DRAFT

For Review Only

Public Health Goal for
Strontium-90
in Drinking Water

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To be added later

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PREFACE

Drinking Water Public Health Goals
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This Public Health Goal (PHG) technical support document provides information on health effects from contaminants in drinking water. PHGs are developed for chemical contaminants based on the best available toxicological data in the scientific literature. These documents and the analyses contained in them provide estimates of the levels of contaminants in drinking water that would pose no significant health risk to individuals consuming the water on a daily basis over a lifetime.

The California Safe Drinking Water Act of 1996 (Health and Safety Code, Section 116365) requires the Office of Environmental Health Hazard Assessment (OEHHA) to perform risk assessments and adopt PHGs for contaminants in drinking water based exclusively on public health considerations. The Act requires that PHGs be set in accordance with the following criteria:

1. PHGs for acutely toxic substances shall be set at levels at which no known or anticipated adverse effects on health will occur, with an adequate margin of safety.
2. PHGs for carcinogens or other substances that may cause chronic disease shall be based solely on health effects and shall be set at levels that OEHHA has determined do not pose any significant risk to health.
3. To the extent the information is available, OEHHA shall consider possible synergistic effects resulting from exposure to two or more contaminants.
4. OEHHA shall consider potential adverse effects on members of subgroups that comprise a meaningful proportion of the population, including but not limited to infants, children, pregnant women, the elderly, and individuals with a history of serious illness.
5. OEHHA shall consider the contaminant exposure and body burden levels that alter physiological function or structure in a manner that may significantly increase the risk of illness.
6. OEHHA shall consider additive effects of exposure to contaminants in media other than drinking water, including food and air, and the resulting body burden.
7. In risk assessments that involve infants and children, OEHHA shall specifically assess exposure patterns, special susceptibility, multiple contaminants with toxic mechanisms in common, and the interactions of such contaminants.
8. In cases of insufficient data for OEHHA to determine a level that creates no significant risk, OEHHA shall set the PHG at a level that is protective of public health with an adequate margin of safety.

9. In cases where scientific evidence demonstrates that a safe dose response threshold for a contaminant exists, then the PHG should be set at that threshold.
10. The PHG may be set at zero if necessary to satisfy the requirements listed above in items seven and eight.
11. PHGs adopted by OEHHA shall be reviewed at least once every five years and revised as necessary based on the availability of new scientific data.

PHGs adopted by OEHHA are for use by the California Department of Health Services (DHS) in establishing primary drinking water standards (State Maximum Contaminant Levels, or MCLs). Whereas PHGs are to be based solely on scientific and public health considerations without regard to economic cost considerations or technical feasibility, drinking water standards adopted by DHS are to consider economic factors and technical feasibility. Each primary drinking water standard adopted by DHS shall be set at a level that is as close as feasible to the corresponding PHG, placing emphasis on the protection of public health. PHGs established by OEHHA are not regulatory in nature and represent only non-mandatory goals. By state and federal law, MCLs established by DHS must be at least as stringent as the federal MCL, if one exists.

PHG documents are used to provide technical assistance to DHS, and they are also informative reference materials for federal, state and local public health officials and the public. While the PHGs are calculated for single chemicals only, they may, if the information is available, address hazards associated with the interactions of contaminants in mixtures. Further, PHGs are derived for drinking water only and are not intended to be utilized as target levels for the contamination of other environmental media.

Additional information on PHGs can be obtained at the OEHHA web site at www.oehha.ca.gov.

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PUBLIC HEALTH GOAL FOR STRONTIUM IN DRINKING WATER

SUMMARY

The Office of Environmental Health Hazard Assessment (OEHHA) proposes a Public Health Goal (PHG) of 0.35 pCi/L for strontium-90 in drinking water. The proposed PHG is based on the known carcinogenic effects of radiation observed in humans. In 1999, U.S. Environmental Protection Agency (U.S. EPA) published "Cancer Risk Coefficients for Environmental Exposure to Radionuclides: Federal Guidance Report 13" on the relative risks of radioactive substances to humans, specifically to provide technical guidance to federal and state risk assessors. This report provides tabulated risk coefficients based on the state-of-the-art methods and models that take into account many factors, including age, gender, and competing causes of death. The methodology can be used to identify risks from water ingestion alone. The estimation of the risk coefficient assumes the linear no threshold model and is especially appropriate for estimating cancer risks at low levels of exposure to radionuclides like strontium.

OEHHA followed general risk assessment practices and used the risk coefficient recommended in Federal Guidance Report 13 to estimate the cancer health risk level for strontium. The proposed PHG was estimated by applying the strontium-90 risk coefficient to a lifetime of exposure to strontium-90 in 2 L/day of drinking water, assuming a *de minimis* excess individual cancer risk level of one in one million (10^{-6}). This proposed PHG level is judged adequate to protect sensitive populations, and also to protect against all non-cancer effects of strontium.

The federal maximum contaminant limit (MCL) for strontium-90 in drinking water is 8 pCi/L, an activity level estimated to provide a radiation dose of 4 mrem/year, which was judged by U.S. EPA to be an acceptable radiation dose from this isotope. The California MCL is set at the same level.

INTRODUCTION

This Public Health Goal (PHG) technical support document provides information on health effects from strontium-90 (^{90}Sr) in drinking water. PHGs are developed for contaminants based on the best available toxicological data in the scientific literature. These documents and the analyses contained in them provide estimates of the levels of contaminants in drinking water that would pose no significant health risk to individuals consuming the water on a daily basis over a lifetime.

This PHG technical support document addresses a substance that is radioactive. Elements that contain unstable nuclei are said to be radioactive or are called radionuclides. To achieve a more stable energy state, radionuclides spontaneously emit one or more alpha or beta particles, followed in some cases by the emission of x-or gamma-ray photons. An alpha particle is defined as a positively charged particle consisting of two protons and two neutrons. A beta particle is either a negatively charged negatron/electron or a positively charged particle (positron). Gamma rays are high

energy, short-wavelength electromagnetic radiation. Radioactive emissions are measured by an activity unit called a *curie* (Ci), representing 3.7×10^{10} disintegrations per second. For drinking water, the common representation of activity is the *picocurie* (pCi), equal to 10^{-12} Ci. Another representation of radioactivity is the *becquerel* (Bq), which is one disintegration per second (1 pCi = 3.7×10^{-2} Bq).

Energetic atoms of radionuclides release their energy either through particles or electromagnetic radiation, which then may in turn interact with other atoms or matter, particularly to knock electrons from off their orbits around the nucleus. This process is defined as ionizing radiation. Ionizing radiation is a particular concern for living tissues as it could lead to changes in important constituents of the cell including DNA, and result in changes in structure and function of the cells or organ systems. Understanding the potential for ionizing radiation to effect changes to cells and tissues requires knowing how much energy is deposited in the tissues as a result of these emissions. This concept is referred to as the absorbed dose and is represented by units of *rad* (radiation absorbed dose), which is the amount of energy (in units of 100 ergs) deposited in one gram of matter or tissue. In International Units, the *gray* (Gy) is used for characterizing absorbed dose, representing one joule/kg of energy deposited and is equivalent to 100 rad.

However, the radiation particles or energy types differ in their ability to affect tissues, and thus an adjustment or quality factor can be used to compensate for the differences. For example an alpha particle deposits its energy in a short range rarely can penetrate the surface layers of tissues, while beta particle and gamma radiation deposit their energies over a greater range. The *rem* (roentgen equivalent man) unit accounts for the difference in the type of radiation by multiplying the absorbed dose in rads by a quality factor, and can also be represented as *sieverts* (Sv), equaling 100 rems. Another fine-tuning of the absorbed dose is to adjust for the different types of organs affected by radioactive emissions; this is referred to as *rem-ede* (effective dose-equivalent).

The radionuclide, strontium-90 (^{90}Sr), is created during the process of nuclear fission, which occurs in a nuclear reactor or an atomic explosion. Although ^{90}Sr does not occur naturally, it is ubiquitous because of the worldwide atmospheric testing of nuclear weapons. These tests, which occurred during the 1950s and 60s, resulted in the deposition of ^{90}Sr onto all continents and water bodies. As such, there is a small amount of ^{90}Sr in most environmental media, including drinking water. ^{90}Sr decays by emitting a beta particle.

The federal government has regulated levels of ^{90}Sr in community water supplies since the mid-1970s. The U.S. EPA promulgated Maximum Contaminant Levels (MCLs) for ^{90}Sr and other radionuclides in community water supplies in their 1976 National Interim Primary Drinking Water Regulation. For most of the beta/photon radionuclides, the MCL was that concentration in water that would yield 4 mrem/year to the total body or any given internal organ. For ^{90}Sr, the U.S. EPA set a separate MCL of 8 pCi/L.

In 1991, the U.S. EPA proposed new MCLs for all beta/photon emitters based on newer dosimetry. They based the MCLs on a 4 mrem/year effective dose equivalent. The proposed rule was never implemented.

In 2000, the U.S. EPA finalized their rule for drinking water. For ^{90}Sr the MCL remains at 8 pCi/L because updated dosimetry and risk levels yielded similar concentrations. This MCL is scheduled for review in the next two to three years for risk management issues. The California MCL for ^{90}Sr is also 8 pCi/L (CCR, 2002).

Other agencies have developed differing health protective levels for radionuclides and provide equivocal guidance for setting a ^{90}Sr PHG. For example, the International Commission on Radiological Protection has recommended a *de minimis* public radiation exposure of 1 mrem/year per source (ICRP, 1999), which is approximately equivalent to a lifetime cancer risk of $5x10^{-5}$. OEHHA has chosen to use a *de minimis* cancer risk level of 10^{-6} for setting PHGs for all non-threshold carcinogens, while U.S. EPA uses a value of zero for the comparable federal guidelines, the MCLGs. The purpose of this document is to review the toxicity of ^{90}Sr and to derive and propose an appropriate, health-protective PHG for ^{90}Sr in drinking water.

