days 14–16 of lactation, approximately 5% of the dose was recovered in the nursing pups 24 h after the end of exposure (Kostial et al., 1969). When lactating mice received an intraperitoneal injection of radioactive strontium, strontium levels in the nursing pups were about 20% of those in the dams (Rönnbäck et al., 1968). These results are consistent with those of the oral exposure study (Kostial et al., 1969), assuming that approximately 25% of the oral dose was absorbed by the dam. The tissue distribution of strontium in lactating mice and their offspring was found to be similar after an intraperitoneal dose to the dams during lactation; concentrations were approximately 1000 times higher in bone than in liver and kidney (Jacobsen et al., 1978). The strontium concentration in calvaria (roof of the skull) of the lactating pups, after 5 days of lactation, was approximately 3 times that of the dams, whereas the concentrations in long bones of pups and dams were similar (Jacobsen et al., 1978). 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.

After dermal application of ^{85}Sr-labelled strontium chloride to the left forearm of volunteers, ^{85}Sr was detected (by external counting) in the patella and right forearm bone 3 and 6 h after the start of exposure, suggesting that some strontium had been absorbed and taken up by bone (Ilyin et al., 1975). Distribution of dermally absorbed strontium is likely to be similar to that of strontium absorbed by the oral route, with most of the body burden in the skeleton (ATSDR, 2004).

7.4 Metabolism

Strontium can bind to proteins and, based on its similarity to calcium, probably forms complexes with various inorganic anions, such as carbonate and phosphate, and carboxylic acids, such as citrate and lactate (Lloyd, 1968; Twardock et al., 1971; Kshirsagar, 1977; Alda & Escanero, 1985).

Strontium is able to interact with ligands that normally bind calcium (Skoryna, 1981a). These include hydroxyapatite, the main component of mineralized bone (Harrison et al., 1959; Schoenberg, 1963), and a variety of calcium-binding and calcium transport proteins that are important in the physiological disposition of calcium in cells, including Ca^{2+}-adenosine triphosphatases (Pfleger & Wolf, 1975; Mermier & Hasselbach, 1976; Berman & King, 1990; Sugihira et al., 1992; Yu & Inesi, 1995), Na^{+}–Ca^{+}-antiport (Niggli, 1989; Richard et al., 1989; McCormack & Osbaldeston, 1990) and Ca^{2+} channels (Gregoire et al., 1993; Fukushi et al., 1995a, 1995b).

7.5 Excretion

Strontium that is absorbed from the gastrointestinal tract is excreted primarily in urine and faeces. In two radium dial painters examined about 10 years after exposure, urinary and faecal excretion of strontium over 24 h accounted for approximately 0.03% and 0.01% of the body burden, respectively (Wenger & Soucas, 1975). The urinary to faecal excretion ratio of 3 is consistent with ratios of 2–6 observed (over several days to weeks) in subjects given an intravenous injection of strontium chloride (Bishop et al., 1960; Snyder et al., 1964; Samachson, 1966; Uchiyama et al., 1973; Likhtarev et al., 1975; Blake et al., 1989a, 1989b; Newton et al., 1990). Thus, urine appears to be the major route of excretion of absorbed strontium. The observation of faecal excretion of radioactive strontium weeks to decades after an oral exposure or over shorter periods after an intravenous exposure suggests the existence of a mechanism for transfer of absorbed strontium into the gastrointestinal tract, either from the bile or directly from the plasma. Evidence for direct secretion of strontium from the plasma into the intestine is provided by studies in animals. The available information does not address the extent to which biliary excretion may also contribute to faecal excretion of strontium (ATSDR, 2004).

Urinary excretion of inhaled and absorbed strontium can be slow. In the case of a worker who accidentally inhaled an unknown amount of ^{90}Sr-labelled strontium chloride, 52% of the total ^{90}Sr excreted in the urine was voided with a half-time of 3.3 days, with subsequent half-times of 17 days (7%) and 347 days (18%). The urinary to faecal excretion ratio was 3:1 during the 800 days after exposure (Petkau & Pleskach, 1972). In a second case, deposition of ^{90}Sr-labelled strontium carbonate occurred in the nasal tract of an exposed worker. Excretion in urine occurred with half-times of 2.2 (>90%), 15 and 175 days, and the urinary to faecal excretion ratio over the first 24 days was 0.71. The lower ratio was presumably due to the relative importance of faecal excretion resulting from mechanical clearance of strontium from the respiratory tract into the gastrointestinal tract over this shorter timescale (Rundo & Williams, 1961). In a third case, two workers accidentally inhaled ^{90}Sr-labelled strontium titanate, and ^{90}Sr was detected in urine over 225 days (Navarro & López, 1998).

Balance data for a "reference" man have been described as follows (in mg/day): intake from food and water (1.9), loss in urine (0.34), loss in faeces (1.5), loss in sweat (0.02) and loss in hair (0.0002) (Snyder et al., 1975).

The long-term (over decades) elimination of strontium was studied in 361 males and 356 females exposed to radiostrontium in the Techa River area of Russia after release of fission products from a plutonium production process. Whole-body elimination half-times were estimated to be 28 years in males and 16 years in females. The difference in these elimination rates was mainly due to a pronounced increase in rate in females after age 50 years, presumably reflecting increased bone resorption after menopause (Tolstykh et al., 1997). A similar mean value of 25 years was estimated for the long-term elimination half-time of strontium in 56 radium dial painters (Müller et al., 1966). In two dial painters, long-term elimination half-times were estimated to be 9 years (Wenger & Soucas, 1975). Estimates of the long-term elimination half-times of strontium reflect primarily the storage of strontium in bone and its release from bone. Over short periods after exposure, elimination rates are faster, reflecting soft tissue elimination and elimination from a relatively rapidly exchangeable pool of strontium in bone. When whole-body elimination of a tracer dose of ^{85}Sr was measured for periods of 42–108 days in nine subjects, the mean elimination half-time was 91 ± 32 days (Likhtarev et al., 1975). In three healthy subjects given a single oral dose of strontium chloride, the estimated average whole-body elimination half-times, studied over 13 days, were 2 days for the first 30% and 59 days for the remaining 70% (Uchiyama et al., 1973). Similar short-term rates of elimination have been observed within days to a few weeks after an intravenous injection of strontium chloride (MacDonald et al., 1965; Newton et al., 1990).

In dogs exposed to ^{85}Sr-labelled strontium chloride (AMAD 1.4–2.7 μm) aerosols for 2–22 min, whole-body elimination half-times were 0.6 (59% of dose), 9 (12%) and 300 days (29%). The rapid early elimination phase reflects mechanical transfer of strontium deposited in the tracheobronchial region of the respiratory tract to the gastrointestinal tract (and then to the faeces), and the slower elimination component reflects elimination from the skeleton (Fission Product Inhalation Project, 1967a). A similar elimination pattern was seen in rats exposed to tracer levels of ^{85}Sr or a mixture of ^{85}Sr and ^{90}Sr aerosols (AMAD 1.8–2.8 μm). The long-term whole-body elimination half-time, measured for 5–230 days after exposure, was 330 days (Fission Product Inhalation Project, 1967b).

After application of ^{85}Sr-labelled strontium chloride to the forearm skin of volunteers, ^{85}Sr was excreted in urine (faecal excretion was not measured in this study) (Ilyin et al., 1975).

As discussed above, absorbed strontium is also eliminated in breast milk during lactation. The mean concentration of strontium in breast milk of 12 healthy women was 74 μg/l (range 39–93 μg/l), and the strontium to calcium concentration ratio was 2.4×10^{-4} (Harrison et al., 1965).

Strontium has been detected in human saliva and seminal fluid. In healthy subjects given a single intravenous injection of strontium chloride, the saliva to plasma concentration ratio was 0.9, and the semen to plasma ratio was 0.6 (Harrison et al., 1967).

7.6 Physiologically based pharmacokinetic modelling

The International Commission on Radiological Protection (ICRP, 1993) has developed a compartmental model of the kinetics of alkaline earth elements, including strontium, for humans. This is applicable to infants, children, adolescents and adults.

8. EFFECTS ON LABORATORY MAMMALS AND IN VITRO TEST SYSTEMS

8.1 Single exposure

The oral median lethal dose (LD_{50}) for strontium nitrate in male mice was 2.35 g/kg body weight as strontium (Llobet et al., 1991). For strontium chloride, the oral LD_{50} was 2.7 and 2.9 g/kg body weight as strontium in female and male mice, respectively (Ghosh et al., 1990). An older paper reported oral LD_{50} values in rats and mice for strontium chloride of 2.25 and 3.1 g/kg body weight, respectively (Woodard & Calvery, 1941). No overt toxicity was seen following administration of strontium carbonate at a strontium dose of 14 g/kg body weight to rats and mice by stomach tube (Zyuzyukin & Makolkina, 1979). Rats (six females) given strontium sulfate at 2 g/kg body weight by gavage (950 mg/kg body weight as strontium) showed no toxic effects or changes in a "full" macroscopic examination of tissues and organs (NIER, 2006a). All of these figures indicate a low acute oral toxicity.

No overt effects or changes in a "full" macroscopic necropsy were seen when strontium sulfate was applied (24 h, covered contact) to the skin of rats (five of each sex) at 2 g/kg body weight, equivalent to a strontium dose of 950 mg/kg body weight. The rats were observed for up to 14 days (NIER, 2006b).

8.2 Short-term exposure

Administration of strontium chloride to monkeys by capsule at 2 g/kg body weight per day for 7 days did not induce any overt toxic effects, but resulted in local

irritation, leading to haemorrhagic and erosive lesions in the oesophagus and upper duodenum (Fisch et al., 2006).

Behaviour, growth, food intake, and the weights and microscopic appearance of the liver and kidney were normal in all groups of young adult rats (130–170 g; three of each sex per group) fed strontium chloride hexahydrate at up to 3000 mg/kg in the diet for 2 weeks (about 50–100 mg/kg body weight per day as strontium, assuming rats ingest food at the equivalent of 5–10% of their body weight daily). There were no clear effects on haematology, and the bones were not examined in this range-finding study (Kroes et al., 1977).

A number of short-term repeated oral dose studies show that a critical target of strontium toxicity is bone and cartilage structure. Bone histology was normal in five young female rats (starting weight 40–60 g) fed 0.19% strontium in the diet (as strontium carbonate) for 20 days (about 190 mg/kg body weight per day as strontium, assuming that young rats consume food equivalent to 10% of their body weight per day). At 0.38% in the diet (probably about 380 mg/kg body weight per day as strontium), there were irregularities in the proximal epiphyseal cartilage plate, areas of uncalcified bone matrix in the distal ends of the metaphyseal trabeculae and proximal end of the diaphysis, and decreased ash content of bone. At higher dietary concentrations (up to 3%), there were more conspicuous irregularities in the organization of the hypertrophic zone cells (distorting the usual parallel arrangement of intercellular matrix columns), in the pattern of calcification and in deposition of osteoid, as well as bands of uncalcified cartilage matrix isolated between areas of osteoid tissue. In tibias, the dry weight, ash weight, ash percentage and calcium in ash were significantly reduced. Growth was generally unaffected at up to 1%, but was reduced at 1.5% and above. The diets also contained 1.6% calcium and 0.9% phosphorus (Storey, 1961).[1]

In an experiment reported in the same publication, bone was unaffected in groups of three adult female rats (200–250 g) given up to 0.75% strontium in the diet for 20 days (about 375 mg/kg body weight per day) as strontium carbonate. Histological changes in the tibia (thicker epiphyseal cartilage plate, increased width of metaphyseal osteoid seams) were noted at 1.5% in the diet (about 750 mg/kg body weight per day as strontium) and above. At 3% in the diet, effects included reduced growth, the deposition of osteoid tissue near vascular canals, a reduction in the area of bone resorption and reductions in the dry weight, ash weight, ash percentage and calcium in ash of bone (Storey, 1961).

Calcium absorption and rates of bone formation and resorption were normal in 36-day-old rats ingesting strontium carbonate in the diet at up to 102 mg/kg body weight per day as strontium for 27 days. At a strontium dose of 510 mg/kg body weight per day, there was a 13% reduction in serum calcium, a 24% reduction in bone formation rate, a 28% reduction in bone resorption rate (based on ^{45}Ca uptake) and a significant reduction in the calcium content of ashed femurs; ash weight was unaltered (Morohashi et al., 1994).

A number of other studies involving higher strontium doses have identified effects on bone formation and structure. For example, rats (100–125 g) ingesting diet supplying strontium (as strontium carbonate) at 500 mg/kg body weight per day for 3 weeks showed numerous bone abnormalities, including reduced ash weight (mineral content) of metaphyseal bone, increased complexed acidic phospholipid content (lipid nucleator of bone mineral), large areas of non-mineralized bone (osteoid) in epiphyseal bone and secondary spongiosa, abnormally wide epiphyseal plates with abnormally long and dense metaphyses, lower bone density areas in the diaphyses, longer primary spongiosa of the proximal tibia, and disorganized trabeculae disconnected from the overlying calcified cartilage. There was no evidence of vitamin D deficiency. The investigators suggested that strontium binds to the surface of initial hydroxyapatite crystallites, reducing their further proliferation and resulting in a smaller crystal size (Neufeld & Boskey, 1994).

In male weanling rats ingesting dietary strontium chloride at a strontium dose of 1520 mg/kg body weight per day for 26 days, growth was reduced, epiphyseal growth plates had abnormally thick hypertrophic zones and impaired calcification and resorption at the metaphyseal side, and cartilage contained 75% less calcium and had a 60% lower rate of synthesis of glycosaminoglycans and collagen (Svensson et al., 1985, 1987). Weanling (21-day-old) male rats ingesting strontium (form unspecified) at 1850 mg/kg body weight per day for 20 days in a diet sufficient in calcium, phosphorus and vitamin D showed reduced growth, a 70% thicker epiphyseal growth plate, larger zones in the epiphyseal regions of long bones (and alterations in the relative sizes: smaller proportional volumes of the resting, proliferative and calcifying zones, and a larger volume of the hypertrophic zone) and an increase in the volume of extracellular matrix in bone, possibly associated with a reduced rate of extracellular matrix vesicle degradation (Reinholt et al., 1984). The epiphyseal cartilage of these rats had alterations in proteoglycan composition (slightly higher galactosamine content), chondroitin sulfate chain lengths (larger), regional distributions of large and small

[1] This study was used to derive the intermediate-duration minimal risk level (MRL) of 2.0 mg/kg body weight per day by ATSDR (2004) and the reference dose (RfD) of 0.6 mg/kg body weight per day by USEPA (1996).

chondroitin sulfate peptides and regional distributions of both non-sulfated chondroitin sulfate disaccharides and hyaluronic acid disaccharides. It was suggested that these strontium-induced alterations in cartilage matrix might affect the process of mineralization (Reinholt et al., 1985). The addition of strontium carbonate to the diet of 4-week-old male rats (giving a strontium dose of 1970 mg/kg body weight per day) for 4 weeks caused reduced growth and bone mineralization, a 33% reduction in tibia length and a 5-fold increase in epiphyseal plate width (Matsumoto, 1976). Inclusion of strontium phosphate in the diet of male weanling (21-day-old) rats at strontium concentrations of 2% (about 2000 mg/kg body weight per day) for 2 weeks resulted in decreased growth and decreased acid phosphatase in the small intestine and liver, whereas alkaline phosphatase was decreased in the small intestine but increased in the bone and unaffected in liver. These effects were reversed by giving the rats a normal low-strontium diet for 2 weeks, and their biological significance is unclear; however, it was suggested that strontium may have stimulated osteoblasts, which secrete osteoid and have a high alkaline phosphatase activity (Kshirsagar, 1976). Young (50–70 g) rats developed a rachitic gait in 3 weeks after ingesting dietary strontium carbonate at a strontium dose of 2160 mg/kg body weight per day (Storey, 1962) (see study description in section 8.3).

Mice seem to have a similar susceptibility to the bone effects of strontium. When 21-day-old male mice ingested strontium chloride at a strontium dose of 350 mg/kg body weight per day in the drinking-water for 29 days, minor bone effects included a 10% increase in osteoid surface (percentage of the endosteal surface covered by an osteoid seam) and an 11% reduction in the number of active osteoclasts. There were no effects on tibial length, bone mineral content (per cent ash, calcium or phosphorus), the osteoblastic surface of the vertebrae (percentage of the endosteal surface showing plump osteoblasts), bone matrix apposition rate, osteoid seam thickness (average width of all endosteal osteoid seams) or calcified bone volume (Marie & Hott, 1986).

Inclusion of strontium (as the chloride) at 2000 mg/l in the drinking-water of rats for 15 days had no effect on exploratory motor activity (Escanero et al., 1985).

