DRAFT

For Review Only

Public Health Goal for

Radium-226 and 228

in Drinking Water

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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 (amended Health and Safety Code, Section 116365), amended 1999, requires the Office of Environmental Health Hazard Assessment (OEHHA) to perform risk assessments and publish PHGs for contaminants in drinking water based exclusively on public health considerations. Section 116365 specifies that the PHG is to be based exclusively on public health considerations without regard to cost impacts. 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 can cause chronic disease shall be based upon currently available data 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 the existence of groups in the population that are more susceptible to adverse effects of the contaminants than a normal healthy adult.
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. In cases of insufficient data to determine a level of no anticipated risk, OEHHA shall set the PHG at a level that is protective of public health with an adequate margin of safety.
7. 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.

8. The PHG may be set at zero if necessary to satisfy the requirements listed above.
9. OEHHA shall consider exposure to contaminants in media other than drinking water, including food and air and the resulting body burden.
10. PHGs published by OEHHA shall be reviewed every five years and revised as necessary based on the availability of new scientific data.

PHGs published 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, drinking water standards adopted by DHS are to consider economic factors and technical feasibility. Each standard adopted 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 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.

LIST OF CONTRIBUTORS

[added at end of review cycle]

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PUBLIC HEALTH GOAL FOR RADIUM-226 AND RADIUM-228 IN DRINKING WATER

SUMMARY

The Office of Environmental Health Hazard Assessment (OEHHA) proposes Public Health Goals (PHGs) of 0.069 pCi/L and 0.019 pCi/L for radium-226 and radium-228, respectively, in drinking water. The proposed PHGs are based on the known carcinogenic effects of radiation observed in humans. The risk estimates for these isotopes utilize the U.S. Environmental Protection Agency (U.S. EPA) report, Cancer Risk Coefficients for Environmental Exposure to Radionuclides: Federal Guidance Report 13, published in 1999. This U.S. EPA report on the relative risks of radioactive substances to humans was produced specifically to provide technical guidance to federal and state risk assessors. The report provides tabulated risk coefficients based on state-of-the-art methods and models that take into account many factors, including age, gender, competing causes of death, and the risks from water ingestion alone. The estimation of the risk coefficients (carcinogenic potencies) assumes the linear no-threshold model and is especially appropriate for estimating cancer risks at low levels of exposure to radionuclides like radium and strontium. OEHHA followed the practices recommended by U.S. EPA to calculate the proposed PHGs for radium-226 and radium-228 by applying the risk coefficients, based on carcinogenic effects observed in radium dial painters, for these radium isotopes to a lifetime of exposure to 2 L/day of drinking water. The PHG values assume a *de minimis* theoretical excess individual cancer risk level of 10^{-6} from exposure to radium.

Public health-protective concentrations for noncancer effects were calculated based on bone necrosis in a human population with less-than-lifetime exposures to radium. In this case, the primary human population used for these assessments was the former radium dial painters, whose median age was 18. Using values based on children's exposures, with a combined uncertainty factor of ten, the health-protective concentrations were estimated as 200 pCi/L for both radium-226 and radium-228. The concentrations estimated to protect against cancer (above) would also be adequate to protect against all non-cancer effects.

The U.S. EPA Maximum Contaminant Level (MCL) for radium in community water supplies, combined for radium-226 and -228, is 5 pCi/L (U.S. EPA, 1976). The California MCL, established in 1997, is also 5 pCi/L for the combined isotopes (DHS, 2004a).

INTRODUCTION

This PHG technical support document provides information on health effects from radium-226 and radium-228 (^{226}Ra, ^{228}Ra) in drinking water. PHGs are developed for contaminants based on the best available toxicological data in the scientific literature.

These documents and the analysis 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 two radioactive isotopic forms of radium. Radioactivity is produced by unstable nuclei, and isotopes of elements with this property are called radionuclides. The instability in the nucleus is manifested as the potential to decay or fall into a lower energy state by releasing principally either alpha or beta particles, or gamma rays. 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} nuclear disintegrations per second. For drinking water, the common representation of activity is the picocurie (pCi), equal to 10^{-12} Ci. Another presentation of radioactivity in the International System of Units is the becquerel (Bq), which is defined as one disintegration per second.