CHEMICAL PROFILE

Chemical Identity

Strontium-90 is a man-made radioactive isotope of strontium. It decays with a half-life of 29 years to yttrium-90 and emits a beta particle (an energetic electron) in the decay process. The energy of the beta particles (maximum 546 keV) is sufficient to produce ionizations and excitations of molecules in their path. The average range of these beta particles in water is less than 0.2 cm. Because of the short range of the beta particles, ^{90}Sr outside of the body does not pose much radiation hazard, except in large quantities and in equilibrium with ^{90}Y (half-life 64.4 hours), which produces a stronger beta radiation (maximum 2,283 keV). However, ^{90}Sr is readily taken into the body because of its similarity to calcium, presenting an internal radiation hazard. Table 1 summarizes some of the more important characteristics of ^{90}Sr.

Table 1. Characteristics of ^{90}Sr

Properties	Value
Atomic number	38
Atomic mass	89.91
Half-life	29 years
Decay constant	0.024 per year
Characteristics of beta particle	
Average energy	200 keV
Average track length	0.2 cm (water)
Maximum energy	546 keV
Specific activity	143 Ci/g (7.09 ng/μCi)

Physical and Chemical Properties

Strontium (atomic number 38) is an alkaline earth element in Group IIA of the periodic table. Because of its high reactivity, elemental (or metallic) strontium is not found in nature. The element exists only as molecular compounds with other elements. Strontium can exist in two oxidation states, but only the +2 form exists under natural environmental conditions, because elemental strontium readily reacts with water and oxygen (ATSDR, 2001). The oxide, hydroxide, nitrate, and chloride salts are soluble in water, while the sulfate and phosphate salts are relatively insoluble (ATSDR, 2001).

Sources

^{90}Sr does not occur naturally, it is nearly ubiquitous because of the worldwide atmospheric testing of nuclear weapons. The tests during the 1950s and 60s resulted in the deposition of ^{90}Sr onto all continents and water bodies. An exception is deep groundwater, more than 50 years old. ^{90}Sr is of environmental significance because of its relatively long half-life (29 years). However, because it has been several decades since the releases, ^{90}Sr levels are at a small fraction of their peak, and are continuing to decline (ATSDR, 2001).

^{90}Sr is used as a radioactive tracer in medical and environmental studies. It is also used in thermoelectric devices for power supplies used in remote locations, luminous signs, and ice detection devices for airplane wings. It is also used in electron tubes, as a radiation source in industrial thickness gauges, and in a device for ophthalmic treatments.

Non-radioactive strontium is found throughout the environment. Strontium compounds are used for many industrial processes including the manufacture of glass and ceramics (ATSDR, 2001). Strontium ranelate, a compound of two non-radioactive strontium ions and a synthetic organic acid (ranelic acid), is now being used to some extent in the treatment of osteoporosis (Marie, 2003; Meunier *et al*., 2004; Health News, 2004).

ENVIRONMENTAL OCCURRENCE AND HUMAN EXPOSURE

^{90}Sr is nearly ubiquitous since the dawn of the nuclear weapons testing, but the environmental levels of ^{90}Sr are low. These levels have been declining since the early 1960s when atmospheric testing of nuclear weapons ceased. Human exposure to ^{90}Sr can result from consumption of food, drinking water, or the incidental ingestion of soil or dust contaminated with ^{90}Sr. Food and drinking water are the largest sources of exposure. Grain, leafy vegetables, and dairy products contribute the greatest percentage of dietary ^{90}Sr to humans (ATSDR, 2001).

Air

The aboveground testing of nuclear weapons released ^{90}Sr to the atmosphere from the mid-1940s to the 1980s. This release resulted in the wide dispersal of ^{90}Sr and other fission product radionuclides. The atmospheric deposition of ^{90}Sr has decreased from a

peak of 3 million curies (10^8 GBq) in 1963 to < 3,000 curies in 1990 (ATSDR, 2001). Other sources of atmospheric ^{90}Sr include the Chernobyl disaster in Ukraine (1986), routine releases from nuclear power stations and Department of Energy operations, and a series of rocket and satellite accidents. The ^{90}Sr released from the Chernobyl accident was mainly localized to Eastern Europe. Similarly, the small releases from nuclear power stations and Department of Energy (DOE) operations are fairly localized in their impact. The total of these other sources of ^{90}Sr is small compared to the total released from weapons testing, approximately 0.01 percent (ATSDR, 2001).

Since the signing of the Nuclear Test Ban Treaty of 1963, the airborne concentrations of ^{90}Sr have dropped steadily due to deposition and radioactive decay. DOE's surveys show small amounts of ^{90}Sr released from nuclear power plants (ATSDR, 2001).

Soil

The ATSDR (2001) reports that ^{90}Sr is found in nearly all soils in the United States. ^{90}Sr levels in soil vary widely depending on climatic conditions (especially rainfall) and proximity to facilities that release ^{90}Sr (nuclear power reactors, DOE facilities). Fresquez *et al*. (1996) reported that the 20-year mean region background for ^{90}Sr in soil near Los Alamos National Laboratory was 320 ± 250 pCi/kg (11.85±9.26 Bq/kg). The DOE (1992) reported that ^{90}Sr concentrations ranged from 0.02 to 540,000 pCi/kg at 91 waste sites located at 18 DOE facilities.

Water

Hamilton *et al*. (1996) reported that ^{90}Sr concentrations in surface water of the north Pacific Ocean were about 0.023-0.081 pCi/L (1-3 mBq/L). The U.S. EPA Environmental Radiation Ambient Monitoring System (ERAMS) program monitors concentrations of ^{90}Sr in drinking water at 78 sites. For 1995, the U.S. EPA reported a median concentration of 0.1 pCi/L of ^{90}Sr (4 mBq/L) for the 78 sites. Sites with above-average concentrations included Detroit and Niagara Falls, with ^{90}Sr concentrations of 0.4 and 0.5 pCi/L, respectively (ATSDR, 2001). Kraybill (1983) reported drinking water concentrations for Los Angeles, California, of 0.09 pCi/L (3 mBq/L) ^{90}Sr. Storm (1994) surveyed 169 public drinking water wells in California, and found that 16 wells had detectable concentrations of ^{90}Sr. The average of these 16 wells was 105 pCi/L (4 Bq/L).

The U.S. EPA lists ^{90}Sr concentrations for surface and groundwater at several locations throughout the United States (U.S. EPA, 2002). Dissolved ^{90}Sr was detected in groundwater at 19 out of 101 sites with median and average concentrations of 1.9 and 1.38 pCi/L (70 and 51 Bq/L), respectively. The surface water concentration of ^{90}Sr was 0.5 pCi/L (19 mBq/L) for one out of nine locations. For 91 waste sites at 18 DOE facilities, the ^{90}Sr concentrations in groundwater ranged from 0.05 to 231,000 pCi/L (DOE, 1992). Scientists from the DOE Environmental Measurement Laboratory reported wet deposition of ^{90}Sr from rainfall in 15 U.S. cities (DOE, 1996). The average annual deposition from all cities was about 5 pCi/m^2 (0.2 Bq/m^2). The cities with the highest ^{90}Sr deposition were New York City and Nome, Alaska (10 and 8 pCi/m^2, respectively).

California municipal drinking water suppliers have monitored public drinking water supply wells from 1994 to 2001 for various radioactive contaminants including strontium. ^{90}Sr was found to exceed the MCL of 8 pCi/L at only one source on one occasion during that period (DHS, 2002).

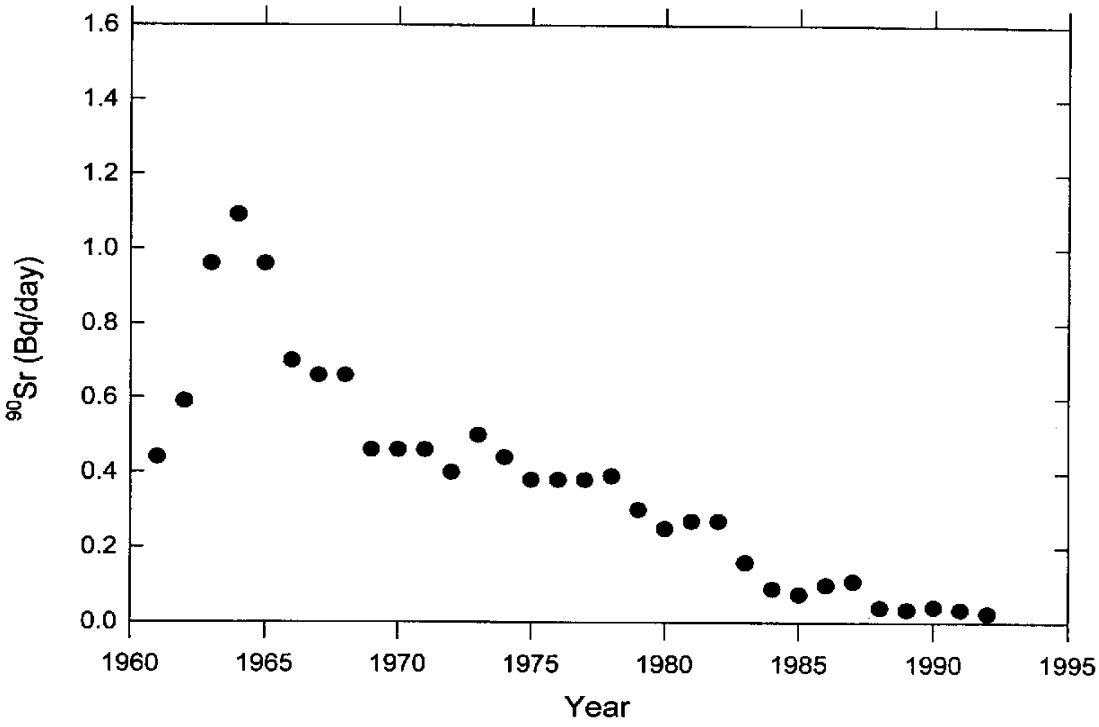
The ATSDR (2001) estimated the average consumption of ^{90}Sr from drinking water to be about 0.2 pCi/day (7 mBq/day). They based this estimate on assuming an average U.S. drinking water concentration of 0.1 pCi/L (3.5 mBq/L) for ^{90}Sr and a water consumption rate of 2 L/day.