Only one study involving repeated inhalation of a strontium salt was identified. A review (Stokinger, 1981) described this early study from the former Soviet Union in which rats inhaling strontium nitrate at 45 mg/m^3 for 4 h/day for 1 month (83% of particles <5 µm) showed functional changes in the liver and kidney and histological changes in the lungs, heart, liver, kidneys and spleen (Zyuzyukin, 1974).

8.3 Medium-term exposure

The most comprehensive repeated oral dose study using the lowest doses showing toxic effects involved inclusion of strontium chloride hexahydrate in the diet of weanling rats (40–60 g; 10 of each sex per group) at 0, 75, 300, 1200 or 4800 mg/kg (strontium doses of 0, 2.5, 10, 40 and 160 mg/kg body weight per day, respectively, assuming young rats consume feed at an amount equivalent to about 10% of their body weight per day) for 90 days (see Table 6). The diet was said to contain "adequate" levels of calcium, magnesium, phosphorus, iodine and vitamin D3. Inclusion of this strontium compound at strontium concentrations up to 10 mg/kg body weight per day had no effect on behaviour, appearance, growth, food intake, survival, haematology, serum chemistry, blood calcium or phosphorus, liver glycogen, urinalysis, weights of the major organs or microscopic appearance of a fairly wide range (25) of tissues, including bone. At 40 mg/kg body weight per day, the only statistically significant finding was a higher thyroid weight in the males. However, this was not clearly related to dose, and the thyroid was microscopically normal. At 160 mg/kg body weight per day, the males showed increased thyroid weight and histological signs of thyroid activation, the females showed lower pituitary weights (without microscopic changes), and liver glycogen levels were lower in both sexes, although the reduction was statistically significant only in the females. Strontium concentrations in the bone were significantly increased at all dose levels (Kroes et al., 1977). The 1200 mg/kg dietary concentration of strontium chloride hexahydrate, providing a strontium dose of about 40 mg/kg body weight per day (assuming young rats consume feed at an amount equivalent to about 10% of their body weight per day), was considered to be the study no-observed-adverse-effect level (NOAEL).

In a recent detailed investigation, reduced spleen weights were seen in female rats given strontium sulfate at 500 mg/kg body weight per day (about 240 mg/kg body weight per day as strontium) or more by gavage for 40–54 days. At a strontium dose of 480 mg/kg body weight per day (administered as strontium sulfate) and above, epididymis and testis weights were increased in the male rats (treated similarly for 42 days). At a strontium dose of 950 mg/kg body weight per day, the females showed reductions in reticulocyte counts and activity of aspartate aminotransferase (AST) (also known as serum glutamic–oxaloacetic transaminase, or SGOT). Survival, growth, sensory and motor functions, urinalysis, and the microscopic appearance of a range (about 30) of tissues and organs (including bone) were unaltered by treatment (NIER, 2006c).

Beneficial effects on bone mineralization (a 17% increase in mineral bone volume and a 70% increase in

Table 6: Findings in male and female rats in the Kroes et al. (1977) study.[a]

	Dose in males (mg/kg body weight per day)					Dose in females (mg/kg body weight per day)				
End-point	**0**	**2.5**	**10**	**40**	**160**	**0**	**2.5**	**10**	**40**	**160**
Liver glycogen content (mg/g) (*n* = 6)	17.7 ± 6.4	22.3 ± 6.2	19.3 ± 6.3	12.4 ± 4.7	10.0 ± 6.4	22.4 ± 6.1	19.9 ± 7.5	17.1 ± 3.1	15.2 ± 5.6	7.8 ± 3.7***
ALT, S-AP, S-urea	—	No changes	No changes	No changes	No changes	—	No changes	No changes	No changes	No changes
Relative pituitary weight (%)	0.0032	0.0029*	0.0033	0.0030	0.0032	0.0074	0.0064	0.0062*	0.0066	0.0056**
Relative thyroid weight (%)	0.0054	0.0066	0.0064	0.0072**	0.0068***	0.0071	0.0082	0.0080	0.0087	0.0074
Histological thyroid activity[b]	1/6/3/0	3/3/3/1	2/4/4/0	1/5/3/0	2/3/3/2	5/3/2/0	3/2/3/1	1/5/4/0	4/4/2/0	3/5/2/0
Bone histology	No pathological changes	No pathological changes	No pathological changes	No pathological changes	No pathological changes	No pathological changes	No pathological changes	No pathological changes	No pathological changes	No pathological changes
B-Ca, B-Mg, B-phosphate	—	No changes	No changes	No changes	No changes	—	No changes	No changes	No changes	No changes
Organ histology	No pathological changes	No pathological changes	No pathological changes	No pathological changes	No pathological changes	No pathological changes	No pathological changes	No pathological changes	No pathological changes	No pathological changes
Relative prostate weight (%)	0.128	0.092*	0.106	0.101*	0.112	—	—	—	—	—
Bone Sr (mg/kg) (*n* = 5)[c]	9 ± 4	273 ± 49	523 ± 87	1430 ± 100	5941 ± 783	—	—	—	—	—

ALT, alanine aminotransferase (also known as serum glutamic–pyruvic transaminase, or SGPT); AP, alkaline phosphatase; B, bone; S, serum. Statistically significant changes have been denoted as follows: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

[a] *n* = 9 or 10 if not otherwise indicated.

[b] Number of animals with histology not activated / very slight activation / slight activation / moderate activation.

[c] At 12 weeks.

the number of bone-forming sites) and no adverse effect on the hydroxyapatite mineral particle size were seen in 28-day-old male rats ingesting strontium (in an unspecified form) at 168 mg/kg body weight per day for 8 weeks (Grynpas et al., 1996). The bone calcification rate was normal or even stimulated in rats given strontium (in the form of strontium chloride) in the drinking-water at 316–525 mg/kg body weight per day for 9 weeks, but was reduced (by 17%) at a strontium dose of 633 mg/kg body weight per day (Marie et al., 1985).

A review briefly describes a limited study in which adult (250 g) male rats (at least 10 per group) were fed strontium chloride at 0.2 (control), 900, 1900 or 3400 mg/l in their drinking-water for 3 months (Skoryna & Fuskova, 1981). Assuming that an adult rat consumes 49 ml of water per day, these concentrations correspond to strontium doses of 0, 70, 147 and 263 mg/kg body weight per day (USEPA, 1996). Adequate amounts of calcium (35 mg/l) and magnesium (6.8 mg/l) were given in the drinking-water. Microscopic examination showed that the tissues (bone and probably heart, liver, muscle, lung, brain, adrenal and kidney) were unaffected by treatment (Skoryna & Fuskova, 1981).

Ingestion of strontium (as an unspecified strontium compound) at 565 mg/kg body weight per day for 43 days by weanling rats resulted in respiratory difficulties, hindlimb paralysis, rickets and osteomalacia (with lower bone sodium, higher bone potassium, reduced bone mineralization as measured by per cent bone ash, and unmineralized osteoid in vertebrae) and deaths. It is not clear whether the paralysis was neurological or muscular, but it could have been related to abnormal calcium signalling in muscle or nerve. It is unlikely that the paralysis was due to the femoral deformation, as even severely rachitic and osteomalacic rodents are not generally paralysed (Johnson et al., 1968).

No effects were noted in groups of 5–6 weanling (21-day-old) rats fed 0.5% strontium in the diet (as strontium phosphate), a concentration supplying strontium at 580 mg/kg body weight per day, for 4–6 weeks. At 1% in the diet (a strontium dose of 1270 mg/kg body weight per day) and above, growth slowed, and alkaline phosphatase activity decreased in the small intestine but increased in the bone. Decreased liver alkaline phosphatase activity, haemorrhage, paralysis, abnormally thick epiphyseal cartilage plates in the long bones and deaths occurred at 2% dietary strontium (2820 mg/kg body weight per day) (Kshirsagar, 1976).

Young (50–70 g) rats ingesting strontium (as dietary strontium carbonate) at a dose of 2160 mg/kg body weight per day for 7 months grew more slowly and developed a rachitic gait. Some rats developed spinal kyphosis, bent tibias and irregular discoloured (tooth) enamel. Histological abnormalities in long bone differentiation included reduced calcification, excess growth and fragmentation of the epiphyseal cartilage plate, abnormal deposition of osteoid (unmineralized bone) in the metaphysis and isolated cartilage nodules. Osteoid accumulated in the skull. Adult rats ingesting 1570 mg/kg body weight per day showed similar but less marked effects. Abnormal depositions of osteoid in long bones and skull were less extensive, and the epiphyseal plate did not fragment. Tooth enamel was abnormally white and pitted (Storey, 1962).

8.4 Long-term exposure and carcinogenicity

No long-term repeated-dose or carcinogenicity studies meeting current guidelines were identified.

8.4.1 Strontium chromate

Chromates are well-recognized mammalian carcinogens. Nine months after the insertion of a strontium chromate pellet into the bronchus of 15 male rats, 1 had developed a squamous cell carcinoma, 7 had carcinoma in situ or dysplasia, 8 had squamous metaplasia and 5 showed goblet cell hyperplasia (Takahashi et al., 2005). In a limited investigation, the carcinogenicity of two commercially available batches of strontium chromate was studied using an intrabronchial pellet implantation technique. Metal pellets were coated with a mixture of cholesterol and strontium chromate and implanted into the left bronchus of 100 male and 100 female young rats. At 24 months, 105 of 198 (53%) of the lungs treated with strontium chromate had a primary keratinizing squamous carcinoma of the bronchial epithelium, compared with 0 of 100 cholesterol controls. The investigators indicated that carcinogenicity was associated with sparingly soluble chromium(VI) compounds, such as strontium, calcium or zinc chromates (Levy et al., 1986). In an older study in which rats were treated with an undisclosed dose of strontium chromate by intrapleural implantation, unspecified tumours were seen at the implantation site in 17 of 28 rats (after 27 months) compared with 0 of 34 controls (of which only 5 survived to 24 months) (Hueper, 1961).

8.4.2 Other strontium compounds

In a limited study that was inadequately reported, adult (250 g) male rats (12 per group) were given strontium chloride in their drinking-water at a concentration of 0.2 (control), 900, 1900 or 3400 mg/l for 3 years (Skoryna, 1981a, 1981b; Skoryna & Fuskova, 1981). Assuming that an adult rat consumes 49 ml of water per day, these concentrations correspond to strontium doses of 0, 70, 147 and 263 mg/kg body weight per day (USEPA, 1996). Adequate amounts of calcium (35 mg/l) and magnesium (6.8 mg/l) were given in the drinking-water. There were no adverse effects on

growth, microscopic appearance of the bone, kidney, lung, adrenal, brain, heart or muscle; organs were not weighed, and tumours were not mentioned. Analysis of strontium in tissues and serum found only the bone to have a predilection for strontium (Skoryna, 1981a, 1981b; Skoryna & Fuskova, 1981; USEPA, 1996).

8.5 Genotoxicity and related end-points

8.5.1 Strontium chromate

In common with other chromium(VI) compounds, strontium chromate induced bacterial mutations in *Salmonella typhimurium* TA100 (only when S9 was included) (Venier et al., 1985) and sister chromatid exchanges in Chinese hamster fibroblasts in culture (Venier et al., 1985) and induced morphological transformation in Syrian hamster embryo cells (Elias et al., 1989, 1991).

8.5.2 Other strontium compounds

According to a limited report, a single gavage dose of strontium chloride induced dose-related increases in chromosomal aberrations in the bone marrow of mice (five of each sex per dose level). Animals were killed 6, 12 or 24 h after treatment at 240–2400 mg/kg body weight (females) or 260–2600 mg/kg body weight (males). The lowest doses equated to strontium doses of 130 and 140 mg/kg body weight for females and males, respectively (Ghosh et al., 1990).

Strontium chloride did not cause chromosome damage (aberrations) or changes in chromosome number when incubated with Chinese hamster oocytes in the absence of any added metabolic activation (Tateno & Kamiguchi, 1997). Strontium sulfate did not induce chromosomal aberrations or polyploidy when incubated with Chinese hamster lung cells, with or without added metabolic activation (NIER, 2006d).

Strontium carbonate did not induce mutations when tested at up to 10 mg/plate in an Ames test using *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 or TA1538 with or without S9 prepared from rat or hamster liver (Yang, 1984). Strontium sulfate similarly showed no mutagenic activity when tested in *S. typhimurium* strains TA98, TA100, TA1535 or TA1537 or in *Escherichia coli* strain WP2*uvr*A at up to 1.25 mg/plate without S9 or 5 mg/plate with rat S9 (NIER, 2006e).

Strontium chloride gave no evidence of an ability to damage bacterial DNA in a rec assay using *Bacillus subtilis* measuring differential killing (Kanematsu et al., 1980) and did not affect the fidelity of DNA synthesis in vitro (Sirover & Loeb, 1976; Loeb et al., 1977); these studies were carried out with and without an added metabolic activation fraction. Strontium chloride also failed to induce cell transformation (Heidelberger et al., 1983) or induce DNA strand breaks in Syrian hamster embryo cells (Casto & DiPaolo, 1983).

8.6 Reproductive and developmental toxicity

8.6.1 Effects on fertility

No effects on mating behaviour, fertility, gestation period or the microscopic appearance of the reproductive tissues and organs were seen when rats (16 of each sex per dose group) were given strontium sulfate by gavage at up to 2 g/kg body weight per day (strontium dose up to 950 mg/kg body weight per day), from 2 weeks before mating until day 4 of lactation. In this screening test for reproductive and developmental toxicity (combined with repeated-dose toxicity), the total dosing period was 42 days for males and 40–54 days for females (NIER, 2006c).

One publication briefly mentioned that the addition of strontium chloride at 0%, 0.09%, 0.19% or 0.34% to the drinking-water did not affect the reproduction of rats over three generations (Skoryna, 1981b). The top dose level would have equated to a strontium dose of about 260 mg/kg body weight per day (USEPA, 1996). The available information is inadequate to allow an assessment of the effects on fertility.

Inclusion of strontium chloride hexahydrate at up to 4800 mg/kg in the diet of weanling rats (10 of each sex per group) for 90 days had no effect on the weights or microscopic appearance of the testes, ovaries, uterus or prostate. This dietary concentration of strontium chloride hexahydrate would provide a strontium dose of about 160 mg/kg body weight per day, assuming young rats consume feed at an amount equivalent to about 10% of their body weight per day (Kroes et al., 1977).

8.6.2 Developmental toxicity

There were no signs of adverse effects on fetal development (implantations, litter size, live births, viability, sex ratio, body weight and length, overt malformations on external examination) in a study in which rats (16 of each sex per dose group) were given strontium sulfate by gavage at up to 2 g/kg body weight per day (strontium doses up to 950 mg/kg body weight per day), from 2 weeks before mating until day 4 of lactation. In this screening test for reproductive and developmental toxicity (combined with repeated-dose toxicity), the total dosing period was 42 days for males and 40–54 days for females (NIER, 2006c).

In a limited study, development of the bone and cartilage was assessed in newborn mice born to mothers

(four per group) fed strontium carbonate at 0% or 2% in the diet throughout pregnancy (strontium dose of 0 or about 1.5 g/kg body weight per day). Treatment did not affect maintenance of pregnancy, fetal numbers or fetal viability. Examination indicated extensive inhibition of calcification of mandibular bone and cartilage, as well as ultrastructural changes in the osteoclasts (on the mandibular alveolar bone) and chondroclasts (in the resorption area of the condylar cartilage), in the strontium group. Additionally, the osteoclasts and chondroclasts showed phagocytic activity, indicating functional changes (Shibata & Yamashita, 2001). In an earlier study, strontium carbonate was mixed in the diet to provide female rats with a 2 g/kg body weight per day dose level throughout pregnancy. The only reported effects involved the fetal bone and included vertebral kyphosis, reduced vertebral calcification and an irregular chondrocyte arrangement and appearance (Miki & Miyamoto, 1968).

Several studies addressed the effects of strontium on bone formation, in particular endochondral ossification, a developmental process that continues long after birth. For example, in a study in which 4-week-old male rats (50–60 g) were fed strontium (as strontium carbonate) at a dose of 1970 mg/kg body weight per day in a diet low in calcium (0.04%), bone mineralization was significantly affected. Tibial length was reduced by 33%, and the tibial proximal and distal epiphyseal plates were both about 5 times wider than normal. Microradiographic and histological analyses of tibial proximal heads revealed that no mineralization was detectable, that the organization of chondroblasts was irregular and that osteoid rather than mineralized bone was deposited (Matsumoto, 1976). Other studies on weanlings were conducted following acute exposure (rat: Kshirsagar, 1976) and repeated exposure (rat: Kroes et al., 1977; Reinholt et al., 1984, 1985; Svensson et al., 1985, 1987; Morohashi et al., 1994; Neufeld & Boskey, 1994; Grynpas et al., 1996; and mouse: Marie & Hott, 1986). Intermediate-duration studies on rats demonstrated that ingestion of strontium resulted in more severe skeletal effects in young animals than in adults (Storey, 1961, 1962). These studies are described in sections 8.2 and 8.3 above.