Energetic atoms of radionuclides release their energy either through ejection of particles or emission of electromagnetic radiation, which then interact with other atoms or matter, particularly to knock electrons out of 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 alterations in the important constituents of the cell including DNA, resulting 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. One gray 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 and rarely can penetrate the surface layers of tissues, while beta particle and gamma radiation deposit their energies over a greater range. The rem (roentgen exposed man) unit accounts for the difference in the type of radiation by multiplying the absorbed dose in rads by a quality factor. Rem can also be represented by the unit, sieverts (Sv), equaling 100 rem. 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 unit of rem-ede is an attempt to take into account the variation of physical properties of organs due to varying composition of lipid, protein, carbohydrate and water that affects their absorption properties for ionizing radiation.

The radionuclides ^{226}Ra and ^{228}Ra are naturally occurring. They are formed from the decay of the primordial radionuclides uranium-238 and thorium-232, respectively, in the earth's crust. As such, there is a small amount of ^{226}Ra and ^{228}Ra in most environmental

media including drinking water. ^{226}Ra decays by emitting an alpha particle, and ^{228}Ra decays by beta particle emissions, in both cases accompanied by gamma emissions.

The federal government has regulated the levels of ^{226}Ra and ^{228}Ra in community water supplies since the mid-1970s. The U.S. EPA promulgated Maximum Contaminant Levels (MCLs) for radium and other radionuclides in community water supplies in their 1976 National Interim Primary Drinking Water Regulation (U.S. EPA, 1976). The combined MCL for ^{226}Ra and ^{228}Ra is 5 pCi/L.

In 1991, the U.S. EPA proposed new MCLs for ^{226}Ra and ^{228}Ra at 20 pCi/L each based on newer dosimetry (U.S. EPA, 1991). The proposed rule was never implemented.

In 2000, the U.S. EPA finalized their rule for drinking water (U.S. EPA, 2000, 2002). For ^{226}Ra and ^{228}Ra the MCL remains at 5 pCi/L (combined) because updated dosimetry and risk levels yielded similar concentrations (U.S. EPA, 2004a). The U.S. EPA estimates the lifetime cancer risk at this level of radioactivity derived from radium to be 1 x 10^{-4} (U.S. EPA, 1991). However, U.S. EPA withdrew the carcinogenicity assessment for lifetime exposure calculation in the Integrated Risk Information System (IRIS) in 1991 (U.S. EPA, 2004b), pending further review by the CRAVE Agency Work Group. The IRIS Web site reports that a screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the cancer assessment for radium 226 and radium 228 conducted in September 2002 did not identify any critical new studies.

Other agencies have developed health protective levels for radium. The purpose of this document is to review the evidence on toxicity of ^{226}Ra and ^{228}Ra and to derive and propose a PHG for them in drinking water based on a *de minimis* risk level.

CHEMICAL PROFILE

Chemical Identity

Radium-226 is a naturally-occurring radioactive isotope that is formed from the decay of uranium-238, a primordial radionuclide. ^{226}Ra decays with a half-life of 1622 years to radon-222 and emits an alpha particle (an energetic helium nucleus) in the decay process. The energy of the alpha particles is 4.6 million electron volts (MeV) for approximately 6 percent of the decays and 4.78 MeV for approximately 94 percent of the decays, which is sufficient to produce ionizations and excitations of molecules in the path of the alpha particles. The average range of these alpha particles in air is about 0.5 cm and about a thousand-fold less in water and tissue. Because alpha particles impart a large amount of energy in a very short distance compared to other types of ionizing radiation (beta and photon), radium-226 poses a relatively large hazard to humans when taken internally. Table 1 summarizes some of the more important characteristics of ^{226}Ra.