Food

Eisenbud (1987) reported a wide range of ^{90}Sr concentrations in food from two U.S. cities, from 0.1 pCi/kg for fresh fish to as high as 69 pCi/kg for whole grain products. He also reported that the average dietary intake ranged from about 3 pCi/day in San Francisco to 54 pCi/day in New York. More recently, Caper and Cunningham (2000) monitored ^{90}Sr in foods as part of the U.S. Food and Drug Administration's Total Diet Study. They detected ^{90}Sr in 65 percent of the food items, with the greatest concentration being in mixed-nuts at 50 pCi/kg. Cunningham *et al*. (1994) evaluated ^{90}Sr activity in food (raw fruits and vegetables, fish and milk) collected from around 33 nuclear reactors. They found that 94 percent of their samples contained ^{90}Sr at concentrations of less than 20 pCi/kg. The remaining six percent had concentrations between 20 and 200 pCi/kg. The U.S. EPA monitors ^{90}Sr in milk at several sites in major U.S. population centers (U.S. EPA, 2003) in July of every year. For 2003, the range of ^{90}Sr levels in milk was from below quantifiable levels to 0.90 pCi/L.

Dietary intake of ^{90}Sr in the U.S. peaked in 1965 at 1.1 Bq/day (30 pCi/day), during the period of atmospheric testing of nuclear weapons. Dietary ^{90}Sr has since fallen to below 0.2 Bq/day (5 pCi/day), as shown in Figure 1 (Cunningham *et al*., 1994).

Figure 1. U. S. Daily Intake of ^{90}Sr, 1961 – 1992 (Cunningham *et al*., 1994)



METABOLISM AND PHARMACOKINETICS

In the U.S., the radiation protection community uses the recommendations of the International Commission on Radiological Protection (ICRP) for its dosimetric, metabolic, and biokinetic models for radionuclides. Most recently, the federal government adopted the new age-specific biokinetic models of the ICRP (U.S. EPA, 1999), and these models are described in a series of documents published between 1989 and 1996 (ICRP, 1989, 1993, 1995a,b, 1996). These are compartmentalized models of the kinetics of alkaline earth elements, including strontium, in humans that are applicable to infants, children, adolescents, and adults. The metabolic and pharmacokinetic information in these ICRP documents is summarized here in terms of what is known about the absorption, distribution, and excretion of strontium.

Absorption

The chemical behavior of strontium is similar to that of calcium (Group 2 in the Periodic Table of Elements), and therefore compounds of strontium are deposited in biological systems analogous to calcium. However it is not as efficiently absorbed or retained as calcium. The ICRP (1993) reports that human data on the absorption of dietary strontium and soluble forms of the element give values ranging from about 15 to 45 percent. Results from other animal species are generally similar. A number of factors have been

found to increase absorption, including fasting and low dietary levels of calcium, magnesium, and phosphorus. Spencer *et al*. (1972) showed that overnight fasting of human volunteers resulted in an increase in strontium absorption from about 25 percent to about 55 percent. A decrease in the calcium content of the diet by 75 percent raised strontium absorption from 20 percent to 40 percent (Shimmins *et al*., 1967). On the basis of the available information, the ICRP adopted a gut to blood transfer factor (f_1) of 0.3 for adults (ICRP, 1993).

The ICRP (1993) reported elevated absorption of strontium during periods of growth. Results obtained by Widdowson *et al*. (1960) suggest that absorption of strontium in 7-day-old infants fed with cow's milk is greater than 73 percent. Bedford *et al*. (1960) reported the absorption of strontium in 5 to 15-year-old children to be the same as adults. Studies in beagles, however, suggest that periods of increased strontium absorption continue well after weaning (ICRP, 1993). Because of this information, the ICRP recommends f_1 values of 0.6 for infants and 0.4 for ages 1 to 15 (ICRP, 1993).

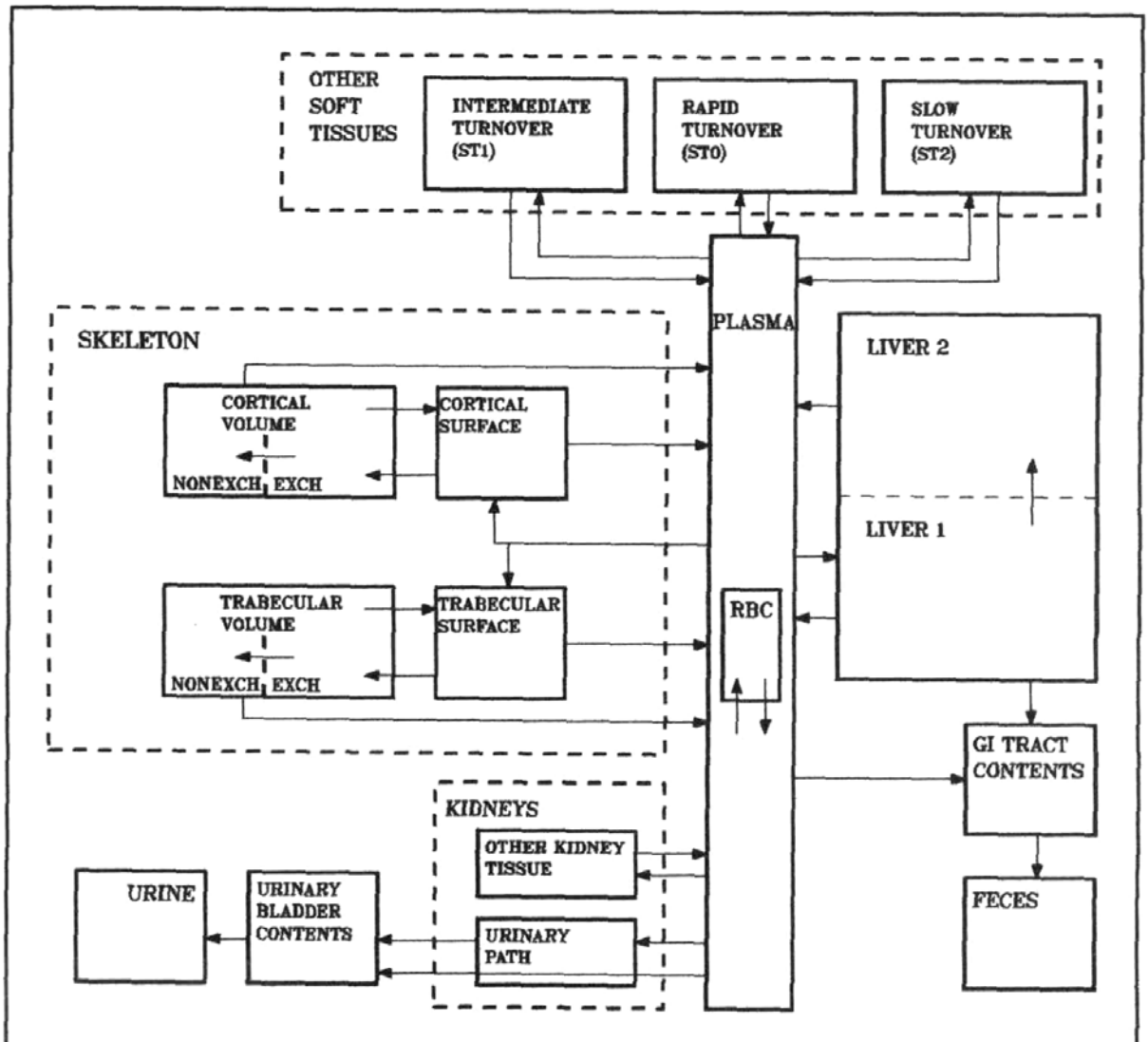
ICRP has developed the biokinetic model for strontium shown in Figure 2. Biokinetic models mathematically characterize the movement, translocation, fate, deposition, and excretion of a substance in a living system. Such models predict where substances go in the body, and how long they remain, which permits the calculation of internal dose and risk to specific tissues and organs as well as the whole body. In the dose computation scheme of the ICRP, information on the biological behavior of radionuclides is contained in three types of biokinetic models: a respiratory model, a gastrointestinal model (GI), and an element-specific systemic model.

The GI model is used to describe the movement of swallowed or endogenously secreted material through the stomach and intestines. Element-specific gut-to-blood transfer factors (f_1) quantify the amount absorbed from the small intestine to the blood (U.S. EPA, 1999). The GI model developed by the ICRP divides the GI tract into four compartments: stomach, small intestine, upper large intestine, and lower large intestine. The ICRP assumes first-order transfer of material from one compartment to the next using simple mass balance and rate equations. The model assumes that 99 percent of strontium that enters the body is not excreted, but is ultimately transferred to the skeleton, while absorption to the blood occurs only through the small intestine.