In rats, subcutaneous injection of strontium (as strontium nitrate) at up to 82 mg/kg body weight per day on days 9–19 of gestation had no effect on resorption frequency, fetal size or weight, litter size, skeletal ossification or the incidence of fetal malformations (Lansdown et al., 1972).

8.7 Mode of action

The toxicity of excess stable strontium is related to its interference in biological processes that normally involve calcium, notably skeletal development. The fact that strontium is chemically similar to calcium allows it to exchange imperfectly for calcium in bone and other cellular compartments that are enriched in calcium. Many enzymes that are calcium dependent will function when strontium is substituted, but changes in kinetic parameters may occur. Strontium can interact with secondary cell messenger systems and transporter systems that normally use calcium. Furthermore, synaptic transmission may be variably affected by strontium. Consequently, at high concentrations, differences in the chemical characteristics of strontium and calcium may be the basis for neurotoxic and neuromuscular perturbations associated with strontium intoxication (ATSDR, 2004).

In animals, large oral doses (≥0.8% in the diet for ≥6 days) suppressed the activation of vitamin D3 in the kidney, which severely reduced the expression of calbindin-D messenger ribonucleic acid (mRNA) and the translation of calbindin-D-9k protein in the duodenum (Omdahl & DeLuca, 1972; Armbrecht et al., 1979, 1998). As a result, duodenal absorption of calcium is reduced. The reported inverse correlation between the amount of strontium that is absorbed and the levels of parathyroid hormone (Vezzoli et al., 1998) suggests that changes in parathyroid hormone levels mediate this effect. Although there are no data on strontium binding to the calcium receptor of the parathyroid gland, it is likely that strontium binds in place of calcium, mimicking calcium and thereby suppressing parathyroid hormone levels. A reduction in parathyroid hormone levels will decrease the level of 1-hydroxylase available to activate vitamin D3 (ATSDR, 2004).

In addition to its effect on calcium absorption, excess absorbed strontium adversely affects bone development in several ways, leading to the development of rickets in young laboratory animals and possibly in children under special circumstances (Özgür et al., 1996). Strontium binds directly to hydroxyapatite crystals, which may interfere with the normal crystalline structure of bone (Storey, 1961). In addition, excess strontium may prevent the normal maturation of chondrocytes in the epiphyseal plates of long bones (Matsumoto, 1976). Excess strontium apparently interferes with the mineralization of complexed acidic phospholipids, which is thought to help initiate the formation of hydroxyapatite crystals in developing bone (Neufeld & Boskey, 1994). As a result, affected bone contains an excess of complexed acidic phospholipid and a significantly lower ash weight. Insufficient mineralization reduces the strength of bones, and the inability to resist compression from increasing body weight results in bone distortion (bowing) (ATSDR, 2004).

Differences in bone physiology suggest that adult rats may have a higher susceptibility to stable strontium

effects compared with adult humans. Unlike most mammals (including humans), adult rats lack a Haversian (bone remodelling) system, and the epiphyseal cartilage growth plate of the long bones of rats never entirely transforms into bone after sexual maturity, so that bone growth continues throughout life (although it is reduced after the age of 12 months) (Leininger & Riley, 1990). Thus, incorporation of strontium into the skeleton is likely to be relatively higher in adult rats than in other mammals, making rats more susceptible to strontium toxicity (ATSDR, 2004).

9. EFFECTS ON HUMANS

9.1 Bone toxicity

A relationship between soil strontium concentrations and childhood rickets was suggested in a study carried out in the Ulaş Health Region of Sivas, Turkey, a region with a high prevalence of childhood rickets (32% compared with 4.4% nationally among children up to 5 years of age). After weaning, the children's diet in this region is based mainly on grains grown in strontium-rich soil. Soils surrounding 55 villages were characterized by strontium concentration (Group 1, >350 mg/kg; Group 2, <350 mg/kg). In total, 2140 children (ages 6–60 months) from these localities (613 in Group 1 and 1527 in Group 2) were examined for signs of rickets. The proportion of children with one or more rachitic signs was higher in Group 1 (37.5% compared with 19.5%), as was the severity of disease (number of rachitic signs per child) ($P < 0.001$). The increased risk of rickets in the areas with strontium-rich soil was irrespective of age, duration of breastfeeding, and height and weight of the children (Özgür et al., 1996).

Strontium has been used to treat patients with osteoporosis or other disorders of bone mineralization. Treatment has involved administration of "low doses" of strontium salts (usually the lactate, gluconate, carbonate or ranelate) over several years. Patients were co-administered calcium and, in some cases, vitamin D (ATSDR, 2004). No adverse side-effects were reported in studies on osteoporosis patients. In one study, 72 postmenopausal patients took daily doses of up to 1.7 g of strontium (as strontium lactate) for 0.25–3 years (strontium dose of about 24 mg/kg body weight per day). Of the 32 patients who were followed up, 84% reported marked improvement (McCaslin & Janes, 1959). In another study, 50 patients ("with various conditions that might be affected by stable strontium") reported subjective improvement after ingesting 1–1.5 g of strontium gluconate per day (183–274 mg of strontium per day or a strontium dose of about 3–4 mg/kg body weight per day) for at least 3 months (Skoryna, 1981b; Skoryna & Fuskova, 1981). In a third study, no toxic effects were reported when an undisclosed number of patients consumed 1537 mg of strontium per day (as strontium lactate) for 24–36 days (Warren & Spencer, 1976).

9.2 Cancer

9.2.1 Strontium chromate

Strontium chromate was implicated as a cause of increased lung cancer mortality in workers in British chromate pigment manufacturing plants. In one factory, strontium chromate was produced from 1950 to 1968, and lead and zinc chromate were produced until 1976. For lung cancer deaths in workers exposed to "high" and "medium" levels of chromates before 1961, when industrial hygiene improvements were introduced, the observed/expected ratio (O/E) was 6/1.61, with a standardized mortality ratio (SMR) of 373 ($P < 0.01$). For workers exposed to "high" and "medium" levels from 1961 to 1967, O/E was 5/0.89 and SMR was 562 ($P < 0.01$) (Davies, 1979, 1984). No excess lung cancer risk was found (3 cases observed, 2.95 expected) among workers in two Japanese factories producing strontium chromate, but it was suggested that improvements in industrial hygiene procedures might have meant only very low exposures to strontium chromate (Kano et al., 1993; ATSDR, 2004). The carcinogenicity of strontium chromate is attributed to chromium(VI) ion, which enters lung cells and is metabolized to a genotoxic agent. Strontium itself contributes to the solubility of strontium chromate, but any associated health effect is expected to be masked by that of the chromate (ATSDR, 2004).

9.2.2 Other strontium compounds

A study carried out on Chongming Island in China found that persons living in communities with a high liver cancer mortality (41–58 cases per 100 000) had strontium concentrations in hair (3.9–10.7 mg/kg) similar to those of persons living in communities with lower liver cancer figures (17–18 cases per 100 000; strontium concentrations 4.0–21 mg/kg) in 1984. In a case–control analysis (matched for area of residence), mean strontium concentrations in cases (3.0 mg/kg) and controls (3.7 mg/kg) were similar (Wang et al., 1990).

9.3 Other effects

A 35-year-old female paramedic developed a sudden anaphylactic reaction upon inhaling fumes from a flare that contained approximately 75% strontium nitrate (~31% strontium), 10% potassium perchlorate, 10% sulfur and 10% sawdust/oil binder. Initial symptoms included coughing, wheezing, severe tachycardia and shortness of breath, unresponsive to albuterol, epinephrine or steroids. The paramedic recovered following sedation, intubation and intensive

care for several days. Upon combustion, each component would yield products that are irritating to the respiratory tract, and the possible role of strontium in the development of anaphylaxis in this case is uncertain (Federman & Sachter, 1997).

In a study of subjects (aged 5–97 years) in families who had resided for at least 10 years within 1 of 24 communities in the lowest quartile of the economic scale in Texas, there was no correlation between strontium concentration in the drinking-water and mortality from arteriosclerotic and degenerative heart disease, other heart diseases, hypertension, general arteriosclerosis or vascular diseases of the central nervous system. Mean strontium concentrations ranged from 0.4 to 37.8 mg/l (Dawson et al., 1978).

A very small study in Newfoundland, Canada, found that the mean concentration of strontium in tap water of 28 mothers who gave birth to a normal infant (0.035 ± 79 mg/l) was slightly, but not significantly, lower than that of 28 mothers who produced an infant with neural tube defects (0.064 ± 103 mg/l). A similar pattern was seen for 12 of the other 13 elements measured. Strontium concentrations above 0.03 mg/l were found for 12 cases with neural tube defects and 5 controls. A few very high concentrations (>100 mg/l) were noted in both groups (Longerich et al., 1991). In an earlier small study carried out in Cardiff, United Kingdom, the mean strontium concentration in domestic tap water of 36 women who gave birth to an infant (live or stillborn) with a neural tube defect (0.09 mg/l; range 0.02–0.13 mg/l) was similar to that of 44 matched women who produced infants without neural tube defects (0.08 mg/l; range 0.03–0.15 mg/l) (St Leger et al., 1980).

A study of 1313 children (aged 12–14 years) living in seven towns in Wisconsin, USA, showed that the extent of enamel mottling of the teeth increased in prevalence and severity as the average concentration of strontium in the drinking-water increased from 0.02 to 34 mg/l. The trend was seen only for the 904 lifelong residents and not for the 405 immigrants. Mottling was not associated with fluoride concentration (Curzon & Spector, 1977). However, the prevalence of dental caries scores in 539 children (aged 12–14 years) in five communities in Ohio, USA, decreased as the mean strontium concentration in drinking-water increased from 0.2 to 15.3 mg/l. There was no association with fluoride concentration (Curzon, 1981).

9.4 Sensitive subpopulations

9.4.1 Children and infants

Strontium is ubiquitous in soils and water supplies. Together with its chemical similarity to calcium, this means that some incorporation of strontium into the human body is inevitable. Because of the requirement for high calcium intake during the period of bone development, the absorption and retention of strontium are higher in children than in adults. Consequently, children could experience a greater potential systemic dose from exposures to strontium than adults would (ATSDR, 2004).

Numerous laboratory animal studies demonstrate abnormal skeletal development (i.e. rickets) in young animals exposed to sufficiently high levels of dietary strontium (Storey, 1961, 1962; Kshirsagar, 1976; Matsumoto, 1976; Reinholt et al., 1985; Svensson et al., 1985, 1987; Morohashi et al., 1994). Young rats were shown to be sensitive to levels of ingested strontium that had no effect on adults (Storey, 1961).

Part of the reason why children and young of other animal species might be more sensitive than adults to excess strontium is faster absorption from the intestine (although this has not been consistently demonstrated in humans). Based on rat studies in which strontium absorption was 4–8 times faster in weanlings than in adults (Harrison et al., 1966; Forbes & Reina, 1972), some biokinetic models assume that the absorbed dose may be 8 times higher in infants than in adults (NCRP, 1991). This age-dependent difference in absorption may be partly explained by the duodenal level of vitamin D–dependent calbindin-D protein (a calcium-binding protein involved in absorption), which is much lower in old rats than in young rats (Armbrecht et al., 1989). The translation of calbindin-D9k mRNA into protein in the rat duodenum declines with age, and this would probably reduce the rates of intestinal absorption of calcium and strontium in older animals (Armbrecht et al., 1998).

Children are particularly vulnerable to excess strontium because the immature skeleton has a high rate of bone remodelling, and strontium adversely affects bone development in several ways, as demonstrated in laboratory animal studies. In rats (and chickens), excess strontium suppresses the activation of vitamin D3 in the kidney, severely reducing the expression of calbindin-D mRNA and the translation of calbindin-D9k protein in the duodenum (Omdahl & DeLuca, 1972; Armbrecht et al., 1979, 1998). As a result, duodenal absorption of calcium is reduced. Strontium also binds directly to hydroxyapatite crystals, which may interfere with the normal crystalline structure of bone in rats (Storey, 1961). In addition, excess strontium may prevent the normal maturation of chondrocytes in the epiphyseal plates of long bones of rats (Matsumoto, 1976). Excess strontium apparently interferes with the mineralization of complexed acidic phospholipids, which is thought to help initiate the formation of hydroxyapatite crystals in developing bone (Neufeld & Boskey, 1994). As a result, affected bone contains an excess of complexed acidic

phospholipid and a significantly lower ash weight. This finding is consistent with the reduced rate of matrix vesicle degradation observed in rachitic cartilage in strontium-treated rats (Reinholt et al., 1984).

Rat and mouse studies indicate that the mammalian placenta does not accumulate strontium or prevent strontium transfer to the fetus following maternal exposure. However, no adequate studies were located that addressed developmental effects following maternal exposure to stable strontium in humans or laboratory animals. Stable strontium is also transferred to nursing infants through breast milk of exposed mothers at a strontium to calcium ratio of approximately 2.4×10^{-4} (Harrison et al., 1965). These levels are unlikely to be high enough to affect fetal bone development. Strontium stored in maternal bone because of prior exposure can be mobilized during pregnancy or lactation, resulting in fetal or infant exposure (Tolstykh et al., 1998).

9.4.2 Other sensitive subpopulations

Those consuming protein-deficient diets may be at increased risk of suffering adverse effects of exposure to excess stable strontium. In adult rats, consumption of a protein-deficient diet increased the intestinal absorption of dietary strontium and its incorporation into bone and reduced faecal and urinary excretion of strontium. When rats were given ethanol in addition to the protein-deficient diet, bone incorporation of strontium was increased further, even though ethanol given with a normal-protein diet tended to reduce strontium incorporation due to diuretic effects (Gonzalez-Reimers et al., 1999).

Plasma levels of strontium were 60% higher in patients with chronic kidney failure than in healthy controls, suggesting a reduced ability to excrete strontium (Apostolidis et al., 1998). Uraemic patients on renal dialysis had significantly higher levels of strontium in serum, muscle and brain tissue than did healthy controls. Serum strontium levels in the patients were correlated with local tap water levels, but it is also possible that uraemic patients may have reduced strontium excretion rates (Alfrey et al., 1975; D'Haese & De Broe, 1996; Couttenye et al., 1999; D'Haese et al., 1999, 2000; Schrooten et al., 1999; Krachler et al., 2000). Bone strontium levels were higher in dialysis patients with osteomalacia (D'Haese et al., 2001).

Part-body retention measurements demonstrated that diseased bone in patients with Paget disease (osteitis deformans) had a relatively higher uptake of strontium following administration of ^{85}Sr compared with healthy bone in the same patients. Pagetic bone contains a higher proportion of small mineral crystals with greater surface area, which accounts for its increased ability to accumulate strontium. Reflecting the high degree of osteoclast activity in Paget disease, diseased bone had an increased turnover of ^{85}Sr compared with healthy bone (Tothill et al., 1983). As bone metabolism is locally accelerated in persons with this disease, they are likely to develop higher body burdens of strontium compared with those in healthy adults (ATSDR, 2004).

Dietary strontium inhibits the formation of 1,25-dihydroxyvitamin D (Armbrecht et al., 1998). Thus, vitamin D–deficient diet or insufficient exposure to sunlight may lead to increased sensitivity to strontium-induced bone effects.

10. EFFECTS ON OTHER ORGANISMS IN THE LABORATORY AND FIELD

10.1 Essentiality

Plants do not require strontium but readily absorb it from soil via their normal calcium uptake pathway (NCRP, 1984).

Strontium is needed for the normal development of some unicellular organisms (Acantharia, Radiolaria) and calcerous algae (Halimeda) (Holmes-Farley, 2003). Reef-building corals form aragonitic carbonate skeletons that contain relatively high amounts of strontium (Ferrier-Pagès et al., 2002). Strontium is required for the normal embryonic development of a variety of marine molluscs, including gastropods (Bidwell et al., 1986), bivalves (Gallager et al., 1989) and cephalopods (Hanlon et al., 1989). Embryos reared in the absence of strontium lack mineralized statoliths or shells. Strontium deficiency can lead to the development of abnormal locomotory behaviour (Bidwell et al., 1986). In fact, the strontium to calcium ratio of skeletal aragonite of calcium carbonate–producing organisms has been used widely to reconstruct past oceanographic conditions (Smith et al., 1979). Similarly, incorporation of strontium into fish otoliths (ear stones) and patterns of strontium to calcium ratios have been used to trace fish movements (Limburg, 1995; Bath et al., 2000; Kraus & Secor, 2004).