Table 1. Characteristics of Radium-226

Properties	Value
Atomic number	88
Atomic mass	226
Half-life	1622 years
Decay constant	4.3×10^{-4} per year
Characteristics of alpha particle	
Energy	4.78 MeV (94%), 4.6 MeV (6%)
Average track length	0.5 cm (air)
Specific activity	0.988 Ci/g

Radium-228 is a naturally-occurring radioactive isotope that is formed from the decay of thorium-232, a primordial radionuclide. ^{228}Ra decays with a half-life of 5.7 years to actinium-228 and emits a beta particle (an energetic electron) in the decay process. The energy of the beta particles (maximum 55 kiloelectron volts (keV), average 14 keV) is sufficient to produce ionizations and excitations of molecules in their path. The average range of these beta particles in air is less than 1 μm in water. Because beta particles travel such short distances in water and tissue, ^{228}Ra poses a radiation hazard to humans when taken internally. Table 2 summarizes some of the more important characteristics of ^{228}Ra.

Table 2. Characteristics of Radium-228

Properties	Value
Atomic number	88
Atomic mass	228
Half-life	5.7 years
Decay constant	0.12 per year
Characteristics of beta particle	
Average energy	14 keV
Average track length	<1 μm (water)
Maximum energy	55 keV
Specific activity	275 Ci/g

Physical and Chemical Properties

The chemical properties of radium are similar to other alkaline earth elements, particularly barium and calcium. Radium exists in only the +2 oxidation state in solution and does not easily complex in water (Ames and Rai, 1978). The carbonate and sulfate salts of radium are very insoluble in water. The chloride, nitrate and bromide forms are soluble.

Water concentrations of radium appear to be controlled by dissolution and sorption (U.S. EPA, 1991). Sorption can remove radium from solution by adsorption and coprecipitation by scavengers such as iron hydroxide and barium sulfate. Radium is most mobile in aquifers with high concentrations of dissolved solids (Benes *et al*., 1984, 1985).

Source

Radium is a naturally–occurring silvery white radioactive metal (atomic number 88) that is formed from the radioactive decay of uranium and thorium. It can exist in several isotopes, radium-226 (^{226}Ra), radium-228 (^{228}Ra), radium-224 (^{224}Ra), and radium-223 (^{223}Ra). ^{226}Ra and ^{228}Ra are the isotopes of primary environmental concern, because their half-lives are long enough to promote substantial environmental accumulation. The half-life of ^{226}Ra is about 1,600 years, and the half-life for ^{228}Ra is about 6 years. ^{226}Ra is part of the uranium-238 decay series and decays to radon-222 by alpha particle emission. ^{228}Ra is a progeny of thorium-232 and decays to actinium-228 by emitting a beta particle.

ENVIRONMENTAL OCCURRENCE AND HUMAN EXPOSURE

Radium is nearly ubiquitous at low concentrations in air, water, soil, rock, and food. The median concentrations of ^{226}Ra and ^{228}Ra in drinking water are generally low, but there are regions where higher concentrations are known to occur. The mining of coal and uranium ore and their use in energy production has resulted in the redistribution of radium in the environment, but the overall effect appears small.

Air

Radium is present in the air at extremely low levels. The U.S. EPA reported outdoor concentrations of about 1.5×10^{-5} pCi ^{226}Ra /m^3 and 2.3×10^{-3} pCi ^{228}Ra /m^3 (U.S. EPA, 1991). Dust samples collected from the atmosphere of New York City were found to contain ^{226}Ra at 8×10^{-5} pCi/m^3 (3.0×10^{-6} Bq/m^3) and ^{228}Ra at 1.5×10^{-4} pCi/m^3 (5.6×10^{-6} Bq/m^3) (ATSDR, 1990).