Distribution

The ICRP summarized the literature on the distribution and retention of strontium in humans (ICRP, 1993). Briefly, strontium follows the movement of calcium in the body but exhibits a slightly different pattern of distribution. It is largely sequestered into bone. Experimental studies show that strontium is less effectively absorbed from the intestines, more effectively excreted by the kidneys, and less readily incorporated into new bone than calcium.

Figure 2. Biokinetic Model for Strontium



The ICRP's generic model structure for calcium-like elements (ICRP, 1993). Abbreviations: RBC = red blood cells, EXCH = exchangeable bone volume, NONEXCH = nonexchangeable bone volume.

Metabolism

The chemical properties of strontium are similar enough to calcium that it can substitute for calcium in reactions which form inorganic anions such as carbonate and phosphate and carboxylic acids such as citrate and lactate (ATSDR, 1991). Strontium exchanges with calcium in bone and other cellular compartments where calcium predominates. At

pharmacologic doses, strontium may affect the rate of bone turnover by increasing osteoblastic activity while decreasing osteoclastic activity (Marie, 2004).

Excretion

Strontium is excreted slowly from the body. The urine appears to be the major avenue of excretion of strontium from the plasma. Radium dial painters had a urinary:fecal excretion ratio of about 3:1 (ATSDR, 2001). Strontium appears to undergo substantial tubular reabsorption in the kidney, and probably uses the same transport mechanisms as calcium (ATSDR, 2001). Fecal excretion of strontium from weeks to decades of strontium exposure has suggested another mechanism for transfer of strontium to the gastrointestinal tract. Studies in animals confirm that strontium appears to be secreted directly from the plasma into the intestine (Palmer and Thompson, 1961).

The strontium systemic biokinetic model as described in ICRP Publication 67 (1993) is a "calcium-like," bone volume-filling model. The model incorporates a central blood plasma (RBC) compartment connected to tissue compartments: skeleton, kidneys, liver and other soft tissues, and to output compartments: GI tract and feces, urinary bladder and urine. The ICRP systemic models for strontium assume that 50 percent of the element leaves the exchangeable bone volume and goes to the non-exchangeable bone tissue. The removal half-time for strontium from the exchangeable bone is about 80 days.

TOXICOLOGY

The toxicity of strontium-90 is due largely to strontium being chemically similar to calcium. As such, strontium is able to exchange for calcium in all tissues, but more significantly in those tissues with high calcium content such as bone. Beta emissions from ^{90}Sr have limited ability to penetrate through tissue and radiostrontium must be internalized or be in close contact with the skin for adverse health effects to occur. The basis for the health concern regarding oral or inhalation exposures is the bone-seeking behavior of the strontium, its long half-life of 29 years, the highly energetic 0.546 MeV beta particles, and the additional exposure to the 2.2 MeV beta particles released during decay of its short-lived ^{90}Y daughter isotopes. Furthermore, strontium may affect other calcium-utilizing processes including enzymes, secondary messenger systems and transporter systems.

Certain conditions are likely to enhance the absorption of strontium relative to calcium. Due to the higher intake of calcium during normal development, it would be expected that younger organisms would be more susceptible to the toxic effects of strontium. Radioactive strontium isotopes can incorporate into bone and irradiate the bone cells, hematopoietic tissues in the bone marrow, and surrounding soft tissues. Hence, immune and erythropoietic systems located in the bone marrow are susceptible to injury as well. All these factors, coupled with the proven carcinogenic effects of ionizing radiation and the long half-life of ^{90}Sr, make it a potential toxic hazard to exposed humans. For the above-mentioned reasons, children may exhibit an enhanced response to strontium

exposure in comparison with adults exposed to the same level of strontium in the environment. Young animals have been shown to be particularly vulnerable to strontium-90 because the immature skeleton has a high rate of bone remodeling and strontium may adversely affect bone development and damage hematopoietic tissues (ATSDR, 2001). In addition, people who are in renal failure may be more susceptible to strontium toxicity, because in this condition they may retain strontium more and fail to excrete strontium and retain calcium (ATSDR, 2001).

Strontium has been reported to enhance bone formation and/or decrease bone loss in osteoporosis patients (Meunier *et al.*, 2004). It is not clear whether this indicates that the elderly could be a sensitive population with regard to uptake of ^{90}Sr into bone.

Toxicological Effects in Animals

The animal database for oral exposures to strontium-90 is relatively substantial. Animal studies include acute and chronic exposures in dogs, monkeys, rodents, cows and pigs. The adverse effects include hematological, bone and kidney damage, immunological and developmental effects, cancer, and death. When attempting to predict human toxicity from animal studies, it would be necessary to bear in mind certain anatomical considerations. One of these is that, unlike humans, rat bones continue to grow through adulthood and therefore, adult rats are probably more susceptible to the toxic effects of strontium on the bone. Bone size is another consideration. Since the range of beta emissions from radioactive strontium and yttrium is about one centimeter, emissions of ^{90}Sr at the surface of bones from large animals (including humans) could not reach the hematopoietic tissues within the marrow. Of course, this protective effect would be diminished for children and infants due to their smaller bones.

Acute Toxicity

Casarett *et al*. (1962) reported increased deaths in a small number of Rhesus monkeys given large amounts of ^{90}Sr (100 μCi/day [3.7 MBq/day] for 5 or 10 days) by gavage. One monkey died four months after treatment, and another after four years. In experiments with young and adult rats, Casarett *et al*. (1962) also reported an 80 percent reduction in survival at five months when weanling rats were given at least 297 μCi/kg-day (11 MBq/kg-day) for 10 days by drinking water. The adult survival was unaffected. The increased mortality of the young rats, 20 times higher than adults, was attributed to the increased skeletal burden of ^{90}Sr in the young. Approximately 19 percent of adult rats ingesting 65 μCi ^{90}Sr/day (2.4 MBq/day) in drinking water for 10 days developed chronic interstitial nephritis. Rats drinking water for five days at doses of greater than 100 μCi/day (3.7 MBq/day) of ^{90}Sr suffered bone abnormalities, malformations, cartilage detachments, and fractures (Casarett *et al*., 1962). Cragel *et al*. (1969) reported deaths in four out of six young cows given 32-36 mCi (1.2-1.7 GBq) of ^{90}Sr orally for five days. Deaths occurred from radiation sickness.

Animal studies showed adverse hematological effects associated with beta irradiation of the bone marrow following incorporation of ^{90}Sr into bone (Casarett *et al*., 1962; Cragel *et al*., 1969; Zapol'skaya *et al*., 1974; Dungworth *et al*., 1969; Clarke *et al*., 1972).

Rhesus monkeys given large daily oral doses of ^{90}Sr (1000 μCi, 37 MBq) died within four months from pancytopenia (Casarett *et al*., 1962). Six young female dairy cattle given well over 40,000 μCi ^{90}Sr (2 GBq) experienced acute radiation sickness including severely decreased leukocytes and platelet counts after 80 days (Cragel *et al*., 1969).

Subchronic Toxicity

Using longer-term oral exposures to ^{90}Sr, several researchers report decreases in rodent survival. Hopkins *et al*. (1966) reported a 36 percent reduction in survival in young Long-Evans rats ingesting 104 μCi/kg-day (3.8 MBq/kg-day) of ^{90}Sr for 30 days. In an intermediate-duration study in rats, moderate hypoplasia of the bone marrow occurred among males and females given 790 μCi (29.2 MBq) ^{90}Sr over 30 days (Casarett *et al*., 1962). Hypoplasia of the bone marrow leading to anemia and thrombocytopenia developed in rabbits fed 6 μCi (218 kBq) ^{90}Sr/kg-day for 31 to 280 days (Downie *et al*., 1959). Downie *et al*. (1959) reported reduced osteocyte numbers in rabbits fed 6 μCi/kg-day for 48 days.

Administration of non-radioactive strontium to rats at 5 to 500 parts per million (ppm) in drinking water for 12 weeks showed a dose-dependent increase in strontium and decrease in calcium in bones. However, no severe toxic effects were noted (Xu *et al.*, 1997). Rats given strontium at 0.05, 0.1, or 0.5 percent in their feed for about four weeks beginning at weaning showed dose-dependent effects on calcium in femurs. At the highest dose, corresponding to 0.875 micromoles/day of strontium, calcium metabolic parameters were markedly suppressed, and calcium was decreased in both serum and femur (Morohashi *et al.*, 1994).

Developmental and Reproductive Toxicity

Clarke *et al*. (1970) studied the multigenerational effects of administered ^{90}Sr in Pittman-Moore swine fed from 1-3,100 μCi/day (0.037-114.7 MBq/day) only during the period of mating. Dosing had no effect on fertility or fecundity. Sows receiving the highest dose did not survive gestation. Offspring of sows fed 625 μCi/day (23.13 MBq/day) showed reduced weight at weaning and did not survive to nine months when fed ^{90}Sr after birth, even though parent sows fed the same doses survived well past breeding age.

CF-1 mice were fed 0.031-31 μCi/kg-day (1.11-1147 kBq/kg-day) ^{90}Sr from the time of conception through the rest of their lives, while their parents received the same amount through conception to lactation (Finkel *et al.*, 1960). No effects on litter size, survival of offspring or increase in malformations were noted. However, survival of offspring was shortened at doses of 3 μCi/kg-day (111 kBq/kg-day) and higher, which was attributed to an increased incidence of bone marrow cancers.

A high concentration of non-radioactive strontium fed to mice throughout pregnancy inhibited bone development in the offspring (Shibata and Yamashita, 2001), presumably by affecting bone calcification.