The regulation of strontium ions has been demonstrated in giant Malaysian freshwater prawns (*Macrobrachium rosenbergii*) and appears to be linked to magnesium regulation. The investigators noted that the observation that strontium is regulated suggests that strontium may be important in the physiology of this species (Funge-Smith et al., 1995).

Studies on squid axons showed that strontium seems to be handled in an essentially similar manner to calcium (Baker & Singh, 1982). Physiological and nutritional variables that affect strontium metabolism are similar to

Table 7: Toxicity of soluble strontium salts to aquatic organisms.

Organism	End-point	Strontium concentration (mg/l)	Reference
Freshwater			
Tubificid worm *Tubifex tubifex*	LC_{50} (96 h)	241	Khangarot (1991)
Water flea *Daphnia magna*	LC_{50} (48 h)	94	Khangarot & Ray (1989)
Water flea *Daphnia magna*	LC_{50} (48 h)	125	Biesinger & Christensen (1972)
Water flea *Daphnia magna*	EC_{50} (21 days) (reproductive impairment)	60	Biesinger & Christensen (1972)
Copepod *Cyclops abyssorum*	LC_{50} (48 h)	300	Baudouin & Scoppa (1974)
Copepod *Eudiaptomus padanus*	LC_{50} (48 h)	180	Baudouin & Scoppa (1974)
Water flea *Daphnia hyalina*	LC_{50} (48 h)	75	Baudouin & Scoppa (1974)
Crayfish *Austropotamobius pallipes pallipes*	LC_{50} (96 h)	440	Boutet & Chaisemartin (1973)
Crayfish *Austropotamobius pallipes pallipes*	LC_{50} (30 days)	320	Boutet & Chaisemartin (1973)
Crayfish *Orconectes limosus*	LC_{50} (96 h)	910	Boutet & Chaisemartin (1973)
Crayfish *Orconectes limosus*	LC_{50} (30 days)	720	Boutet & Chaisemartin (1973)
Rainbow trout *Oncorhynchus mykiss*	LC_{50} (28 days) (embryo-larval test)	0.2	Birge (1978)
Goldfish *Carassius auratus*	LC_{50} (7 days) (embryo-larval test)	8.6	Birge (1978)
Eastern narrow-mouthed toad *Gastrophryne carolinensis*	LC_{50} (7 days) (embryo-larval test)	0.2	Birge (1978)
Marine			
European shore crab *Carcinus maenas*	LC_{50} (96 h)	5.5–55.2[a,b]	Amiard (1976)
European shore crab *Carcinus maenas*	LC_{50} (9 days)	55.2	Amiard (1976)
Pink shrimp *Palaemon serratus*	LC_{50} (96 h)	276–2760[a,b]	Amiard (1976)
Pink shrimp *Palaemon serratus*	LC_{50} (9 days)	0.6–5.5[a,b]	Amiard (1976)
Mysid shrimp *Mysidopsis bahia*	LC_{50} (48 h)	>525[a,c,d]	Pillard et al. (2000)
Plaice *Pleuronectes platessa*	LC_{50} (96 h)	2760[a,b]	Amiard (1976)
Shanny *Blennius pholis*	LC_{50} (96 h)	2760[a,b]	Amiard (1976)
Striped bass *Morone saxatilis*	LC_{50} (96 h)	>93[a,e]	Dwyer et al. (1992)
Inland silverside minnow *Menidia beryllina*	LC_{50} (48 h)	210[a,b,d]	Pillard et al. (2000)
Sheepshead minnow *Cyprinodon variegatus*	LC_{50} (48 h)	>525[a,c,d]	Pillard et al. (2000)

[a] Concentrations refer to "added" strontium.
[b] "Background" strontium concentration given as 8–13 mg/l; however, these values were taken from the literature.
[c] No significant effect at highest concentration tested.
[d] "Background" strontium concentration in artificial seawater = 12 mg/l.
[e] "Background" strontium concentration in "instant ocean" = 2.4 mg/l.

those that affect calcium metabolism. It should be noted that the rates of calcium-mediated processes, including muscular contraction, are slowed when strontium is substituted for calcium (NAS, 2000).

10.2 Aquatic environment

The toxicity of strontium to aquatic organisms is summarized in Table 7. Strontium has low acute toxicity to freshwater organisms. Most tests are based on strontium chloride, with 48 h and 96 h LC_{50}s ranging from 75 to 910 mg/l; a 21-day EC_{50}, based on reproductive impairment in daphnids, was 60 mg/l. In embryo-larval tests, an LC_{50} of 0.2 mg/l was reported for both rainbow trout (28 days) and eastern narrow-mouthed toad (7 days). Acute 48 h and 96 h LC_{50}s in marine organisms suggest that they are less sensitive than freshwater organisms to strontium. Acute 48 h and 96 h LC_{50}s range from 5.5 to 2760 mg/l for "added" strontium, with a 9-day LC_{50} in pink shrimp (*Palaemon serratus*) ranging from 0.6 to 5.5 mg/l for "added" strontium. However, the marine data are difficult to

interpret, with the lowest LC_{50} values derived from a study that did not measure the "background" strontium concentration. Inhibition of calcification in the freshwater green alga *Gloeotaenium* was observed at a strontium concentration of 150 mg/l after 37 h (Devi Prasad, 1984).

Spangenberg & Cherr (1996) found no adverse effect on mussel (*Mytilus californianus*) embryos exposed for 48 h post-fertilization to strontium chloride at strontium concentrations ranging from 0.1 to 20 mg/l.

10.3 Terrestrial environment

Fischer & Molnár (1997) exposed the earthworm *Eisenia foetida* to a mixture of peaty marshland soil and horse manure spiked at different strontium concentrations for 10 weeks. No effect on the body weight gain of introduced worms was found at a strontium concentration of 10.6 g/kg dry weight; however, the concentration resulted in a significant reduction in reproduction. Tatara et al. (1998) reported the 24 h LC_{50} for total strontium at 15.9 g/l and for the free ion at 10.4 g/l for the free-living soil nematode *Caenorhabditis elegans* exposed to strontium nitrate. Williams & Dusenbery (1990) reported a 96 h LC_{50} of 465 mg/l for strontium in the same species.

11. EFFECTS EVALUATION

11.1 Evaluation of health effects

11.1.1 Hazard identification and dose–response assessment

This CICAD covers naturally occurring strontium compounds (i.e. stable isotopic forms). A number of radioactive isotopes exist but are not reviewed here.

Strontium is similar to calcium in its physiological behaviour and can act as an imperfect surrogate for calcium. The typical human body burden of strontium is about 0.3–0.4 g, and 99% is found in the skeleton.

Acute toxicity data are very limited. A low acute oral toxicity was demonstrated for strontium chloride, strontium carbonate, strontium sulfate and strontium nitrate in rats and/or mice. Strontium sulfate had only a low acute dermal toxicity in rats. Local damage to the oesophagus and duodenum occurred in monkeys given strontium chloride by capsule daily for 1 week.

The most comprehensive repeated oral dose study using the lowest doses showing toxic effects involved inclusion of strontium chloride hexahydrate in the diet of weanling rats (40–60 g; 10 of each sex per group), giving strontium doses of 0, 2.5, 10, 40 or 160 mg/kg body weight per day, for 90 days (see Table 6). The diet was said to contain adequate levels of calcium, magnesium, phosphorus, iodine and vitamin D3. Administration of strontium at doses up to 10 mg/kg body weight per day had no effect on behaviour, appearance, growth, food intake, survival, haematology, serum chemistry, blood calcium or phosphorus, liver glycogen, urinalysis, weights of the major organs or microscopic appearance of a fairly wide range (25) of tissues, including the bone. At 40 mg/kg body weight per day, the only statistically significant finding was a higher thyroid weight in the males. However, this was not clearly related to dose, and the thyroid was microscopically normal. At 160 mg/kg body weight per day, the males showed increased thyroid weight and histological signs of increased thyroid activity, and the females showed lower pituitary weights (without microscopic changes). Liver glycogen levels were lower in both sexes, although the reduction was statistically significant only in the females. No effects on the bone were seen in this study, but strontium concentrations in the bone were significantly increased at all dose levels (Kroes et al., 1977).

In a recent study involving a fairly detailed examination, reduced spleen weights were seen in female rats given strontium sulfate at 500 mg/kg body weight per day (a strontium dose of about 240 mg/kg body weight per day) or more by gavage for 40–54 days. At a strontium dose of 480 mg/kg body weight per day (administered as strontium sulfate) and above, epididymis and testis weights were increased in male rats (treated similarly for 42 days). At a strontium dose of 950 mg/kg body weight per day, the females showed reductions in reticulocyte counts and AST activity. Survival, growth, sensory and motor functions, urinalysis, and the microscopic appearance of a range (about 30) of tissues and organs (including bone) were unaltered by treatment (NIER, 2006c).

Numerous other studies in laboratory animals have indicated that a key target tissue following repeated exposure to strontium is the bone. Bone histology was normal in young rats fed strontium at 0.19% in the diet (about 190 mg/kg body weight per day) for 20 days (Storey, 1961). The appearance of the cartilage plate was altered in rats given 0.38% strontium in the diet (about 380 mg/kg body weight per day) and in young mice given drinking-water supplying 350 mg/kg body weight per day for 29 days. In several studies, higher repeated oral doses caused numerous bone and cartilage abnormalities, including impaired calcification, reduced mineral content, increased complexed acidic

phospholipids, non-mineralized (osteoid) regions, spongiosa, wide epiphyseal plates, lower bone densities, disorganized trabeculae, smaller bones and rickets. Markers of bone effects included changes in serum levels of activated vitamin D and calbindin-D proteins and changes in acid and alkaline phosphatase activities in certain organs. No adequate lifetime studies involving chronic repeated exposure were identified.

No carcinogenicity studies meeting current guidelines were identified for strontium compounds. Chromium(VI) compounds are known to be genotoxic mammalian carcinogens, and strontium chromate induced local tumours when implanted into the respiratory tract of rats; the chromium(VI) was considered to be responsible.

Genotoxicity data on strontium compounds are few. A limited study reported that a single oral dose of strontium chloride induced chromosomal aberrations in the bone marrow of mice. Strontium chloride did not induce chromosome damage in hamster oocytes in culture, DNA damage in bacteria or hamster embryo cells or cell transformation in hamster embryo cells in culture. Strontium sulfate did not damage the chromosomes of hamster lung cells. Neither strontium carbonate nor strontium sulfate was mutagenic in Ames bacterial tests. In common with other chromium(VI) compounds, strontium chromate induced bacterial mutations in an Ames test, sister chromatid exchanges in hamster fibroblast cells in culture and cell transformation in hamster embryo cells in culture.

No effects on reproduction/fertility or fetal development were seen in a screening study in which rats (both sexes) were given strontium sulfate by gavage for about 6–8 weeks starting 2 weeks before mating. According to a brief report, fertility was unaffected by the inclusion of strontium chloride in the drinking-water of rats over three generations. A developmental study in mice demonstrated adverse bone effects in the newborn offspring following repeated oral dosing of the pregnant females with strontium carbonate. Repeated oral dose studies on weanling and adult rats indicated that the younger animals were more sensitive than adults to the effects of strontium on bone.

Very little information is available on the toxicity of stable strontium to humans. A study in Turkey suggested a relationship between dietary strontium and childhood rickets. There is some evidence that occupational exposure to strontium chromate can cause lung cancer, but chromium(VI) compounds (such as chromates) are recognized genotoxic carcinogens, and the chromate moiety is believed to be responsible for the carcinogenic activity of strontium chromate.

The requirement for calcium is high during the period of bone development, growth and remodelling, and thus children tend to absorb and retain strontium to a greater extent than adults. Consequently, the young are at increased risk from exposure to excess strontium. Others who might be at increased risk from strontium exposure include patients with kidney failure (whose ability to excrete strontium may be limited) or osteomalacia, those consuming a protein-deficient diet and people who do not receive adequate exposure to sunlight.

11.1.2 Criteria for setting tolerable intakes and tolerable concentrations

Human data are inadequate for setting a TDI for oral exposure to strontium. The study in which strontium chloride hexahydrate was included in the diet of weanling rats at 0, 75, 300, 1200 or 4800 mg/kg for 90 days (Kroes et al., 1977) was selected as the pivotal study, being a well-reported, detailed examination providing evidence of effects at lower doses and over a longer exposure duration than for other candidate studies. The 1200 mg/kg dietary concentration of strontium chloride hexahydrate, providing a strontium dose of about 40 mg/kg body weight per day (assuming young rats consume feed at an amount equivalent to about 10% of their body weight per day) was considered to be the study NOAEL (see section 8.3). This study was used to derive a TDI.

An uncertainty factor of 10 was applied to account for interspecies differences between rats and humans. To account for possible differences in interindividual susceptibility, a factor of 3 was applied. The default factor of 10 was not warranted because the critical study was performed in young animals, a recognized sensitive subpopulation. As no strontium accumulation was observed after 2 weeks of administration, no additional uncertainty factor was considered to be needed to compensate for the use of a study that is of shorter duration than would normally be used to derive a TDI (IPCS, 1994). However, an uncertainty factor of 10 was applied to account for deficiencies in the database: lack of adequate data on carcinogenicity and reproductive toxicity. This leads to a TDI of 0.13 mg/kg body weight per day (40 mg/kg body weight per day / [10 × 3 × 10]).[1]

[1] In the 20-day study on the effects of strontium on bone in rats (Storey, 1961), the NOAEL was 190 mg/kg body weight per day. Using 10 as the uncertainty factor for species-to-species extrapolation, 3 for interindividual variation, 3 to compensate for the use of a study with only short duration and investigation of bone effects and growth only and 10 for other deficiencies in the database would have resulted in a TDI of 0.2 mg/kg body weight per day.

In the absence of adequate data, a tolerable concentration for chronic inhalation exposure to strontium cannot be established.

11.1.3 Sample risk characterization

11.1.3.1 Exposure of the sample populations

Average strontium concentrations in urban air are generally below 0.1 µg/m^3, with higher concentrations near coal-burning plants. Average concentrations in drinking-water in Germany and the USA were reported to be about 0.34 and 1.1 mg/l, respectively. Food plants absorb strontium from the soil, where average concentrations of strontium of about 240 mg/kg and 89 mg/kg (topsoils in Europe) have been reported. In food samples taken in the developed world, the highest concentrations were measured in leafy vegetables (e.g. 64 mg/kg dry weight in cabbages).

The source document estimated that for adults in the USA, the total daily intake of strontium is about 3.3 mg/day, made up of 2 mg/day from drinking-water, 1.3 mg/day from foodstuffs (mainly leafy vegetables, grains and dairy products) and an insignificant 0.4 µg/day from air (ATSDR, 2004). This ATSDR estimate (3.3 mg/day) fits well with other estimates of intake from drinking-water (about 0.7–2 mg/day) and food (another 1.2–2.3 mg/day) for populations in Australia, Finland, Germany, Japan, the United Kingdom and Viet Nam.

Certain populations might experience substantially higher oral exposures than the averages discussed above. Data on drinking-water are few, but the highest concentrations reported in Wisconsin and Texas (33.9 and 37.8 mg/l, respectively) are about 100 and 30 times higher than the mean concentrations (about 0.34 mg/l and 1.1 mg/l) reported for Germany and the USA, respectively. In a hot climate, an adult drinking daily 3 litres of water containing strontium at 37.8 mg/l could ingest up to 110 mg/day from this source alone. This would equate to about 1.8 mg/kg body weight per day for an adult weighing 64 kg. An additional contribution to total daily intake from foodstuffs would be expected. Data on concentrations in food plants are also limited, but concentrations could vary considerably as a result of varying strontium levels in soil, from which plants take up strontium. In European topsoils, the average strontium concentration was 89 mg/kg, but concentrations ranged widely from 8 to 3120 mg/kg. Therefore, certain populations who live in areas where strontium concentrations in soil and water are high and who consume predominantly locally grown produce might have strontium intakes that are substantially higher than 3.3 mg/day. Prediction of strontium levels in surface water and soil from underlying geology is difficult; for a discussion of factors likely to contribute to high surface strontium, see the web site of the Forum of the European Geological Surveys Directors (FOREGS), which also presents maps of strontium concentrations in water and soil across Europe (http://www.gtk.fi/foregs/geochem/index.htm).