Soil

Radium-226 and Radium-228 can be found in soil throughout the country. Myrick *et al*. (1981) reported the mean concentration of ^{226}Ra in 356 surface soil samples collected

from 33 states was 1.1 pCi/g (0.041 Bq/g). This mean concentration is very similar to those for ^{226}Ra reported by Eisenbud (1973) for typical igneous rock, 1.3 pCi/g (0.048 Bq/g). Concentrations by rock type included the following:

- Sandstone, 0.71 pCi/g (0.026 Bq/g)
- Limestone, 0.42 pCi/g (0.016 Bq/g)
- Shale, 1.1 pCi/g (0.41 Bq/g)

Coal burning and uranium mining/milling operations have produced elevated levels of radium in soil. Deposition of coal fly ash has caused levels of ^{226}Ra to be as high as 8.1 pCi/g in industrial areas (U.S. EPA, 1990). Kalin (1988), Landa (1984), and Tracy *et al*. (1983) reported the concentration of ^{226}Ra in soils that were contaminated by mining and milling activities to range from 1 to 37,000 pCi/g (0.037 to 137 Bq/g).

Using uranium concentrations as an indicator of radium levels, national radioactivity surveys indicate that elevated radium levels in soil are expected in the Western third of the continental U.S., including large areas of California and Idaho (ATSDR, 1990). In addition, these surveys predict elevated levels of radium in Wisconsin, Minnesota, the Appalachian Mountains, and Florida.

Water

Various studies investigated the occurrence of radium in ground, surface, and treated drinking water (Aieta *et al*., 1987; Cech *et al*., 1988; U.S. EPA, 1985; Hess *et al*., 1985; Longtin, 1988; Lucas, 1985; Michel and Cothern, 1986; USGS, 1998; Watson *et al*., 1884). In general, shallow groundwater has less radium than deep aquifers, and treated water has less radium than raw groundwater. The radium content of surface water is usually very low, lower than most groundwater supplies.

Radium-226, a progeny of U-238, is more commonly found in groundwater than ^{228}Ra a progeny of thorium-232 because uranium has a relatively higher solubility than thorium. The geochemical properties of ^{226}Ra differ from those of U-238, and co-occurrence is not common (USGS, 1998) because the degree and chemical conditions of mobilization of the parent and progeny are different.

The most extensive region in the nation where ^{226}Ra occurs in elevated concentrations in groundwater is in north central states including Minnesota, Wisconsin, Illinois, Iowa, and Missouri (USGS, 1998). In these states, drinking water is drawn from deep aquifers that tend to have limited sorption sites, and radium solubility is enhanced by the ionic effect of high dissolved solids.

Radium-226 is also found at high levels in water derived from aquifers in the east from New Jersey to Georgia (USGS, 1998). These aquifers are composed of unconsolidated sand that contain uranium-bearing minerals. This sand also tends to have limited sorption capacity, enhancing the solubility of radium.

Although ^{228}Ra is chemically similar to ^{226}Ra, its distribution in groundwater is very different for several reasons. The relatively short half-life of ^{228}Ra limits the potential for transport without the parent being present. Consequently, ^{228}Ra cannot migrate far from

its source before it decays to another progeny. Thorium-232, the parent of ^{228}Ra, is extremely insoluble and is not subject to mobilization in most groundwater environments (USGS, 1998). The insolubility of thorium (unlike uranium) limits the distribution of ^{228}Ra in groundwater. Areas associated with the presence of ^{228}Ra include the East coastal plain and high plains aquifers.

Several nation-wide surveys measured the levels of ^{226}Ra and ^{228}Ra in the nation's drinking water supply (U.S. EPA, 1986, 1988, 1997; Longtin, 1988; and USGS, 1998). The U.S. EPA considers the National Inorganics and Radionuclide Survey (NIRS, U.S. EPA, 1988), performed by the Office of Drinking Water, to be the most suitable for deriving estimates of national radium concentrations in drinking water (U.S. EPA, 1990). Table 3 below summarizes the findings of the NIRS.