Neurotoxicity

No studies were found which report neurological effects of strontium-90 on experimental animals.

Immunotoxicity

Longer-term exposures to ^{90}Sr resulted in impaired immune function in animals. Howard (1970) reported that pigs fed 625 µCi/day (23.13 MBq/day) for nine months had significantly reduced antibody response to *Brucella* bacteria, about 50 percent of the controls. He also reported the loss of response to phytohemagglutinin stimulation. In a six-year chronic study in which beagles were fed ^{90}Sr at 0.4 µCi/kg-day, Dungworth *et al*. (1969) reported that about 1 percent of the exposed subjects developed myeloid metaplasia of the spleen.

Genetic Toxicity

Radioactive strontium is known to increase micronuclei formation, induce unscheduled DNA synthesis, aneuploidy, chromosomal breaks, and exchanges in various *in vivo* and *in vitro* test systems (ATSDR, 2001).

Chronic Toxicity

In albino rats fed 0.5 or 2 µCi/kg-day (18.5 to 74 kBq/kg-day) of ^{90}Sr for their postweaning lifetimes, Zapol'skaya *et al*. (1974) reported lifespans shortened by 18 to 30 percent compared to controls. They plotted mortality against absorbed dose and showed that the maximum mortality rate of 40 percent correlated with 4,000 rad (40 Gy) to the skeleton. Rats receiving more than 0.5 µCi/kg-day (18.5 kBq/kg-day) had significantly depressed hematopoiesis.

Large-scale, long-term exposure studies to ^{90}Sr were conducted at the University of California, Davis starting in 1961. These long-term oral exposure studies evaluated the health and survival of nearly 500 beagle dogs treated with ^{90}Sr (Dungworth *et al*., 1969; Momeni *et al.*, 1975; Book *et al.*, 1982; Raabe *et al*., 1981; White *et al*., 1993) and followed the same experimental protocol. Groups of pregnant beagle dogs were fed ^{90}Sr in their diets, and their pups were thus exposed from gestational day 21 through postnatal day 44, and up to 1.5 years when they reached adulthood. This exposure up to 1.5 years of age assured that the adult dog skeleton would be uniformly labeled with ^{90}Sr. Some animals were dosed throughout their lifetime (Book *et al*., 1982); the rest were maintained for the rest of their lives.

Dungworth *et al*. (1969) reported interim findings from dogs exposed to 0, 0.02, 0.07, 0.44, 1.33, 4 or 12 µCi/kg-day (based on an average 10 kg dog weight) (0.074-530 kBq/kg-day) of ^{90}Sr as described above for the first six years. Myeloproliferative disorder was a major finding in the two highest dose groups, 4 and 12 µCi/kg-day. Other effects seen were abnormal erythrocyte morphology, a drop in hematocrit, radiation-induced leukopenia (which progressed to wide fluctuations in leukocyte count), an abnormal amount of immature granulocytes, reduction in platelets, and splenomegaly. A

no-observed-adverse-effect level (NOAEL) of 1.33 µCi/kg-day) was selected). Several years later, Momeni *et al.* (1975) evaluated these dogs exposed to the same concentrations with an additional high-end group of 36 µCi/day. Increased skeletal changes (endosteal and periosteal cortical sclerosis and thickening) were noted for dogs exposed at doses above 1.33 µCi/day. Thus a NOAEL of 1.33 µCi/day (5 kBq/kg-day) can be identified for this study based on skeletal changes.

In the summary report by White *et al.* (1993), beagles given 0.02 to 36 µCi/kg-day of ^{90}Sr for 540 days and maintained until death had reduced survival of 18, 64, and 85 percent at the three highest dose levels (4, 12, and 36 µCi/day, respectively) when compared with controls. Concentrations of ^{90}Sr in feed at or below 0.44 µCi/day had no apparent effect on survival and there were no reported bone sarcoma deaths in that group, whereas bone sarcomas were noted in the higher dose groups. Thus, a NOAEL of 0.044 µCi/kg-day (1.6 kBq/kg-day) was identified based on the level of mortality being similar to that of the control group.

In a concurrent study, Book *et al*. (1982)) exposed 15 beagle dogs from gestational age day 21 throughout their lifetime to 0, 1.3, 4 or 12 µCi ^{90}Sr/kg-day. The median survival times of the groups were 15, 12.5, 6.5 and 5.2 years, respectively. Osteodystrophy was observed in the highest dose group. The two main causes of radiation-induced mortality were myeloproliferative syndrome and skeletal sarcomas. One case of ^{90}Sr–associated myeloproliferative disorder was noted in the lowest dose, 1.3 µCi/day (5 kBq/kg-day). This dose can be considered a lowest-observed-adverse-effect level (LOAEL), as it appears that there is some lifespan shortening - at least one incident of a ^{90}Sr –associated disease. However, the derivation of a LOAEL must be considered rather weak, since there was a small group size (7 dogs).

In a multigenerational study of female miniature swine, the ingestion of ^{90}Sr caused mortality before the first pregnancy and in individuals of the subsequent generation (Clarke *et al*., 1970; McClellan *et al*., 1963; Ragan *et al.*, 1973). Sows ingesting 3,100 µCi/day from age nine months did not survive the first pregnancy, succumbing from the destruction of hematopoietic tissue in the bone marrow. Sows exposed to 25, 125 and 625 µCi/day (0.93, 4.62 or 23.12 MBq/day), showed increased mortality after 11, 5, and 1 year, respectively. Effects on the F_1 females exposed from time of conception were more severe. None of the F_1 females exposed to the highest dose survived to nine months. Sows of the parental generation receiving the lowest dose (25 µCi/day) (0.93 MBq/day) showed significantly increased cumulative mortality after 7 years, rather than 11.

Finkel *et al*. (1960), exposed two groups of mice, females (over two hundred breeding females) and progeny to 0, 0.01, 0.1, 1.0, 2.5, 5.0, 10.0 µCi (0.037-370 kBq) of ^{90}Sr/g Ca for nearly a lifetime (the study was not completed). They reported a 40 percent shortened lifetime in mice exposed to 10.0 µCi of Sr/g Ca (estimated: 36 µCi/kg-day) from conception to death. Longer lifetimes were reported for mice exposed at adulthood. No consistent dose-related effects were noted for exposures below the highest dose.

Chronic exposures to ^{90}Sr caused suppression of hematopoiesis in rats, beagles, and swine ingesting at least 0.4 µCi/kg-day (Zapol'skaya *et al*., 1974; Dungworth *et al*., 1969; Clarke *et al*., 1972).

Bone injury was notable in chronic studies with beagles fed ^{90}Sr (Momeni, 1975; Book *et al*., 1982; Raabe *et al*., 1983; White *et al*., 1993). The effects noted included trabecular osteopenia, sclerosis, osteolytic lesions, and radiation-induced osteodystrophy. These effects were noted at exposures down to 0.4 µCi/kg-day. Radiation osteonecrosis was a common finding among swine that died with hematopoietic disorders or bone marrow hyperplasia after ingesting a diet containing ^{90}Sr at levels of between 1 and 3,100 µCi/day (Clarke *et al*., 1972).

Carcinogenicity

Numerous animal studies show that oral exposure to ^{90}Sr increases the incidence of bone and bone marrow cancers. In a small study in which monkeys were given ^{90}Sr by gavage, one given 11 µCi/kg-day (0.42 MBq/kg-day) for five days died of leukemia with a final skeletal dose of 4,300 rad (43 Gy). Two others died from bone-related cancers within 36 months after treatment with estimated skeletal doses of 4,700–9,500 rad, 47-97 Gy (Casarett *et al*., 1962). Adult and weanling rats developed osteosarcomas when fed 33 to 65 µCi/day (1.2-2.4 MBq/day) of ^{90}Sr over 10 days (Casarett *et al*., 1962). In longer-term exposures, rats fed a total of 790 µCi (29.2 MBq) ^{90}Sr over 30 days showed a 27 percent increase in the incidence of osteosarcoma, a 11 percent increase in skin sarcoma and a 6 percent increase in leukemia incidence (Casarett *et al*., 1962). Young rabbits that were fed an average of 6 µCi/kg-day (218 kBq/kg-day) for 224 to 280 days developed multiple osteosarcomas in the skull and the rapidly growing ends of the long bones within 6 to 8 months (Downie *et al*., 1959).

Acute exposures in rats have shown that young individuals that incorporate more ^{90}Sr into the growing skeleton were more vulnerable to cancer (Casarett *et al*., 1962). Seventeen percent of the weanling rats developed osteosarcoma while no adult showed any cancer. In addition, other cancers, including leukemia and skin cancer, were increased two–fold over the controls when rats were given 33 to 65 µCi/day (1.2-2.4 MBq/day) for 10 days.

Relatively large studies in rats, mice, dogs and pigs demonstrated an increased tumor incidence following chronic ingestion of ^{90}Sr (Zapol'skaya *et al*., 1974; Finkel *et al*., 1960; White *et al*., 1993; Clarke *et al*., 1970). Albino rats fed 2 µCi/kg-day (18.5 to 74 kBq/kg-day) for a lifetime showed an 18 percent increase in malignancies over the controls. The malignancies included lymphosarcoma, osteosarcoma, and leukemia. The cumulative absorbed dose averaged between 1,350 and 2,200 rad (Zapol'skaya *et al*., 1974). Mice (n = 230) fed 36 µCi/kg-day (1.33 MBq/kg-day) (estimated) from age 110-250 days showed a higher incidence of reticular tumors in the blood-forming tissue but no evidence of bone cancer. Mice exposed from conception at the highest dose levels showed an increased rate of reticular tissue tumors but also developed bone cancer by 525 days (Finkel *et al*., 1960).