11.1.3.2 Health risks in the sample populations

For many populations in developed countries, estimates of total intake vary up to about 4 mg/day, virtually all of which is ingested. The source document intake figure of 3.3 mg/day is equivalent to 0.05 mg/kg body weight per day for an adult weighing 64 kg.

The estimated human intake of 4 mg/day, or 0.06 mg/kg body weight per day for an adult weighing 64 kg, is about half of the TDI of 0.13 mg/kg body weight derived in this CICAD. Thus, there is no evidence that background intakes of about 4 mg/day are likely to pose any risks to bone health in humans.

Certain populations who live in areas where strontium concentrations in soil and water are high and who consume predominantly locally grown produce could easily have intakes that are substantially higher than this 4 mg/day figure. For example, an adult drinking daily 3 litres of water containing strontium at 37.8 mg/l could ingest up to 110 mg/day. This would equate to about 1.8 mg/kg body weight per day for an adult weighing 64 kg. As foodstuffs are also likely to contribute to strontium intake, the total daily intake in such areas could easily exceed the TDI of 0.13 mg/kg body weight.

A study in Turkey suggested a relationship between strontium exposure and childhood rickets. Exposure was classified by soil concentration of strontium. The diet in the endemic area was largely dependent upon grains grown in the area (Özgür et al., 1996; ATSDR, 2004).

11.1.4 Uncertainties in the evaluation of health risks

There are few data in the source document on concentrations in food, water and air, leading to uncertainties in intake estimates, especially for children.

The only study involving chronic administration of a strontium compound was inadequately reported, with very little experimental detail (Skoryna, 1981a, 1981b; Skoryna & Fuskova, 1981). It is uncertain whether adequate chronic studies would identify a lower NOAEL and lowest-observed-adverse-effect level (LOAEL) than those seen in subchronic studies.

No studies meeting modern guidelines on the carcinogenicity, genotoxicity, immunotoxicity, neurotoxicity or reproductive/developmental toxicity of strontium compounds were identified. In the case of strontium chromate, any carcinogenic or genotoxic

potential of strontium would be expected to be masked by that of the chromate.

While the working group reached a consensus on the NOAEL (40 mg/kg body weight per day) and the TDI (40 mg/kg body weight / [10 × 3 × 10] = 0.13 mg/kg body weight), long discussions were held on several details in this process:

- A NOAEL of 10 mg/kg body weight per day could also have been justified; while it is true that the change in the thyroid weight observed at 40 mg/kg body weight per day was limited to males and there was practically no change in the response over a 50-fold range of doses, it may also be argued that as histological evidence of thyroid effects was observed at the next higher dose, the change of weight is the first step in the continuum of adverse thyroid effects, and this dose level (40 mg/kg body weight per day) could be considered a LOAEL rather than a NOAEL.
- The uncertainty factor of 10 for species-to-species extrapolation can be argued to be excessive, as the thyroid function of rats is quite different from that of humans, rats being considerably more sensitive than humans to thyrotoxic chemicals.
- The uncertainty factor of 3 for interindividual variability can be argued to be too small, as no actual chemical-specific data on the interindividual variation of strontium toxicity in humans are available.
- The uncertainty factor of 10 for deficiencies in the database may be argued to be excessive, as there is no accumulation of strontium on continued dosing and as there are some (albeit admittedly limited) data on long-term toxicity, reproductive and developmental toxicity, and genotoxicity of strontium.

11.2 Evaluation of environmental effects

Strontium can be released into the air (mainly as strontium oxide) by natural processes (e.g. weathering of rocks, particle entrainment, wind resuspension and sea spray) or as a result of human activities (e.g. milling, processing, coal burning and fertilizer use). In air, the oxide rapidly forms the hydroxide or carbonate. Atmospheric strontium is returned to the ground by deposition. Strontium is released to surface water and groundwater by natural weathering of rocks and soils. In water, it exists as a hydrated cation. Aqueous strontium can sorb to the surface of certain minerals. Like calcium, strontium has moderate mobility in soils and sediments and sorbs moderately to metal oxides and clays. Plants readily absorb strontium via their normal calcium uptake pathway. Earthworms do not accumulate strontium in soils high in calcium; however, strontium accumulation may occur in acidic, calcium-poor soils. Strontium is readily accumulated in otoliths, vertebrae and opercula of fish. In fact, strontium chloride solutions have been used to deliberately mark salmon fry for later identification in the wild. In higher organisms, bioaccumulation occurs in bone due to strontium's similarity to calcium.

Strontium has low acute toxicity to aquatic organisms in the laboratory. For freshwater organisms, most tests are based on strontium chloride, and 48 h and 96 h LC_{50}s range from 75 to 910 mg/l; a 21-day EC_{50}, based on reproductive impairment in daphnids, was 60 mg/l. In embryo-larval tests, an LC_{50} for strontium of 0.2 mg/l was reported for both rainbow trout (28 days) and eastern narrow-mouthed toad (7 days). Acute 48 h and 96 h LC_{50}s in marine organisms suggest that they are less sensitive than freshwater organisms to strontium.

Under internationally agreed and national regulatory systems, data-poor elements are assessed for risk using a deterministic approach based on uncertainty factors. For strontium, this would give the results described below.

There are no chronic no-observed-effect concentrations (NOECs) for aquatic organisms. According to the European Commission's technical guidance document (EC, 2003) and the Organisation for Economic Co-operation and Development (OECD, 2002), a factor of 1000 is applied to the lowest freshwater acute LC_{50} or EC_{50} if the base set of toxicity data is incomplete. In the case of the strontium freshwater data set, there are no applicable algal studies. The lowest acute LC_{50} for strontium in freshwater organisms is 75 mg/l (*Daphnia hyalina*). Applying a factor of 1000 gives a predicted no-effect concentration ($PNEC_{aquatic}$) for strontium in freshwater organisms of 75 µg/l. There are insufficient data to allow the derivation of a PNEC for saltwater organisms; however, it would appear from the acute toxicity data that marine organisms are less sensitive than freshwater species to strontium.

Natural strontium concentrations in European rivers range over 4 orders of magnitude, from 0.001 to 13.6 mg/l; the median concentration was 0.11 mg/l. Freshwater strontium concentrations are directly related to the underlying geology of rivers and streams. Similarly, in surface waters in the USA, the ranges were equally wide, differing slightly between different studies; all studies showed average values in the order of 0.4–1.5 mg/l. In seawater, the average concentration of strontium is approximately 8 mg/l.

Where elements are essential to living organisms, it is permitted under regulatory systems to adjust guidance values to reflect natural background concentrations. This avoids uncertainty factors pushing guidance values below natural levels of the element. This is not possible for strontium, for two reasons: the element is not regarded as essential by the normal criteria for

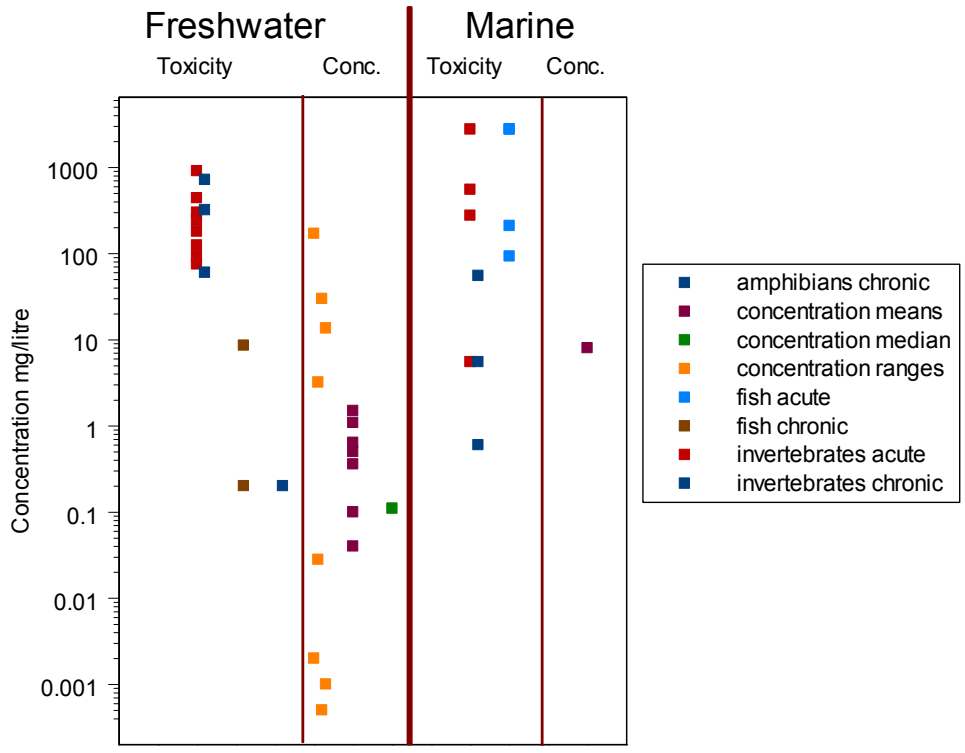


Figure 1: Distribution of strontium toxicity values for freshwater and marine organisms compared with strontium concentrations in surface waters

essentiality, and natural levels of strontium substantially overlap the derived PNEC and even some of the "toxic" values derived from laboratory tests (see Figure 1).

It is clear that for fresh water, many of the test organisms in the laboratory studies were acclimatized not to natural waters but to strontium-deficient ones or were derived from populations in low-strontium areas. Furthermore, marine toxicity values represent strontium "added" beyond the normal concentration in seawater (around 8 mg/l), and in some of the marine studies, the "background" strontium concentration was not measured. Realistic exposure/effect ratios cannot, therefore, be derived for strontium from the available information.

12. PREVIOUS EVALUATIONS BY INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS (IOMC) BODIES

The International Agency for Research on Cancer (IARC) has not evaluated the carcinogenic potential of stable strontium compounds as a group. In its evaluation of "chromium and chromium compounds", an IARC working group evaluated a number of chromium(VI) compounds, including strontium chromate. IARC concluded that there was "sufficient evidence" for the carcinogenicity of strontium chromate in laboratory animals and sufficient evidence in humans for the carcinogenicity of chromium(VI) compounds as encountered in various chromium/chromate industries. Overall, IARC concluded that chromium(VI) is carcinogenic to humans (Group 1) (IARC, 1990).[1]

[1] Note added in press: IARC has recently re-evaluated chromium(VI) compounds and confirmed the classification of chromium(VI) compounds as carcinogenic to humans (Group 1); the evidence in humans is sufficient for cancer of the lung and limited for cancer of the nasal cavity and paranasal sinuses (IARC, in press).

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APPENDIX 1—ACRONYMS AND ABBREVIATIONS

ALT	alanine aminotransferase
AMAD	activity median aerodynamic diameter
AOAC	Association of Official Analytical Chemists
AP	alkaline phosphatase
AST	aspartate aminotransferase
ASTM	American Society for Testing and Materials
ATSDR	Agency for Toxic Substances and Disease Registry (USA)
BCF	bioconcentration factor
CAS	Chemical Abstracts Service
CICAD	Concise International Chemical Assessment Document
DNA	deoxyribonucleic acid
EC_{50}	median effective concentration
EDTA	ethylenediaminetetraacetic acid
EU	European Union
FAAS	flame atomic absorption spectroscopy
FAO	Food and Agriculture Organization of the United Nations
GFAAS	graphite furnace atomic absorption spectroscopy
IARC	International Agency for Research on Cancer
ICP-AES	inductively coupled plasma atomic emission spectroscopy
ICP-MS	inductively coupled plasma mass spectrometry
ICSC	International Chemical Safety Card
IOMC	Inter-Organization Programme for the Sound Management of Chemicals
IPCS	International Programme on Chemical Safety
K_d	distribution coefficient
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
LOAEL	lowest-observed-adverse-effect level
MRL	minimal risk level
mRNA	messenger ribonucleic acid
NOAEL	no-observed-adverse-effect level
NOEC	no-observed-effect concentration
NTA	nitrilotriacetic acid
O/E	observed/expected ratio
OECD	Organisation for Economic Co-operation and Development
OSW	Office of Solid Waste (USEPA)
PIXE	proton-induced X-ray emission
PNEC	predicted no-effect concentration
RfD	reference dose
SGOT	serum glutamic–oxaloacetic transaminase
SGPT	serum glutamic–pyruvic transaminase
SIDS	Screening Information Data Set (OECD)
SMR	standardized mortality ratio
TDI	tolerable daily intake
TMAH	tetramethylammonium hydroxide
TNA	thermal neutron activation and radiometric measurement
TRXF	total reflection X-ray fluorescence
USA	United States of America
USEPA	United States Environmental Protection Agency
WHO	World Health Organization

APPENDIX 2—SOURCE DOCUMENT

ATSDR (2004)

The source document was the toxicological profile for strontium and compounds, prepared by the Agency for Toxic Substances and Disease Registry (ATSDR) through a contract with the Syracuse Research Corporation. Copies of the profile can be obtained from the ATSDR web site (http://www.atsdr.cdc.gov/toxpro2.html) or from:

Division of Toxicology
Agency for Toxic Substances and Disease Registry
Division of Toxicology/Toxicology Information Branch
United States Department of Health and Human Services
1600 Clifton Road NE, Mailstop E-29
Atlanta, Georgia 30333
USA

A peer review panel was assembled for strontium and compounds. The panel consisted of the following members:

Adele L. Boskey, Ph.D., Professor of Biochemistry, Starr Chair in Mineralized Tissues, Hospital for Special Surgery, Weill Medical College of Cornell University, New York, NY

Marvin Goldman, Ph.D., Emeritus Professor of Radiation Biology, Department of Surgical and Radiological Sciences, University of California, Davis, CA

Richard Leggett, Ph.D., Life Sciences Division, Oak Ridge National Laboratory, Knoxville, TN

Bruce Muggenburg, D.V.M., Ph.D., Senior Scientist and Veterinary Physiologist, Toxicology Division, Lovelace Respiratory Research Institute, Albuquerque, NM

These experts collectively have knowledge of strontium and its compounds' physical and chemical properties, toxicokinetics, key health end-points, mechanisms of action, human and laboratory animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(I)(13) of the *Comprehensive Environmental Response, Compensation, and Liability Act*, as amended. Scientists from ATSDR reviewed the peer reviewers' comments and determined which comments would be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record. The citation of the peer review panel should not be understood to imply its approval of the profile's final content. The responsibility for the content of this profile lies with the ATSDR.

***

In May 2006, a comprehensive literature search was conducted by Toxicology Advice & Consulting Ltd in order to identify critical data published since publication of the source document. Searches were carried out in the TRACE database and in a range of other well-established toxicity databases and databanks (accessed via the Toxnet system), including Toxline (which incorporates the toxicity subset of Medline), Chemical Carcinogenesis Research Information System (CCRIS), Developmental and Reproductive Toxicology Database (DART), Genetic Toxicology Data Bank (GENETOX), Hazardous Substances Data Bank (HSDB), Integrated Risk Information System (IRIS) and Registry of Toxic Effects of Chemical

Substances (RTECS). A further wide selection of online toxicity data sources was interrogated using the ToxSeek meta-search and clustering engine.

TRACE includes information from peer-reviewed toxicology and nutrition journals as well as secondary sources and web sites. In addition to primary literature on the health effects of chemicals, TRACE covers official publications and evaluations issued by authoritative groups, including:

- World Health Organization (WHO)/IPCS reports and evaluations (including CICADs and Environmental Health Criteria, IARC, Joint FAO/WHO Expert Committee on Food Additives and Joint FAO/WHO Meeting on Pesticide Residues monographs) and the WHO Air Quality Guidelines and Guidelines for Drinking-water Quality
- OECD Screening Information Data Set (SIDS) dossiers/SIDS initial assessment reports
- International Uniform Chemical Information Database data sets
- European Union (EU) risk assessment reports
- EU expert committee opinions (including EU scientific committees and European Food Safety Authority scientific panels) and other reports from EU agencies and institutes (including European Chemicals Agency, European Centre for the Validation of Alternative Methods, European Medicines Agency and Consumer Products Safety & Quality)
- European Centre for Ecotoxicology and Toxicology of Chemicals, Humanities in the European Research Area, Council of Europe and other pan-European programmes
- United Kingdom government agency (including Department for Environment, Food and Rural Affairs, Environment Agency, Food Standards Agency, Department of Health, Health and Safety Executive, Health Protection Agency, Pesticides Safety Directorate and Veterinary Medicines Directorate) and advisory committee (e.g. Committee on Toxicity, Veterinary Products Committee, Veterinary Residues Committee and Advisory Committee on Releases to the Environment) reports and evaluations
- Opinions from other United Kingdom organizations, such as the Royal Society
- United States agency reports and evaluations (Environmental Protection Agency, ATSDR, Food and Drug Administration, National Toxicology Program, Occupational Safety and Health Administration, National Center for Environmental Assessment, Center for Food Safety and Nutrition, Center for the Evaluation of Risks to Human Reproduction, National Institute of Environmental Health Sciences, Centers for Disease Control and Prevention, Office of Environmental Health Hazard Assessment and American Conference of Governmental Industrial Hygienists)
- Health Canada evaluations
- German Advisory Committee on Existing Chemicals (BUA), German Research Foundation (DFG), BG Chemie and Federal Institute for Risk Assessment (BfR) reports and monographs
- Gezondheidsraad opinions, including those from its various committees, such as Dutch Expert Committee on Occupational Standards
- National Institute for Public Health and the Environment (RIVM) reports
- Danish Environmental Protection Agency reviews
- Reports and other information provided by Swedish governmental organizations, including the National Food Administration and the Swedish Chemicals Agency
- Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals
- Australian agency reviews, including National Industrial Chemicals Notification and Assessment Scheme Priority Existing Chemical Assessments, Australian Pesticides and Veterinary Medicines Authority reports and (jointly with New Zealand) Food Standards Australia New Zealand assessments
- Japanese Chemical Industry Ecology-Toxicology & Information Center reports
- Cosmetic Ingredient Review, Research Institute for Fragrance Materials and other specialist industry groups
- bibra toxicity profiles

Literature searches in November 2009 did not identify any new critical toxicity or ecotoxicity data.