White *et al*. (1993) reported beagles fed between 0.12 and 3.4 µCi/kg-day developed bone sarcoma, chondrosarcoma, hemangiosarcoma, fibrosarcoma, leukemia and undifferentiated sarcoma. Multiple tumors occurred only at the highest dose levels. Skeletal doses for the four highest dose groups at the time of death ranged from 5,000 to 10,700 rads. As the dose of ^{90}Sr increased, there was more likely to be an early onset of

sarcomas, particularly osteosarcomas. Doses ranging from 0.002 to 0.044 µCi/kg-day did not result in increased osteosarcoma deaths. Of the 66 sarcomas reported in this study, 75 percent were osteosarcomas; other types were chondrosarcoma, hemangiosarcoma, fibrosarcoma, and undifferentiated sarcoma.

In a multigenerational study in miniature swine, pigs fed between 1 and 3,100 µCi/day (0.037-114.7 MBq/day) for life developed a range of different cancers (Clarke *et al*., 1970). Lymphoid and myeloid cancers were elevated in the 1-125 µCi/day (0.037-3.7 MBq/day) range. In the parental generation, myeloid neoplasms were observed but no bone cancer developed. The F1 and F2 offspring exposed from conception developed osteosarcoma at 125 µCi/day. Osteosarcoma had a longer latency period than the other cancers and occurred at the higher exposures. Myeloid metaplasia and myeloid and lymphoid neoplasms developed sooner and more frequently in the F1 and F2 generations than in the parental generation.

Ovarian tumors were reported in mice treated as fetuses (Ronnback and Nilsson, 1982). Pregnant CBA mice (3-8/group) were injected with 0, 1.25, 2.5, 5, 10, and 20 µCi/animal (46.3, 92.5, 185, 370, 740 kBq) ^{90}Sr on the 19th day of gestation. Female offspring were killed after 10 months, upon which their ovaries were examined. In the two highest dose groups there were no multiple corpora lutea and a decrease in number of offspring. Furthermore, there was an increase in proliferation of tubular structures along with a higher rate of tubular adenomas (12 neoplasms/21 animals evaluated).

Toxicological Effects in Humans

The database for oral exposure to ^{90}Sr in humans is derived mostly from long-term and ongoing studies of a population that was exposed to contaminated drinking water and food following the release of large quantities of radioactive material into the Techa River from a Soviet nuclear weapons facility between 1949 and 1956 (ATSDR, 2001). This population received a mixed exposure to external radiation and to internal radiation from ^{89}Sr, ^{90}Sr, and ^{137}Cs.

Acute Toxicity

No reports were found on the acute toxicity of strontium to humans.

Neurotoxicity

The Techa River cohort was reported to suffer from various nervous system disorders including: weakness, apathy, and fatigue. These effects where observed in those individuals having an absorbed dose of 40-50 rad/year (ATSDR, 2001).

Immunotoxicity

Exposed Techa River inhabitants were reported to have immunological changes, which included granulocytopenia, decreased antigen expression of differentiating T-lymphocytes, and decreased T-lymphoblast transformation (ATSDR, 2001).

Genetic Toxicity

In the Techa River cohort progeny, a slight apparent increase in lethal chromosomal anomalies was observed (Kossenko *et al.*, 1994). In exposed individuals the mean genomic translocation frequency was elevated when compared with nonexposed populations (ATSDR, 2001).

Reproductive and Developmental Toxicity

No significant reproductive or developmental effects were noted for the Techa River exposed cohorts. There was no apparent difference in fertility, birthrate, and spontaneous abortion between the study and control populations.

Chronic Toxicity

Epidemiological studies of the effects of ^{90}Sr on human populations exposed by fallout have found little or no association with health effects. The only studies that suggest adverse effects from ^{90}Sr exposure are those that evaluate the exposure of inhabitants near the Techa River, Russia (Kossenko, 1996). Radiation releases from a nuclear weapons facility in the area resulted in contamination of water and food with radioisotopes of strontium, cesium, and gamma radiation emitters during the period of 1949-1956. In the exposed group, the standardized morality rate during the followup period (1950-1982) was 140 per 100,000, compared with 105 per 100,000 in the control group. The absorbed doses to the bone marrow ranged from 17.6 to 164 rad. Because of the nature of a mixed exposure to a number of radioisotopes, the effects reported cannot be solely attributed to ^{90}Sr.

Carcinogenicity

Epidemiological studies have found little or no association between oral exposure to ^{90}Sr from fallout and cancer in humans (ATSDR, 2001). In an epidemiological study using the Danish cancer registry, Sala and Olsen (1993) found no association between the incidence of thyroid cancer in Denmark between 1943 and 1988 and the levels of skeletal incorporation of ^{90}Sr from fallout. Hole *et al*. (1993) used data collected between 1959 and 1970 from a ^{90}Sr monitoring program in Scotland to identify three risk cohorts for leukemia, non-Hodgkin's lymphoma, acute myeloid leukemia, all childhood cancers, and bone cancer. Based on the degree of fallout, three cohorts were identified including: a high-risk group born between 1963 and 1966, a medium-risk group born between 1959 and 1962, and a low-risk group born after 1966. The study found no evidence for increased risk of total cancers, leukemia, non-Hodgkin's lymphoma, or acute myeloid leukemia for cohorts born during the highest fallout period (1963-1966). The few cases of bone tumors showed a statistically non-significant increase for children born during the high-risk period.

In contrast, the Techa River population, exposed to contaminated water and food from radionuclide releases from a nuclear weapons facility, exhibited a significant increase in the incidence of leukemia (Kossenko, 1996; Kossenko *et al*., 1997, 2000). An excess of

leukemia cases was observed in groups of individuals with estimated bone marrow doses of 10 rem (0.1 Sv) or greater, and the risk of mortality from leukemia increased with increasing dose. This finding can be related to the body burdens of ^{90}Sr, which in the Techa River population have been more than 100 times higher than fallout-related exposures during the same period (ATSDR, 2001). No increase in cancer rates has been observed in the progeny of the Techa River cohort. The increase in leukemia cases cannot be attributed solely to the effects of ingesting ^{90}Sr because of other possible exposures to other radionuclides, including ^{89}Sr and ^{137}Cs.

DOSE-RESPONSE ASSESSMENT

Noncarcinogenic Effects

Human health effects data are mostly from long-term and ongoing studies of a population that was exposed to contaminated drinking water and food following a release of large quantities of radioactive material into the Techa River from a Soviet nuclear weapons facility. This population received a mixed external radiation and internal radiation exposure from ^{89}Sr, ^{90}Sr and ^{137}Cs (Akleyev *et al*., 1995; Kossenko *et al*., 2000). Animal data include several large, long-term studies in dogs, pigs and rodents.

Several non-cancer adverse health effects were found in the Techa River population including: hematological effects (leukopenia, thrombocytopenia, and granulocytopenia), skeletal lesions, immunological effects (decreased expression of antigens) and nervous system disorders (weakness, apathy and fatigue). Although these findings are based on long-term chronic human exposure, we could not use the results to determine a NOAEL or LOAEL (No Observed Adverse Effects Level, Lowest Observed Adverse Effects Level). Multiple exposure routes with gamma radiation from external sources, as well as multiple radionuclides (^{89}Sr, ^{90}Sr and ^{137}Cs) occurring in these epidemiological studies make it impossible to separate out the effects due solely to ^{90}Sr.

Seven studies in dogs, rodents and pigs that reported non-cancer effects from chronic oral exposure to ^{90}Sr make the best studies for estimating a LOAEL or NOAEL for non-cancer effects because they are based on lifetime exposures. The studies deemed suitable for further risk analysis are summarized in Table 3. A dose of 0.15 µCi/kg-day of ^{90}Sr in beagles was the lowest dose producing an apparent dose-related decrease in survival.

Howard (1970) gave strontium chloride to Pitman Moore miniature pigs for 9 months at ^{90}Sr doses of 625 µCi/day. At the end of the study, he observed reduced antigen response to the bacterium *Brucella abortus*. Assuming an average weight of 70 kg, we estimated the resulting dose to be about 8.92 µCi/kg-day.

Table 3. Summary of Chronic Effects for Oral Exposure to ^{90}Sr in Animals

Study	Species and Effect	Dose Rates (µCi/kg-d)	NOAEL (µCi/kg-d)	LOAEL (µCi/kg-d)	Comments
Dungworth *et al*., 1969	Beagles, cardiovascular, hematological, immunological	0.002 to 1.2	0.15	0.4	
Howard, 1970	Pitman Moore miniature pigs, immunological	8.9	-	8.9	Dose estimate based on reported intakes, assuming average body weight of 70 kg
Clark *et al*., 1972	Pitman Moore miniature pigs, survival	0.014 to 1000	0.07	0.35	Dose estimate based on reported intakes, assuming average body weight of 70 kg
Zapol'skaya *et al*., 1974	Albino rats, hematological	0.5, 2.0	-	0.5	
Momeni *et al.* 1976	Beagles, skeletal changes	0.02-3.6	0.15	0.4	
Book *et al*., 1982	Beagles, premature death	0.13-1.2	-	0.13	Lifetime dosing
White *et al*., 1992	Beagles, survival	0.02-3.6	0.044	0.15	

Clark *et al*. (1972) fed female Pitman Moore miniature swine 0, 1, 5, 25, 125, 625 and 3,100 µCi/day of ^{90}Sr from age nine months to the first pregnancy. All pigs in the 3,100 µCi/day group died before the first pregnancy from the destruction of hematopoietic tissue in bone marrow, which resulted in anemia, leukopenia, thrombocytopenia and hemorrhagic syndrome. Pigs at doses above 25 µCi ^{90}Sr/day had shortened lifespans. Doses of 1 and 5 µCi/day did not result in any changes. Thus, 5 µCi/day is considered to be the highest no-effect dose, and assuming an average weight of 70 kg, is estimated to provide a NOAEL of 0.071 µCi/kg-day.