APPENDIX 3—CICAD PEER REVIEW

The draft CICAD on strontium and strontium compounds was sent for review to institutions and organizations identified by IPCS after contact with IPCS national Contact Points and Participating Institutions, as well as to identified experts. An open invitation to participate in the peer review process was also published on the IPCS web site. Comments were received from:

R. Benson, Denver, CO, USA
S. Bull, London, United Kingdom
S. Dobson, Monks Wood, United Kingdom
H. Gibb, Sciences International Inc., Alexandria, VA, USA
R. Hertel, Federal Institute for Risk Assessment (BfR), Berlin, Germany
J. Kielhorn, Fraunhofer Institute for Toxicology and Experimental Medicine, Hanover, Germany
F.K. Muchirim, Nairobi, Kenya
M. Nordberg, Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden
M.S.T Pham, Sydney, New South Wales, Australia
J. Stauber, Sydney, New South Wales, Australia
F.M. Sullivan, United Kingdom
K. Ziegler-Skylakakis, Freising-Weihenstephan, Germany

The Final Review Board (see Appendix 4) recommended that the health risk assessment on strontium should be based on the Kroes et al. (1977) study and that a TDI should be derived using the procedure described in Environmental Health Criteria 170 (IPCS, 1994). This was done by the authors and secretariat in collaboration; thereafter, the document was subjected to a final peer review by the peer reviewers of the original document (above), as well as by the members of the Final Review Board (Appendix 4).

APPENDIX 4—CICAD FINAL REVIEW BOARD

Helsinki, Finland
26–29 March 2007

Members

Dr A. Aitio, Finnish Institute of Occupational Health, Helsinki, Finland

Professor H. Bouwman, School of Environmental Sciences and Development, North-West University, Potchefstroom, South Africa

Dr C. De Rosa,[1] Agency for Toxic Substances and Disease Registry, Atlanta, GA, USA

Dr S. Devotta, National Environmental Engineering Research Institute, Nagpur, India

Dr S. Dobson, Centre for Ecology and Hydrology, Monks Wood, United Kingdom

Dr L. Fructengarten, Centro de Controle de Intoxicacoes de Sao Paulo, Sao Paulo, Brazil

Dr H. Gibb, Sciences International Inc., Alexandria, VA, USA

Dr R. Hertel, Federal Institute for Risk Assessment (BfR), Berlin, Germany

Mr P. Howe, Centre for Ecology and Hydrology, Monks Wood, United Kingdom

Dr S. Keith, Agency for Toxic Substances and Disease Registry, Atlanta, GA, USA

Dr J. Kielhorn, Fraunhofer Institute for Toxicology and Experimental Medicine, Hanover, Germany

Ms M.E. Meek, Health Canada, Ottawa, Ontario, Canada

Dr T. Santonen, Finnish Institute of Occupational Health, Helsinki, Finland

Dr B. Sonawane, National Center for Environmental Assessment, Office of Research and Development, Environmental Protection Agency, Washington, DC, USA

Dr J. Stauber, CSIRO Centre for Environmental Contaminants Research, Sydney, Australia

Dr M. Sweeney, Division of Surveillance, Hazard Evaluations & Field Studies, National Institute for Occupational Safety and Health, Cincinnati, OH, USA

Ms D. Willcocks, Australian Department of Health and Ageing, Sydney, Australia

Dr K. Ziegler-Skylakakis, Secretariat of the Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK Commission), Munich, Germany

[1] Invited but unable to participate.

Secretariat

Dr J. Bartram, Assessing and Managing Environmental Risks to Health, World Health Organization, Geneva, Switzerland

Mrs S. Marples, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

Ms L. Onyon, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

Mr M. Shibatsuji, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

Mr P. Watts, bibra - toxicology advice & consulting, Sutton, United Kingdom

STRONTIUM

ICSC: 1534
October 2004

CAS #	**7440-24-6**	**Sr**
RTECS #	**WK7700000**	
EC/EINECS #	**231-133-4**	**Atomic mass: 87.6**

TYPES OF HAZARD / EXPOSURE	**ACUTE HAZARDS / SYMPTOMS**	**PREVENTION**	**FIRST AID / FIRE FIGHTING**
FIRE	Not combustible but forms flammable gas on contact with water or damp air.	NO contact with water.	NO water. Dry sand, special powder.
EXPLOSION			
EXPOSURE		**PREVENT DISPERSION OF DUST!**	
Inhalation		Ventilation.	Fresh air, rest.
Skin		Protective gloves.	Rinse skin with plenty of water or shower.
Eyes		Safety spectacles.	
Ingestion		Do not eat, drink, or smoke during work.	Rinse mouth.

SPILLAGE DISPOSAL	**PACKAGING & LABELLING**
Personal protection: particulate filter respirator adapted to the airborne concentration of the substance. Sweep spilled substance into sealable containers. Do NOT let this chemical enter the environment.	
EMERGENCY RESPONSE	**STORAGE**
	Dry. Keep under inert gas. Well closed. Keep in a well-ventilated room. Store in an area without drain or sewer access.

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International Programme on Chemical Safety

WHO ILO UNEP

SEE IMPORTANT INFORMATION ON BACK

STRONTIUM

ICSC: 1534

IMPORTANT DATA

PHYSICAL STATE; APPEARANCE
SILVERY, WHITE SOLID IN VARIOUS FORMS

CHEMICAL DANGERS
Reacts with water forming flammable/explosive gas (hydrogen - see ICSC0001).

OCCUPATIONAL EXPOSURE LIMITS
TLV not established.
MAK: IIb, value not established but data is available; (DFG 2009).

ROUTES OF EXPOSURE
The substance can be absorbed into the body by inhalation of its aerosol.

INHALATION RISK
A nuisance-causing concentration of airborne particles can be reached quickly when dispersed.

PHYSICAL PROPERTIES

Boiling point:	1384°C
Melting point:	757°C
Density:	2.64 g/cm³
Solubility in water:	reaction

ENVIRONMENTAL DATA

Bioaccumulation of this chemical may occur along the food chain.

NOTES

Reacts violently with fire extinguishing agents such as water. The recommendations on this Card DO NOT APPLY to radioactive strontium. Card has been partially updated in March 2010: see Spillage Disposal, Storage.

ADDITIONAL INFORMATION

STRONTIUM CHROMATE

ICSC: 0957
April 2004

CAS # 7789-06-2
RTECS # GB3240000
EC Annex 1 Index # 024-009-00-4
EC/EINECS # 232-142-6

C.I. Pigment yellow 32
Chromic acid strontium salt
$SrCrO_4$
Molecular mass: 203.6

TYPES OF HAZARD / EXPOSURE	ACUTE HAZARDS / SYMPTOMS	PREVENTION	FIRST AID / FIRE FIGHTING
FIRE	Not combustible.		In case of fire in the surroundings: all extinguishing agents allowed.
EXPLOSION			
EXPOSURE		**PREVENT DISPERSION OF DUST! AVOID ALL CONTACT!**	
Inhalation	Cough. Sore throat. Wheezing.	Closed system and ventilation.	Fresh air, rest. Refer for medical attention.
Skin	Redness. Pain.	Protective gloves. Protective clothing.	Remove contaminated clothes. Rinse skin with plenty of water or shower. Refer for medical attention.
Eyes	Redness. Pain.	Safety goggles, face shield, or eye protection in combination with breathing protection.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.
Ingestion	Abdominal pain. Diarrhoea. Nausea. Vomiting.	Do not eat, drink, or smoke during work. Wash hands before eating.	Rinse mouth. Refer for medical attention.

SPILLAGE DISPOSAL

Chemical protection suit including self-contained breathing apparatus. Sweep spilled substance into containers; if appropriate, moisten first to prevent dusting. Carefully collect remainder, then remove to safe place. Do NOT let this chemical enter the environment.

PACKAGING & LABELLING

Do not transport with food and feedstuffs.
EU Classification
Symbol: T, N
R: 45-22-50/53
S: 53-45-60-61
Note: E

EMERGENCY RESPONSE

STORAGE

Provision to contain effluent from fire extinguishing. Separated from combustible and reducing substances, food and feedstuffs. Store in an area without drain or sewer access.

IPCS
International Programme on Chemical Safety

WHO ILO UNEP

Prepared in the context of cooperation between the International Programme on Chemical Safety and the Commission of the European Communities

SEE IMPORTANT INFORMATION ON BACK

STRONTIUM CHROMATE

ICSC: 0957

IMPORTANT DATA

PHYSICAL STATE; APPEARANCE
YELLOW CRYSTALLINE POWDER

CHEMICAL DANGERS
The substance is a strong oxidant and reacts with combustible and reducing materials.

OCCUPATIONAL EXPOSURE LIMITS
TLV: (as Cr) 0.0005 mg/m³ as TWA; A2 (suspected human carcinogen); (ACGIH 2008).
MAK: (as Cr) skin absorption (H); sensitization of skin (Sh); Carcinogen category: 1; Germ cell mutagen group: 2 (DFG 2009).

ROUTES OF EXPOSURE
The substance can be absorbed into the body by inhalation of its aerosol and by ingestion.

INHALATION RISK
A harmful concentration of airborne particles can be reached quickly when dispersed.

EFFECTS OF SHORT-TERM EXPOSURE
The substance is irritating to the eyes, the skin and the respiratory tract.

EFFECTS OF LONG-TERM OR REPEATED EXPOSURE
Repeated or prolonged contact may cause skin sensitization. Repeated or prolonged inhalation exposure may cause asthma. The substance may have effects on the respiratory tract and kidneys, resulting in nasal septum perforation and kidney impairment. This substance is carcinogenic to humans.

PHYSICAL PROPERTIES

Melting point (decomposes)
Density: 3.9 g/cm³

Solubility in water, g/100 ml at 15°C: 0.12

ENVIRONMENTAL DATA

This substance may be hazardous in the environment; special attention should be given to aquatic organisms. It is strongly advised not to let the chemical enter into the environment because it persists in the environment.

NOTES

Do NOT take working clothes home. Deep Lemon Yellow and Strontium Yellow are common names. Anyone who has shown symptoms of asthma due to this substance should avoid all further contact. The symptoms of asthma often do not become manifest until a few hours have passed and they are aggravated by physical effort. Rest and medical observation are therefore essential. Card has been partially updated in March 2010: see Occupational Exposure Limits, Storage, Spillage Disposal.

ADDITIONAL INFORMATION

STRONTIUM CARBONATE

ICSC: 1695
April 2007

CAS #	**1633-05-2**	**Strontianite**
RTECS #	**WK8305000**	**Carbonic acid, strontium salt (1:1)**
EC/EINECS #	**216-643-7**	**SrCO3**
		Molecular mass: 147.6

TYPES OF HAZARD / EXPOSURE	ACUTE HAZARDS / SYMPTOMS	PREVENTION	FIRST AID / FIRE FIGHTING
FIRE	Not combustible.		In case of fire in the surroundings: all extinguishing agents allowed
EXPLOSION			
EXPOSURE		**PREVENT DISPERSION OF DUST!**	
Inhalation	Cough.	Avoid inhalation of dust.	Fresh air, rest.
Skin		Protective gloves.	Rinse and then wash skin with water and soap.
Eyes	Redness.	Safety goggles	Rinse with plenty of water (remove contact lenses if easily possible).
Ingestion		Do not eat, drink, or smoke during work.	Rinse mouth. Give one or two glasses of water to drink.

SPILLAGE DISPOSAL	PACKAGING & LABELLING
Personal protection: particulate filter adapted to the airborne concentration of the substance. Sweep spilled substance into containers; if appropriate, moisten first to prevent dusting.	
EMERGENCY RESPONSE	**STORAGE**
	Separated from acids.

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STRONTIUM CARBONATE

ICSC: 1695

IMPORTANT DATA

PHYSICAL STATE; APPEARANCE
WHITE ODOURLESS POWDER.

CHEMICAL DANGERS
Reacts with acids.

OCCUPATIONAL EXPOSURE LIMITS
TLV not established.
MAK: IIb (not established but data is available) (DFG 2006).

INHALATION RISK
A nuisance-causing concentration of airborne particles can be reached quickly.

EFFECTS OF SHORT-TERM EXPOSURE
May cause mechanical irritation the eyes and the respiratory tract.

EFFECTS OF LONG-TERM OR REPEATED EXPOSURE
See Notes.

PHYSICAL PROPERTIES

Decomposes at >1200 °C
Density: 3.5 g/cm³

Solubility in water, g/100 ml at 18°C: 0.011 (very poor)

ENVIRONMENTAL DATA

NOTES

Strontium ion has effects on the calcium content of the bones and teeth, but data concerning harmful doses of strontium carbonate are inadequate. Strontium carbonate occurs naturally in the environment as strontianite. The physico-chemical properties and its natural occurence as strotianite in the environment indicate also the $SrCO_3$ is stable and rather inert in its solid form. It can be expected that it is persistent and distributes mainly to the soil compartment.

ADDITIONAL INFORMATION

STRONTIUM SULFATE

ICSC: 1696
April 2007

CAS #	**7759-02-6**	**Celestite**
RTECS #	**WT1210000**	**Sulfuric acid, strontium salt (1:1)**
EC/EINECS #	**231-850-2**	**Celestine**
		Strontium sulphate
		$SrSO_4$
		Molecular mass: 183.7

TYPES OF HAZARD / EXPOSURE	ACUTE HAZARDS / SYMPTOMS	PREVENTION	FIRST AID / FIRE FIGHTING
FIRE	Not combustible. Gives off irritating or toxic fumes (or gases) in a fire.		In case of fire in the surroundings: all extinguishing agents allowed
EXPLOSION			
EXPOSURE		**PREVENT DISPERSION OF DUST!**	
Inhalation	Cough.	Avoid inhalation of dust.	Fresh air, rest.
Skin		Protective gloves.	Rinse and then wash skin with water and soap.
Eyes	Redness.	Safety goggles.	Rinse with plenty of water (remove contact lenses if easily possible).
Ingestion		Do not eat, drink, or smoke during work.	Rinse mouth. Give one or two glasses of water to drink.

SPILLAGE DISPOSAL	PACKAGING & LABELLING
Personal protection: particulate filter adapted to the airborne concentration of the substance. Sweep spilled substance into containers; if appropriate, moisten first to prevent dusting.	
EMERGENCY RESPONSE	**STORAGE**

IPCS
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STRONTIUM SULFATE

ICSC: 1696

IMPORTANT DATA

PHYSICAL STATE; APPEARANCE
ODOURLESS WHITE CRYSTALLINE POWDER.

CHEMICAL DANGERS
The substance decomposes on heating slowly >1580°C producing toxic and corrosive fumes including sulfur oxides.

OCCUPATIONAL EXPOSURE LIMITS
TLV not established.
MAK: IIb (not established but data is available) (DFG 2006).

INHALATION RISK
A nuisance-causing concentration of airborne particles can be reached quickly.

EFFECTS OF SHORT-TERM EXPOSURE
May cause mechanical irritation the eyes and the respiratory tract.

EFFECTS OF LONG-TERM OR REPEATED EXPOSURE
See Notes.

PHYSICAL PROPERTIES

Melting point:	1605°C
Density:	3.96 g/cm³

Solubility in water, g/100 ml at 25°C: 0.0135 (very poor)

ENVIRONMENTAL DATA

NOTES

Strontium ion has effects on the calcium content of the bones and teeth, but data concerning harmful doses of strontium sulfate are inadequate.
Occurs naturally in environment as the mineral celestine.

ADDITIONAL INFORMATION

RÉSUMÉ D'ORIENTATION

Le présent document concis d'évaluation chimique internationale (CICAD)[1] relatif au strontium naturel et à ses composés (isotopes stables) a été préparé conjointement par Toxicology Advice & Consulting Ltd[2] et le Centre for Ecology and Hydrology (*Centre d'écologie et de d'hydrologie*) du Royaume-Uni. Les sections consacrées à la physicochimie de ces substances et à leur toxicité pour les mammifères s'inspirent du profil toxicologique établi en 2004 par l'Agency for Toxic Substances and Disease Registry (*Agence pour les produits toxiques et Registre des maladies*) (ATSDR, 2004) des Etats-Unis d'Amérique (USA). Une version préliminaire de ce profil toxicologique était déjà disponible en 2001 et la version définitive de 2004 contient un certain nombres de données essentielles parues entre temps dans la littérature. En mai 2006, Toxicology Advice & Consulting Ltd a procédé à une recherche bibliographique de grande envergure dans les bases de données portant sur la période 2000-2006 afin de relever toute référence essentielle qui aurait été publiée postérieurement à celles qui sont prises en compte dans le document de base de l'ATSDR.[3] En juin 2006, le Centre for Ecology and Hydrology a également effectué des recherches bibliographiques approfondies afin d'obtenir des informations relatives aux aspects environnementaux de la question. Des renseignements sur la disponibilité du document de base et son examen par des pairs sont donnés à l'appendice 2. L'appendice 3 donne des indications sur l'examen par des pairs du présent CICAD. Les fiches internationales sur la sécurité chimique (ICSC) du strontium (ICSC 1534), du carbonate de strontium (ICSC 1695), du sulfate de strontium (ICSC 1696) et du chromate de strontium (ICSC 0957) établies par le Programme international sur la sécurité chimique (IPCS) sont également reproduites dans le présent CICAD (IPCS, 2004a, 2004b, 2006a, 2006b).

A l'état métallique, le strontium réagit rapidement avec l'eau et l'oxygène et il n'existe par conséquent qu'à l'état d'oxydation + II. A l'état naturel, le strontium n'est pas radioactif et il existe sous quatre formes isotopiques stables : ^{88}Sr (82,6 %), ^{86}Sr (9,9 %), ^{87}Sr (7,0 %) et ^{84}Sr (0,6 %). Le strontium représente 0,02 à 0,03 % de l'écorce terrestre où il est présent principalement sous forme de célestine (sulfate de strontium) ou de strontianite (carbonate de strontium). Les isotopes radioactifs du strontium ne sont pas examinés dans le présent CICAD.

Ces dernières années, les importations de strontium aux Etats-Unis sont restées relativement stables, de l'ordre de 31 000 à 39 000 tonnes par an. En 2001, plus de 85 % du strontium utilisé aux Etats-Unis servait à la confection de céramiques et d'objets en verre, principalement les dalles de verre des téléviseurs. On utilise également des dérivés du strontium pour la confection d'aimants de ferrite (ferrite de strontium) et autres applications des céramiques et du verre, de produits pyrotechniques (nitrate de strontium), de pigments pour peintures (chromate de strontium), de lampes à fluorescence (phosphate de strontium), de dégazeurs (getters) pour la production de zinc (carbonate de strontium), d'alliages pour le moulage de l'aluminium (strontium métallique) et de médicaments (chlorure de strontium, peroxyde de strontium). La quantité totale de dérivés du strontium qui sont commercialisés chaque année au Canada est actuellement d'environ 5 400 tonnes.

Le strontium peut être libéré dans l'atmosphère (principalement sous forme d'oxyde) par des processus naturels (par exemple la météorisation des roches, l'entraînement de particules, la resuspension éolienne et la formation d'embruns marins) ou par suite d'activités humaines (par ex. broyage et traitements divers, combustion du charbon et utilisation d'engrais phosphatés). Dans l'air, l'oxyde se transforme rapidement en hydroxyde ou en carbonate. Le strontium entraîné dans l'atmosphère se redépose sur le sol. La météorisation des roches et des sols entraîne le strontium dans les eaux superficielles et souterraines. Dans l'eau, il est présent sous forme de cation hydraté. Le strontium présent dans l'eau peut se fixer par sorption à la surface de certains minéraux. Comme le calcium, le strontium est modérément mobile dans les sols et les sédiments et il se fixe modérément par sorption aux oxydes métalliques et aux argiles. Les végétaux absorbent facilement le strontium par leur voie normale d'absorption du calcium. Dans les sols riches en calcium, les lombrics n'accumulent pas le strontium; mais cette accumulation peut se produire dans des sols acides pauvres en calcium. Le strontium s'accumule facilement dans les otolithes, les vertèbres et les opercules des poissons. On utilise d'ailleurs des solutions de chlorure de strontium pour marquer le fretin de saumon et procéder à une identification ultérieure dans le milieu naturel. Chez les organismes supérieurs, le strontium s'accumule dans les os du fait de sa ressemblance avec le calcium.

Dans l'air, la concentration du strontium est généralement inférieure à 0,1 $\mu g/m^3$, mais elle peut être plus élevée à proximité des installations où l'on brûle du

[1] On trouvera à l'appendice 1 la liste des acronymes et abréviations utilisés dans le présent rapport.

[2] Qui s'appelle maintenant bibra-toxicology advice & consulting.

[3] Après avoir recherché en novembre 2009 s'il existait de nouvelles publications apportant des informations essentielles, l'un des auteurs a conclu qu'il n'en existait aucune (voir l'appendice 2).

charbon. La teneur moyenne de l'eau de mer en strontium est d'environ 8 mg/l. Aux Etats-Unis, le strontium est présent dans presque toutes les eaux douces de surface; les concentrations qui ont été mesurées étaient comprises entre 0,3 et 1,5 mg/l en moyenne. Dans les cours d'eau d'Europe, on trouve des concentrations qui s'échelonnent sur 4 ordres de grandeur, allant de 0,001 à 13,6 mg/l, avec une valeur médiane de 0,11 mg/l. Dans des cours d'eau contaminés par d'anciennes exploitations minières, on a relevé des teneurs moyennes en strontium allant jusqu'à 2 mg/l. Dans les sédiments des cours d'eau européens, la concentration médiane de strontium est de 126 mg/kg. Dans les sédiments des cours d'eau contaminés par ces anciennes exploitations, des concentrations de strontium pouvant atteindre 225 mg/kg de poids sec ont également été mesurées. Dans l'ensemble du monde, la concentration moyenne de strontium dans les sols avoisine 240 mg/kg. En Europe, la teneur médiane en strontium dans le sous-sol est de 95 mg/kg et elle atteint 89 mg/kg dans la couche arable. En Allemagne et aux Etats-Unis, on a relevé une concentration en strontium dans l'eau de boisson respectivement égale à 0,34 mg/l et à 1,1 mg/l. En ce qui concerne les plantes vivrières, c'est dans les légumes-feuilles que les teneurs les plus élevées en strontium ont été observées (par exemple, 64 mg/kg de poids sec dans les choux).

Chez l'être humain adulte, on estime que l'apport total de strontium peut atteindre environ 4 mg par jour dans de nombreuses régions du monde. L'eau de boisson y contribue pour environ 0,7-2 mg par jour et les aliments (principalement les légumes-feuilles, les céréales et les produits laitiers) pour 1,2-2,3 mg par jour. Comparativement, l'apport dû à l'air est négligeable. Ces apports peuvent être sensiblement plus élevés dans les zones où la concentration de strontium dans l'eau de boisson atteint la limite supérieure des valeurs mesurées. Là où le sol est riche en strontium, les plantes vivrières peuvent contribuer beaucoup plus à la dose journalière ingérée, notamment si ces plantes vivrières sont, pour l'essentiel, consommées localement.

Chez l'adulte la teneur totale de l'organisme en strontium est généralement d'environ 0,3 à 0,4 g dont 99 % dans le squelette. L'organisme humain absorbe le strontium ingéré dans la proportion de 11 à 30 %. Chez le rat, la résorption gastro-intestinale du strontium s'est révélée plus élevée chez les sujets âgés de 15 jours que chez ceux dont l'âge était de 89 jours. Chez l'Homme en revanche, on n'a pas constaté de relation entre l'âge et l'absorption du strontium. Au niveau du poumon, l'absorption des dérivés solubles est rapide, tandis que celle des dérivés insolubles est lente. L'absorption transcutanée des dérivés du strontium est également lente. Le strontium peut se substituer plus ou moins bien au calcium; une fois absorbé, il se répartit dans l'organisme comme le fait le calcium et au niveau des os, il peut y avoir échange entre calcium et strontium. L'administration concomitante de calcium, de phosphates ou de sulfates réduit l'absorption du strontium au niveau des voies digestives ainsi que sa rétention par le squelette. Le strontium maternel peut passer chez le fœtus pendant la grossesse puis être ensuite transmis au nourrisson lors de l'allaitement. Chez l'être humain, le rapport du strontium au calcium dans les os est de 3×10^{-4} à la naissance est il s'élève ensuite jusqu'à environ 5×10^{-4} chez l'adulte. Dans l'organisme, le strontium forme probablement des complexes avec l'hydroxyapatite, les carbonates, les phosphates, les citrates et les lactates et il peut également réagir avec diverses protéines qui fixent ou transportent le calcium. Une fois absorbé, le strontium est excrété principalement dans les urines et les matières fécales. Après ingestion ou inhalation, on observe assez vite une phase excrétoire rapide qui correspond à l'élimination du strontium non absorbé. Une phase excrétoire lente lui succède (la demi-vie biologique est estimée à des valeurs allant de quelques semaines à 28 ans), qui correspond vraisemblablement à l'élimination plus lente du strontium retenu par le squelette.

On a constaté que le chlorure, le carbonate, le sulfate et le nitrate de sodium présentaient une faible toxicité aiguë par voie orale pour le rat ou la souris. Chez le rat, la toxicité dermique aiguë du sulfate de strontium reste faible. Chez des singes ayant reçu quotidiennement des capsules de chlorure de strontium pendant une semaine, on a observé des lésions oesophagiennes et duodénales localisées.

Le strontium est susceptible de perturber la minéralisation osseuse du squelette en développement. De fait, de nombreuses études montrent que l'os constitue un tissu cible de première importance en cas d'exposition répétée au strontium par voie orale. L'étude la plus informative qui ait été trouvée (complétude des examens, administration des plus faibles doses et durée la plus longue) n'a pas révélé d'effets indésirables imputables au traitement chez des ratons qui avaient reçu quotidiennement du strontium dans leur alimentation à raison d'environ 40 mg/kg de poids corporel pendant 90 jours, des modifications étant toutefois observées dans la structure et le poids de la thyroïde, dans la teneur du foie en glycogène et dans le poids de l'hypophyse à la dose quotidienne de 160 mg/kg de poids corporel. Chez les ratons qui avaient reçu pendant 20 jours du strontium dans leur alimentation à la dose quotidienne de 190 mg/kg de poids corporel, l'examen histologique du tissu osseux s'est révélé normal. La même étude a révélé des effets mineurs sur les os chez les ratons qui avaient reçu du strontium à la dose quotidienne d'environ 380 mg/kg de poids corporel de même que chez des souris qui en avaient reçu quotidiennement 350 mg/kg de poids corporel dans leur eau de boisson pendant 29 jours. Des études de plus longue durée n'ont pas permis de trouver

une valeur plus faible pour la dose sans effet. Selon plusieurs études, une exposition répétée à des doses plus élevées administrées par voie orale a entraîné de nombreuses anomalies au niveau des os et des cartilages, notamment une mauvaise calcification, une teneur réduite en minéraux, un accroissement des phospholipides acides complexés, une augmentation des régions non minéralisées (ostéoïdes), un accroissement du tissu spongieux, une extension des plaques épiphysaires, une diminution de la densité, une désorganisation du réseau trabéculaire, des os plus petits et du rachitisme. Une modification du taux sérique de la forme active de la vitamine D et des calbindines-D ou des variations dans l'activité de la phosphatase acide et de la phosphatase alcaline dans certains organes sont des marqueurs d'une atteinte osseuse.

Aucune étude de cancérogénicité respectant les directives actuelles n'a été retrouvée au sujet des dérivés du strontium. L'implantation de chromate de strontium dans les voies respiratoires de rats a provoqué l'apparition de tumeurs locales. On sait toutefois que les dérivés du chrome (VI) sont cancérogènes pour les mammifères, aussi a t-on estimé que c'est à l'ion chromate qu'il faut imputer l'activité cancérogène du chromate de strontium.

Les données de génotoxicité relatives au strontium sont rares. Selon une étude limitée, une seule dose de chlorure de strontium administrée par voie orale a provoqué des aberrations chromosomiques dans la moelle osseuse de souris. Les composés du strontium se sont toutefois révélés dénués d'activité in vitro. Mis en présence d'ovocytes de hamster en culture, le chlorure de strontium n'a pas provoqué de lésions chromosomiques. Il n'a pas causé non plus de lésions de l'acide désoxyribonucléique (ADN) bactérien, ni de transformation parmi des cellules embryonnaires de hamster. Le sulfate de strontium n'a pas provoqué de lésions chromosomiques dans des cellules pulmonaires de hamster en culture ni de mutations dans le test bactérien d'Ames. Le carbonate de strontium ne s'est pas non plus révélé mutagène dans ce même test. Le seul dérivé du strontium qui ait manifesté une activité génotoxique in vitro est le chromate de strontium. Ce dérivé du chrome (VI) a provoqué des mutations bactériennes dans le test d'Ames, des échanges entre chromatides sœurs dans des fibroblastes de hamster en culture et la transformation de cellules embryonnaires de hamster. On estime que c'est l'ion chromate qui est responsable de l'activité observée.

Une étude de criblage dans laquelle des rats des deux sexes ont reçu du sulfate de strontium par gavage pendant 6 à 8 semaines en commençant 2 semaines avant l'accouplement, n'a révélé aucun effet sur la reproduction ou la fécondité, ni sur le développement des fœtus. Selon une analyse de la littérature, aucun effet sur la fécondité n'a été constaté chez des rats ayant reçu du chlorure de strontium dans leur eau de boisson pendant 3 générations. Après administration répétée de carbonate de strontium par voie orale à des souris gestantes, on a observé des effets indésirables sur les os de leur progéniture. Des études comportant l'administration répétée de strontium par voie orale à des ratons juste sevrés et à des rats adultes montrent que les jeunes animaux sont plus sensibles que les adultes aux effets osseux du strontium.

Il existe très peu d'informations au sujet de la toxicité des isotopes stables du strontium pour l'être humain. Une étude effectuée en Turquie incite à penser qu'il pourrait y avoir une relation entre une exposition au strontium et le rachitisme chez l'enfant. La concentration du strontium dans le sol était le seul indicateur témoignant d'une exposition probable. Dans la zone d'endémie, l'alimentation est largement basée sur les cultures céréalières locales.

En se basant sur une étude qui n'a révélé aucun effet indésirable (l'examen a notamment comporté une étude des os au microscope) chez des ratons qui avaient ingéré du strontium pendant 90 jours à la dose quotidienne de 40 mg/kg de poids corporel, on peut établir que la dose journalière tolérable (DJT) est de 0,13 mg/kg de poids corporel. S'il est vrai que dans de nombreuses régions du monde les apports estimés sont inférieurs à cette valeur, ils pourraient être supérieurs chez certaines populations qui vivent dans des régions où la teneur en strontium de l'eau de boisson ou des plantes vivrières est élevée. Les données disponibles sont insuffisantes pour établir une concentration tolérable par inhalation.

Le strontium est nécessaire au développement normal de certains organismes unicellulaires, des algues calcaires, des coraux, des gastéropodes, des bivalves et des céphalopodes. Au laboratoire, le strontium présente une faible toxicité aiguë pour les organismes aquatiques. Dans le cas des organismes dulçaquicoles, la plupart des tests utilisent du chlorure de strontium et la valeur de la concentration létale médiane de strontium à 48 h et à 96 h (CL_{50}) va de 75 à 910 mg/l. En se basant sur la perturbation de la fonction de reproduction chez la daphnie, on a obtenu pour le strontium une concentration médiane effective (CE_{50}) à 21 jours de 60 mg/l. Les valeurs de la CL_{50} aiguë pour les organismes marins indiquent que ceux-ci seraient moins sensibles au strontium que les organismes dulçaquicoles.