Zapol'skaya *et al*. (1979) fed albino rats 0, 0.5 or 2.0 µCi/kg-day of ^{90}Sr from weaning to the end of life. They reported that hematopoiesis was significantly depressed and the numbers of leukocytes were reduced by 20 percent in the low dose group compared to the controls. Thus 0.5 µCi ^{90}Sr/kg-day can be considered the LOAEL for this study.

The series of UC Davis studies on beagles provide some of the most sensitive measures of strontium-90 toxicity, with exposures of 0, 0.02, 0.07, 0.44, 1.33, 4, 12 and 36 µCi/day of ^{90}Sr. Dungworth *et al*. (1969) found that doses of 0.4 and 1.2 µCi/kg-day produced abnormal erythrocyte morphology and dose-related leukopenia, reduced platelet counts,

anemia, and myeloid metaplasia. Momeni *et al*. (1975) showed skeletal changes at the same doses as Dungworth *et al*. (1969). However, life-shortening aspects of ^{90}Sr exposure (White *et al.* (1993; Book *et al*. 1982) could not be addressed until all the dogs had died. The White *et al.* (1993) and Book *et al.* (1982) studies both demonstrated the same LOAEL of 0.133. However, due to limited dose groups, Book *et al.* (1982) did not have a dose below the LOAEL of 0.133 µCi/kg-day. Thus White *et al.* (1993) provides the most sensitive basis for a NOAEL of 0.044 µCi/kg-day, based on shortened lifespan.

Finkel *et al*. (1960) fed breeding CF-1 female mice a diet containing ^{90}Sr at doses of 0.03 to 36 µCi/kg-day throughout gestation and lactation. Then they fed the offspring the same dose regime from weaning to day 414. Survival of adults and offspring was significantly shortened at 36 µCi/kg-day. Because this was not a completed study, perhaps due to poor animal health, and because of uncertainty over the estimated dose, this study was not considered further for risk analysis.

Carcinogenic Effects

The Techa River population exposed to water and food contaminated with ^{90}Sr exhibited a significant increase in the incidence of leukemia (ATSDR, 2001). Scientists observed an excess of leukemia cases in groups of individuals with estimated bone marrow doses of 10 rem (0.1 Sv) or greater, and the risk of mortality from leukemia increased with increasing dose.

The U.S. EPA classifies all emitters of ionizing radiation as Group A carcinogens based on sufficient epidemiological evidence. The U.S. EPA also considers agents emitting ionizing radiation to be mutagens and teratogens. In 1999 the U.S. EPA estimated the radiogenic cancer risks from ionizing radiation and calculated the overall mortality and morbidity risk to be about 5.75×10^{-4} and 8.46×10^{-4} per person-gray, respectively (U.S. EPA, 1999).

More recently, the U.S. EPA developed carcinogenic potencies or risk coefficients for almost all radionuclides including ^{90}Sr. These values were developed based on the incidence of cancer in Japanese atomic blast survivors and are listed in U.S. EPA's Cancer Risk Coefficients for Environmental Exposure to Radionuclides: Federal Guidance Report No. 13 (U.S. EPA, 1999). The risk coefficients apply to an average member of the public in that estimates of risk are averaged over age and gender distributions of a hypothetical closed population with an unchanging gender ratio whose survival functions and cancer mortality rates are based on the 1989-91 U.S. life table statistics (NCHS, 1997) and U.S. cancer mortality data for the same period (NCHS, 1992, 1993a,b). The U.S. EPA provides mortality and morbidity risk coefficients for each radionuclide and exposure route (inhalation and ingestion of food, water and soil). The five steps in computing the risk coefficients for internal exposure are as follows:

- Step 1. Lifetime risk per unit absorbed dose at each age: Radiation risk models are used to calculate gender-specific lifetime risks per unit of absorbed dose for 14 cancer sites.
- Step 2. Absorbed dose rates as a function of time post-acute intake at each age: Age-specific biokinetic models are used to calculate the time dependent inventories of

activity in various regions of the body following an acute intake of a unit of radionuclide activity. Six ages are used: 100 days and 1, 5, 10, 15, 20-25 years.

- Step 3. Lifetime cancer risk per unit intake at each age: For each cancer site, the gender-specific values of lifetime risk per unit absorbed dose received at each age (from the first step) are used to convert the calculated absorbed dose rates to lifetime cancer risks for the case of acute intake of one unit of activity at each age x_i.
- Step 4. Lifetime cancer risk for chronic intake: The U.S. EPA assumed that the concentration of the radionuclide in the environmental medium remains constant and that all persons in the population are exposed throughout their lifetimes.
- Step 5. Average lifetime cancer risk per unit activity intake: Because a risk coefficient is an expression of the radiogenic cancer risk *per unit activity intake*, the calculated lifetime cancer risk from chronic intake of the environmental medium must be multiplied by the expected lifetime intake.

A more detailed explanation of these five steps is presented in the U.S. EPA's Federal Guidance Report No. 13 (U.S. EPA, 1999).

Analyses involving the risk coefficients should be limited to estimation of prospective risks in large existing populations, rather than being applied to specific individuals. Also the risk coefficients may not be suitable for assessing the risk to an average individual in an *age-specific* cohort. The U.S. EPA performed all computations of dose and risk using DCAL, a comprehensive biokinetic-dose-risk computational system designed for radiation dosimetry (U.S. EPA, 1999). DCAL has been extensively tested and has been compared with several widely used solvers for biokinetic models and systems of differential equations. DCAL was used by a task group of the ICRP to derive or check the dose coefficients given in its series of documents on age specific doses to members of the public from the intakes of radionuclides (ICRP, 1989, 1993, 1995, 1996a,b).

The risk coefficients from The Federal Guidance Report No. 13 for ^{90}Sr are listed in Table 4 below for the water ingestion exposure route in both units of Bq^{-1} and pCi^{-1}.

Table 4. Drinking Water Risk Coefficients for ^{90}Sr

Radionuclide	Risk Coefficient [1] (Bq^{-1})		Risk Coefficient [2] (pCi^{-1})	
	Mortality	Morbidity	Mortality	Morbidity
^{90}Sr	1.34×10^{-9}	1.51×10^{-9}	4.96×10^{-11}	5.59×10^{-11}

[1] Values taken from U.S. EPA, 1999.
[2] Converted from Bq^{-1} to pCi^{-1} by multiplying by 0.037 Bq/pCi.

The scientific community has been aware for many years of the possibility that low doses of ionizing radiation may result in changes in cells and organisms, which reflect an ability to adapt to the effects of radiation. There is also a suggestion that low doses of

ionizing radiation protect against cancer rather than conferring cancer risk (radiation hormesis), based both on experimental results showing adaptive responses and on interpretations of epidemiological studies (UNSCEAR, 1994; NCRP, 2001).

The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR, 1994) states that there is substantial evidence that the number of radiation-induced chromosomal aberrations and mutations can be reduced by a small prior conditioning dose of radiation in proliferating mammalian cells *in vitro* and *in vivo*. It seems likely that this effect is linked to an increased capacity for DNA repair. While it has been observed under specified and defined conditions, it has not been seen with all cell systems.

UNSCEAR (1994) also states that there is increasing evidence that cellular repair mechanisms are stimulated after radiation-induced damage. There appears to be a similar overlap in regard to the type of DNA damage that induces adaptive responses. However, extensive data from animal experiments and limited human data provide no evidence to support the view that the adaptive response in cells decreases the incidence of late effects such as cancer induction in humans after low doses (UNSCEAR, 1994).

The National Council on Radiation Protection and Measurements (NCRP, 2001) reviewed the most recent epidemiological evidence and concluded that there is no strong support for hormesis in the radiation epidemiological literature. It was judged that all epidemiological evidence implicating hormesis was either a statistical anomaly that disappeared as more and better data became available, or was due to confounding factors such as better health for radiation workers. The NCRP also concluded that low-dose cancer studies are equivocal because of the intrinsic limitations in their precision and statistical power. Because of these limitations there is a danger of over-interpreting either individual negative studies or individual highly-positive studies.

CALCULATION OF PHG

Calculations of concentrations of chemical contaminants in drinking water associated with negligible risks for both cancer and noncarcinogenic endpoints must take into account the toxicity of the chemical itself, as well as the potential exposure of individuals using the water. Tap water is used directly as drinking water, for preparing foods and beverages. It is also used for bathing or showering, and in washing, flushing toilets and other household uses, resulting in potential dermal and inhalation exposures.

Noncarcinogenic Effects

The study selected for determining the noncarcinogenic health protective concentration is White *et al.* (1993). This lifetime study, in which beagle dogs were given ^{90}Sr at 0, 0.02, 0.07, 0.44, 1.33, 4, 12 or 36 µCi/day, provides the most sensitive NOAEL among all the reviewed studies. The NOAEL of 0.044 µCi/kg-day, calculated assuming a 10 kg average weight of the dogs, is based on shortened lifespan observed in this study.

Using the 0.044 µCi/kg-day dose as the NOAEL, we calculated the public-health protective concentration (C) for noncarcinogenic endpoints using the equation below:

$$C = \frac{NOAEL \times BW \times RSC}{UF \times WC}$$

where:

NOAEL	=	No Observable Adverse Effect Level (44,000 pCi/kg-day);
BW	=	adult body weight of 70 kg;
RSC	=	relative source contribution of 0.04 (four percent), based on ATSDR's (2001) estimate of 0.2 pCi/day from drinking water and Cunningham *et al*. (1994) total dietary intake of 5 pCi/day; 0.2/5 = 0.04;
UF	=	uncertainty factor of 100, including a factor of 10 for interspecies differences and 10 for human interindividual differences in sensitivity;
WC	=	drinking water ingestion rate for an adult of 2 L/day.