Comme l'éventail des concentrations de strontium dans les eaux de surface recouvre celui des concentrations de cet élément qui se révèlent toxiques pour les organismes aquatiques, il apparaît que nombre des organismes utilisés dans les tests portant sur les eaux douces se sont certainement acclimatés, non pas aux eaux naturelles, mais à celles qui sont pauvres en strontium ou bien qu'ils proviennent de populations

vivant dans des zones ou la teneur en strontium est faible. De plus les concentrations qui se sont révélées toxiques pour les organismes marins correspondent à des concentrations de strontium supérieures à sa concentration normale dans l'eau de mer (environ 8 mg/l) et dans certaines des études portant sur des organismes marins, la teneur de fond en strontium n'a pas été mesurée. Par conséquent, les données disponibles ne permettent pas de déterminer un ratio exposition/effet réaliste pour le strontium.

RESUMEN DE ORIENTACIÓN

Este documento abreviado de evaluación internacional de productos químicos (CICAD)[1] sobre el estroncio natural y sus compuestos (isótopos estables) fue preparado conjuntamente por Toxicology Advice & Consulting Ltd[2] y por el Centro de Ecología e Hidrología de Monks Wood (Reino Unido). Las secciones de fisicoquímica y toxicología de mamíferos se basaron en el perfil toxicológico de 2004 preparado por la Agencia para el Registro de Sustancias Tóxicas y Enfermedades (ATSDR, 2004) de los Estados Unidos de América. En 2001 se publicó un proyecto de versión de este perfil toxicológico y en la versión final de 2004 se incluyeron algunos documentos fundamentales aparecidos en ese periodo intermedio. En mayo de 2006, Toxicology Advice & Consulting Ltd realizó una búsqueda bibliográfica amplia en las bases de datos pertinentes para el periodo de 2000–2006 con objeto de identificar las referencias críticas publicadas después de las incorporadas al documento original de la ATSDR.[3] En junio de 2006, el Centro de Ecología e Hidrología de Monks Wood llevó a cabo búsquedas bibliográficas exhaustivas para identificar información pertinente relativa a los aspectos ambientales. La información sobre el carácter del examen colegiado y la disponibilidad del documento original se presenta en el apéndice 2. La información sobre el examen colegiado del presente CICAD aparece en el apéndice 3. También se reproducen en este documento las Fichas internacionales de seguridad química (ICSC) para el estroncio (ICSC 1534), el carbonato de estroncio (ICSC 1695), el sulfato de estroncio (ICSC 1696) y el cromato de estroncio (ICSC 0957), preparadas por el Programa Internacional de Seguridad de las Sustancias Químicas (IPCS, 2004a, 2004b, 2006a, 2006b).

El estroncio metálico reacciona rápidamente con el agua y el oxígeno, por lo que sólo se encuentra en la naturaleza en el estado de oxidación 2+. En su forma natural no es radiactivo y existe en cuatro formas isotópicas estables: ^{88}Sr (82,6%), ^{86}Sr (9,9%), ^{87}Sr (7,0%) y ^{84}Sr (0,6%). Representa el 0,02–0,03% de la corteza terrestre, en la que se encuentra fundamentalmente como celestita (sulfato de estroncio) o estroncianita (carbonato de estroncio). En el presente CICAD no se examinan los isótopos radiactivos.

En los últimos años, las importaciones de estroncio a los Estados Unidos se han mantenido relativamente

[1] La lista completa de las siglas y abreviaturas utilizadas en este informe figura en el apéndice 1.
[2] Denominada ahora Bibra – Toxicology Advice & Consulting.
[3] Uno de los autores hizo una búsqueda de nuevos documentos críticos en noviembre de 2009 y llegó a la conclusión de que no había ninguno (véase el apéndice 2).

constantes en unas 31 000 y 39 000 toneladas al año. En 2001, más del 85% del estroncio consumido en los Estados Unidos se utilizó en la fabricación de productos de cerámica y vidrio, fundamentalmente en el vidrio de las pantallas de los televisores. Los compuestos de estroncio también se utilizan en los imanes de ferrita cerámica (ferrita de estroncio) y otras aplicaciones de cerámica y vidrio, pirotecnia (nitrato de estroncio), pigmentos para pinturas (cromato de estroncio), lámparas fluorescentes (fosfato de estroncio), adsorbentes en la producción de zinc (carbonato de estroncio), aleaciones para fundiciones de aluminio (estroncio metálico) y medicamentos (cloruro de estroncio, peróxido de estroncio). El volumen total de compuestos de estroncio comercializados en el Canadá asciende ahora a unas 5400 toneladas al año.

El estroncio se puede liberar en el aire (principalmente como óxido de estroncio) mediante procesos naturales (por ejemplo, meteorización de rocas, arrastre de partículas, nueva suspensión en el viento y espuma marina) o como resultado de las actividades humanas (por ejemplo, molturación, elaboración, combustión de carbón y uso de fertilizantes fosfatados). En el aire, el óxido se transforma con rapidez en hidróxido o carbonato. El estroncio atmosférico vuelve al suelo por deposición. Pasa a las aguas superficiales y freáticas mediante la meteorización natural de las rocas y el suelo. En el agua existe como catión hidratado. El estroncio acuoso se puede adsorber en la superficie de ciertos minerales. Al igual que el calcio, tiene una movilidad moderada en el suelo y los sedimentos y se adsorbe de manera moderada en los óxidos metálicos y las arcillas. Las plantas lo absorben fácilmente por las vías normales de incorporación de calcio. Las lombrices de tierra que se encuentran en suelos ricos en calcio no acumulan estroncio; sin embargo, se puede producir dicha acumulación en suelos ácidos con un escaso contenido de calcio. El estroncio se acumula fácilmente en los otolitos, las vértebras y los opérculos de los peces. En realidad, se han utilizado deliberadamente soluciones de cloruro de estroncio para marcar alevines de salmones a fin de poderlos identificar más tarde en el estado libre. En los organismos superiores se registra bioacumulación en los huesos debido a la semejanza del estroncio con el calcio.

Las concentraciones medias de estroncio en el aire suelen ser inferiores a 0,1 $\mu g/m^3$, aunque se pueden alcanzar valores más elevados cerca de plantas de combustión de carbón. Su concentración media en el agua de mar es de unos 8 mg/l. Está presente en casi toda las aguas dulces superficiales de los Estados Unidos, en concentraciones medias que varían entre 0,3 y 1,5 mg/l. Su concentración en las aguas de los ríos europeos tiene una fluctuación de cuatro órdenes de magnitud, de 0,001 a 13,6 mg/l, con un valor mediano de 0,11 mg/l. Se han notificado niveles medios de estroncio de 2 mg/l en el agua de ríos contaminados por antiguas explotaciones mineras. La concentración mediana de estroncio en el sedimento de los ríos europeos era de 126 mg/kg, pero se han notificado concentraciones medias de hasta 225 mg/kg de peso seco en los sedimentos de ríos contaminados por antiguas explotaciones mineras. El promedio de la concentración de estroncio en el suelo en todo el mundo es de unos 240 mg/kg. Las concentraciones medianas de estroncio en los suelos europeos eran de 95 mg/kg en el subsuelo y de 89 mg/kg en la capa superficial. En Alemania y los Estados Unidos se notificaron concentraciones medias en el agua de bebida de unos 0,34 mg/l y 1,1 mg/l, respectivamente. En las plantas alimenticias las concentraciones más elevadas se midieron en las hortalizas de hoja (por ejemplo, 64 mg/kg de peso seco en la col).

Se estima que la ingesta diaria total de estroncio de las personas adultas de muchas partes del mundo puede ser de hasta unos 4 mg/día. El agua de bebida contribuye con 0,7–2 mg/día y los alimentos (principalmente las hortalizas de hoja, los cereales y los productos lácteos) con otros 1,2–2,3 mg/día. En comparación, la contribución del aire es insignificante. La ingesta puede ser sustancialmente más elevada en las zonas donde las concentraciones de estroncio en el agua de bebida están en el extremo más alto de la gama medida. En regiones con concentraciones altas en el suelo, las plantas alimenticias pueden contribuir también de manera sustancial a la ingesta diaria, en particular si se consumen sobre todo alimentos vegetales de producción local.

La carga normal de estroncio en el organismo de los adultos es de unos 0,3–0,4 g, encontrándose el 99% en el esqueleto. En las personas se absorbe alrededor del 11–30% del estroncio ingerido. La absorción gastrointestinal de estroncio era más elevada en ratas de 15 días que en las de 89 días; en las personas no se ha observado esta dependencia de la edad de la absorción gastrointestinal. La absorción a partir de los pulmones es rápida para los compuestos de estroncio solubles, pero lenta para los insolubles. La absorción cutánea de compuestos de estroncio es lenta. El estroncio puede sustituir de manera imperfecta el calcio; la distribución del estroncio absorbido se asemeja a la del calcio, de manera que se pueden intercambiar en los huesos. Mediante la administración conjunta con calcio, fosfatos o sulfatos se reduce su absorción del tracto gastrointestinal y la retención esquelética. El estroncio se puede transferir de la madre al feto durante el embarazo y a los niños pequeños mediante la lactancia materna. La relación estroncio:calcio en los huesos de las personas es al nacer de 3×10^{-4} y aumenta hasta alrededor de 5×10^{-4} en los adultos. En el organismo probablemente forma complejos con la hidroxiapatita, el carbonato, el fosfato, el citrato y el lactato y se puede producir una interacción con diversas proteínas fijadoras y

transportadoras de calcio. El estroncio absorbido se excreta fundamentalmente en la orina y las heces. Tras la ingestión o la inhalación hay una fase rápida de excreción, correspondiente al material no absorbido. A continuación sigue una fase lenta (las estimaciones de las semividas biológicas varían entre varias semanas y 28 años), probablemente debido a que se elimina despacio del esqueleto.

El cloruro de estroncio, el carbonato de estroncio, el sulfato de estroncio y el nitrato de estroncio muestran una toxicidad aguda baja por vía oral en ratas y/o ratones. La toxicidad aguda cutánea del sulfato de estroncio en ratas era baja. Se observaron daños locales en el esófago y el duodeno de monos a los que se había suministrado a diario cloruro de estroncio en cápsulas durante una semana.

El estroncio puede interferir en la mineralización de los huesos durante la formación del esqueleto. Es más, numerosos estudios han puesto de manifiesto que un tejido destinatario fundamental tras la exposición repetida por vía oral al estroncio es el óseo. En el estudio más informativo encontrado (tomando como base el alcance del examen, el uso de las dosis más bajas y la duración más prolongada) no se observaron efectos adversos relacionados con el tratamiento en ratas jóvenes a las que se administraron con los alimentos unos 40 mg de estroncio/kg de peso corporal al día durante 90 días, mientras que con 160 mg/kg de peso corporal al día se detectaron cambios en la estructura y el peso del tiroides, el contenido de glucógeno del hígado y el peso de la hipófisis. La histología ósea era normal en las ratas jóvenes que recibieron 190 mg de estroncio/kg de peso corporal al día con los alimentos durante 20 días. En el mismo estudio se observaron efectos menores en los huesos de ratas jóvenes a las que se habían administrado unos 380 mg de estroncio/kg de peso corporal al día y en ratones que habían recibido 350 mg/kg de peso corporal al día con el agua de bebida durante 29 días. En estudios más prolongados no se determinó el nivel más bajo sin efectos. En varios estudios, la exposición repetida a dosis orales más elevadas produjo numerosas anomalías en huesos y cartílagos, en particular calcificación defectuosa, reducción del contenido de minerales, aumento de los fosfolípidos ácidos complejos, regiones no mineralizadas (osteoides), tejido esponjoso, placas epifisarias más anchas, densidad ósea más baja, trabéculas desorganizadas, huesos más pequeños y raquitismo. Los marcadores de los efectos en los huesos incluían cambios en las concentraciones de vitamina D y proteínas de calbindina-D activadas en el suero y cambios en la actividad de las fosfatasas ácida y alcalina en determinados órganos.

No se encontraron estudios de carcinogenicidad para los compuestos de estroncio que se ajustaran a las directrices presentes. La implantación de cromato de estroncio en las vías respiratorias de ratas indujo tumores locales. Sin embargo, los compuestos de cromo (VI) son carcinógenos para los mamíferos y se consideró que la actividad del cromato de estroncio se debía al ión cromato.

Son escasos los datos de genotoxicidad relativos a los compuestos de estroncio. En un estudio limitado se informó de que una dosis oral única de cloruro de estroncio inducía aberraciones cromosómicas en la médula ósea de ratones. Sin embargo, los compuestos de estroncio no mostraron actividad *in vitro*. El cloruro de estroncio no provocó daños cromosómicos en cultivos de oocitos de hámster, en el ácido desoxirribonucleico (ADN) de bacterias o en células embrionarias de hámster ni transformación celular en éstas últimas. El sulfato de estroncio no indujo daños cromosómicos en cultivos de células de pulmón de hámster o mutaciones en una prueba bacteriana de Ames. El carbonato de estroncio no resultó mutagénico en una prueba de Ames. El único compuesto de estroncio con actividad genotóxica identificada *in vitro* fue el cromato de estroncio. Este compuesto de cromo (VI) indujo mutaciones bacterianas en una prueba de Ames, intercambio de cromátidas hermanas en cultivos de fibroblastos de hámster y transformación celular en células embrionarias de hámster. La actividad observada es atribuible al núcleo de cromato.

No se observaron efectos en la reproducción/fecundidad o el desarrollo fetal en un estudio de detección en el que se administró sulfato de estroncio a ratas (de ambos sexos) mediante sonda durante unas 6–8 semanas, comenzando dos semanas antes del apareamiento. Según un examen, no se detectaron efectos en la fecundidad cuando las ratas recibieron cloruro de estroncio en el agua de bebida durante tres generaciones. Tras la administración de dosis orales repetidas de carbonato de estroncio a ratas preñadas, se observaron efectos adversos en los huesos de las crías. En estudios de dosis orales repetidas en ratas recién destetadas y adultas se puso de manifiesto que los animales más jóvenes eran más sensibles que los adultos a los efectos del estroncio en los huesos.

Hay muy poca información sobre la toxicidad del estroncio estable en las personas. En un estudio realizado en Turquía se indicó una relación entre la exposición al estroncio y el raquitismo infantil. La concentración de estroncio en el suelo era el único indicador de la posible exposición. La alimentación en la zona endémica es muy dependiente del cultivo local de cereales.

A partir de un estudio en el que no se observaron efectos adversos (el examen incluyó una evaluación microscópica de los huesos) en ratas jóvenes a las que se

administró una dosis de estroncio de 40 mg/kg de peso corporal al día durante 90 días, se puede derivar una ingesta diaria tolerable (IDT) de 0,13 mg/kg de peso corporal al día. Aunque las ingestas estimadas en muchas partes del mundo son inferiores a este valor, lo pueden superar ciertas poblaciones que viven en regiones donde las concentraciones de estroncio en el agua de bebida o las plantas alimenticias son elevadas. Los datos disponibles son insuficientes para obtener una concentración tolerable por inhalación.

El estroncio es necesario para el desarrollo normal de algunos microorganismos unicelulares, algas calcáreas, corales, gasterópodos, bivalvos y cefalópodos. Tiene una toxicidad aguda baja para los organismos marinos en el laboratorio. Con respecto a los organismos de agua dulce, la mayor parte de las pruebas se basan en el cloruro de estroncio; las concentraciones letales medianas de estroncio (CL_{50}) a las 48 h y las 96 h oscilan entre 75 y 910 mg/l; una concentración efectiva mediana para el estroncio (CE_{50}) a los 21 días, basada en el trastorno de la reproducción de los dáfnidos, fue de 60 mg/l. Las CL_{50} agudas en organismos marinos parecen indicar que son menos sensibles al estroncio que los organismos de agua dulce.

La superposición de la gama de niveles naturales de estroncio en las aguas superficiales con las concentraciones de estroncio que provocan toxicidad en los organismos acuáticos pone de manifiesto que muchos de los organismos de prueba en los estudios de agua dulce deben haberse aclimatado no a las aguas naturales, sino a las que presentan deficiencia de estroncio o se derivan de poblaciones localizadas en zonas con una concentración baja de estroncio. Además, los valores de la toxicidad marina representan concentraciones “añadidas” de estroncio por encima de la normal del agua de mar (alrededor de 8 mg/l) y en algunos de los estudios marinos no se midió la concentración de estroncio “de fondo”. Por consiguiente, de la información disponible no se pueden derivar relaciones exposición:efectos realistas.

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