Thus:

$$C = \frac{44{,}000 \text{ pCi/kg-day} \times 70 \text{ kg} \times 0.04}{100 \times 2 \text{ L/day}} = 600 \text{ pCi/L (rounded)}$$

The estimated health-protective concentration for noncarcinogenic effects of 600 pCi/L was based on shortening of lifespan in dogs, the critical effect noted in White *et al.* (1994).

Carcinogenic Effects

The U.S. EPA (1999) has determined a cancer coefficient for ^{90}Sr using the DCAL model dose estimates as well as modeling the response with the linearized multistage model. The health-protective concentration, C, for strontium in drinking water, corresponding to a *de minimis* cancer morbidity risk (1 in 1 million), was calculated as in the following equation:

$$C = \frac{R}{EP \times CRC \times WC}$$

where:

R	=	*de minimis* cancer risk of one in a million;
EP	=	exposure period of 70 years (25,568 days);
CRC	=	cancer risk coefficient (5.59×10^{-11}/pCi);

WC = drinking water ingestion rate (2 L/day).

Thus:

$$C = \frac{1 \times 10^{-6}}{25{,}568 \text{ day} \times 5.59 \times 10^{-11}/\text{pCi} \times 2 \text{ L/day}} = 0.35 \text{ pCi/L}$$

The estimated drinking water concentration resulting in a 1 in a million cancer morbidity risk for ^{90}Sr is 0.35 pCi/L. Since the calculated health-protective concentration based on carcinogenic risks is lower (0.35 pCi/L) than the concentration developed for noncarcinogenic effects (600 pCi/L), the PHG is proposed to be set at 0.35 pCi/L. This level is also judged adequate to protect sensitive subpopulations, including pregnant women, infants, and children.

RISK CHARACTERIZATION

The primary sources of uncertainty in the development of a PHG for ^{90}Sr in drinking water include some of the general issues of uncertainty in any risk assessment, particularly dose-response modeling and estimation of exposures. However, there is a considerable amount of certainty in key areas in the risk assessment of radioactive compounds such as ^{90}Sr, unlike the case with many other chemicals. These areas are: mode of action, inter- and intra-species extrapolation, and the relative source contribution (RSC). This certainty is based on a substantial body of information on the carcinogenic effects of radionuclides, including ^{90}Sr, on human subjects. U.S. EPA (as well as other entities) has developed models to estimate human body exposures to radionuclides, adding to the certainty of the estimations.

The proposed PHG of ^{90}Sr of 0.35 pCi/L was calculated based on the carcinogenic potency of 5.59×10^{-11} per pCi developed by U.S. EPA (1999), and an assumed *de minimis* excess individual lifetime cancer risk level of 10^{-6}. The corresponding radioactivity concentrations for lifetime cancer risk levels of 10^{-5} and 10^{-4} are 3.5 pCi/L and 35 pCi/L, respectively.

No additional assumptions are needed with respect to the use of an RSC for ^{90}Sr for the cancer calculation; the U.S. EPA's risk value is specific for water ingestion of ^{90}Sr.

The U.S. EPA MCL of 8 pCi/L was developed based on the 4 mrem assumed to be an acceptable level of exposure to beta/photon emitters, and is not based on analytical or Best Available Technology (BAT) limitations. The 4 mrem standard is applied to all beta particle and photon emitters and represents the absorbed dose of radiation. U.S. EPA (1990) estimated that consumption of 4 mrem of alpha particle and photon emitters in drinking water over a lifetime may result in an individual cancer risk of 5.6×10^{-5}. The ^{90}Sr MCL of 8 pCi/L falls within the U.S. EPA risk goal range of 10^{-4}–10^{-6} which they consider to be an acceptable human exposure level for radionuclides (U.S. EPA, 2000).

Although this risk assessment is for ^{90}Sr, it might also be useful to consider that Sr compounds themselves present some risk of exposure. Excessive exposures to strontium

compounds have been associated with a form of rickets, probably as a consequence of the ability of strontium to substitute for calcium, especially in bone. However, there also are potential beneficial effects of strontium compounds, as noted earlier for osteoporosis (Marie, 2003; Meunier *et al.*, 2004) and other bone disorders (Schrooten *et al.*, 2003). The U.S. EPA RfD for strontium is 0.6 mg/kg-day (U.S. EPA, 2004), based on effects on bone development. Converting the RfD to an appropriate drinking water level, this would amount to 21 mg/L. Comparing this value with the ^{90}Sr noncarcinogenic value derived here of 4.2 x 10^{-6} mg/L (600 pCi/L converted on a mg/L basis based on the specific activity for ^{90}Sr), shows a great difference between radioactive and non-radioactive forms of strontium with regard to toxicity potential.

OTHER REGULATORY STANDARDS

As early as 1928, both the international and U.S. radiation protection communities established agencies to ensure the safe use of ionizing radiation. These agencies are now called the International Commission on Radiological Protection (ICRP) and the National Council on Radiation Protection and Measurements (NCRP).

The NCRP was chartered by the U.S. Congress to (1) disseminate information of public interest and recommend radiation levels to protect the public, (2) support cooperation among organizations concerned with radiation protection, (3) develop basic concepts about radiation protection, and (4) cooperate with the ICRP. Even though the NCRP is a nongovernmental organization, it guides the establishment of federal radiation policies, requirements, and statutes. Based on the recommendation of the NCRP, the U.S. EPA sets radiation protection policy and guidance for all of the federal governmental agencies and state cooperating radiation safety programs.

The federal government has several different agencies that regulate the safe use of radioactive material. The Nuclear Regulatory Commission (NRC) regulates commercial power reactors, research and test reactors, nuclear fuel cycle facilities, and the transport, storage, and disposal of nuclear materials and waste. The U.S. EPA regulates the individual radiation dose for the nuclear fuel cycle, the level of radionuclides emitted to the air and in drinking water, along with residual levels of radiation at uranium and thorium mills, and the release of radionuclides from high-level waste disposal facilities. The Food and Drug Administration (FDA) develops standards for equipment that emits ionizing radiation, and the Department of Transportation (DOT), in conjunction with the NRC, regulates the transport of radioactive material. All these agencies follow the recommendations of the NCRP.

Table 5 summarizes the international and national guidelines and standards pertinent to human exposure to ionizing radiation and ^{90}Sr. These include the guidelines from the ICRP and NCRP, relevant federal standards from the NRC, U.S. EPA, and the DOT. We also include current state standards applicable to Sr in drinking water (Table 6).

The U.S. EPA promulgated MCLs for ^{90}Sr and other radionuclides in community water supplies in their 1976 National Interim Primary Drinking Water Regulation. For most of the beta/photon radionuclides, the MCL was that concentration in water that yielded 4

mrem/year to the total body or any given internal organ based on the dose conversion factors at the time (NBS Handbook 69) and assuming a drinking water rate of 2 L/day. For ^{90}Sr they set a separate MCL of 8 pCi/L. This was set because the gross beta screening measurement of 50 pCi/L yielded a ^{90}S dose greater than the target risk of 4 mrem/yr.

Table 5. Relevant Radiation Protection Guidelines and Regulations (ATSDR, 2001)

Agency	Description	Guideline or Regulation
ICRP	**Guideline** dose for the protection of individuals in the general public	100 mrem/year
NCRP	**Guideline** dose for the protection of individuals in the general public	100 mrem/year
NCRP	**Guideline** dose for any individual radiation source or practice	10 mrem/year
NRC	**Regulation** for the protection of individuals in the general public	100 mrem/year (10 CFR 20)
NRC	**Regulation** for the protection of individuals in the general public from Low-level Radioactive Waste Disposal Facilities	25 mrem/year (10 CFR 61)
NRC	**Regulation** for the protection of the general public from Decommissioned Facilities	25 mrem/year (10 CFR 20)
U.S. EPA	**Regulation** for safe drinking water concentrations. Maximum Contaminant Level in community water systems – average annual concentrations assumed to produce a total body or organ dose of 4 mrem/yr ^{90}Sr. Bone is the critical organ	^{90}Sr, 8 pCi/L 4 mrem/yr (40 CFR 141)
DOT	**Regulation** for transport in normally occupied space.	2 mrem/hour (49 CFR 173)

In 1991, the U.S. EPA proposed new MCLs for all beta/photon emitters based on newer dosimetry. They based the MCLs on a 4 mrem/year effective dose equivalent using the RADRISK Computer Code and a 2 L/day drinking water rate. The proposed rule was never implemented.

In 2000, the U.S. EPA finalized their rule for drinking water. For ^{90}S the MCL remains at 8 pCi/L because updated dosimetry and risk levels yielded similar concentrations. This MCL is scheduled for review in the next two to three years for risk management issues.

Table 6. State Standards and Guidelines for Strontium-90 in Drinking Water (ATSDR, 2001)

State	Standard or Guideline	Concentration (pCi/L)
Alabama	Guideline	8
Alaska	MCL	8
California	Primary MCL	8
Colorado	Standard	8
Connecticut	Guideline	8
Florida	MCL	8
Idaho	Standard	8
Illinois	Drinking water Guideline Water quality standard.	8 1-2
Indiana	MCL	8
Maine	Guideline	2.400 µg/L
Michigan	MCL	8
New Hampshire	Guideline	8
Wisconsin	Guideline	8

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