Table 3. Summary of Radium Concentrations (pCi/L) Measured in Drinking Water in the National Inorganics and Radionuclide Survey (NIRS) (U.S. EPA, 1988)

Radionuclide	Mean	Maximum	Number of Samples
^{226}Ra	0.4	15	990
^{228}Ra	0.7	12	990

Most recently, the U.S. Geological Survey (USGS) performed a reconnaissance survey to provide additional information concerning radium in drinking water. This survey was designed to assess the co-occurrence of the different radium isotopes in the nation's drinking water supply (USGS, 1998). They found poor correlation between the concentrations of ^{226}Ra and ^{228}Ra, but co-occurrence is common, as described below for 525 out of 707 water sources in California. Table 4 below summaries the radium concentrations measured by the USGS reconnaissance survey.

Table 4. Summary of Radium Concentrations (pCi/L) in Drinking Water from the USGS Reconnaissance Survey (USGS, 1998)

Radionuclide	Mean	Median	Standard Deviation	Maximum	Number of samples
^{226}Ra	1.6	0.4	2.8	16.9	99
^{228}Ra	2.1	0.5	7.9	72.3	99

The State of California has measured over 19,600 public drinking water sources from 1984 to 2000 for various radioactive contaminants. ^{226}Ra and ^{228}Ra were detected in only about ten percent of the water sources, presumably those that were judged to have the most potential for significant contamination. Radium-226 was found in 427 of the 1,369 sampled sources, ^{228}Ra in 146 of the 571 sampled sources, and ^{226}Ra + ^{228}Ra 8 (specific radioactivity not distinguished) in 525 out of 707 sampled sources (DHS, 2004a). The

MCL of 5 pCi/L was exceeded 100 times in this time period (1984 to 2000) (DHS, 2004b). For 2001, there were four wells with a level of radium-228 that exceeded the MCL while only one well was found with a radium-226 level greater than the MCL (DHS, 2004c).

Food

Radium occurs in many different foods, and the reported concentrations vary considerably. Eisenbud (1973) estimated the mean ^{226}Ra content of diets in 11 U.S. cities to be between 0.52 to 0.73 pCi/kg (0.019 to 0.027 Bq/kg). Watson *et al*. (1984) estimated the mean concentrations of ^{226}Ra in milk and beef to be about 0.23 pCi/L and 0.22 pCi/kg, respectively.

The U.S. EPA reported that eggs, pasta, bread and other bakery products, and potatoes are the major source of ^{226}Ra in the diet (U.S. EPA, 1991). They estimated the average adult dietary intake of ^{226}Ra and ^{228}Ra to be between 1 and 2 pCi/day, and that drinking water supplies would contribute less than 50 percent of the total intake.

The National Council on Radiation Protection and Measurements (NCRP) found a similar pattern in intake levels of ^{226}Ra and ^{228}Ra for three U.S. cities, where dietary intake was greater from food sources than from water (NCRP, 1975). Their results are summarized in Table 5. The low levels of radium in drinking water in these three cases may be related to derivation of drinking water from surface sources rather than groundwater.

Table 5. Estimates of Total Dietary Intake (pCi/d) of ^{226}Ra and ^{228}Ra (NCRP, 1975).

	^{226}Ra			^{228}Ra	
	New York	**San Francisco**	**San Juan**	**New York**	**San Francisco**
Cereals and grain products	0.56	0.39	0.14	0.42	0.37
Meat, fish, eggs	0.46	0.07	0.01	0.14	0.08
Milk and dairy products	0.14	0.05	0.02	0.05	0.10
Green vegetables and fruits	0.54	0.24	0.53	0.44	0.38
Root vegetables	0.06	0.04	-	0.12	0.08
Water	0.02	0.03	0.01		
Total	1.8	0.8	0.7	1.2	1.0

METABOLISM AND PHARMACOKINETICS

In the United States, 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, 2000), and these models are described in a series of documents published between 1989 and 1996 (ICRP, 1989, 1993, 1995ab, 1996). We used the metabolic and pharmacokinetic information in these ICRP documents to summarize what is known about the absorption, distribution, and excretion of radium.

Absorption

The ICRP estimated that gastrointestinal absorption of radium is about 15-21 percent of the ingested amount based on data for whole body ^{226}Ra in adult humans who drank water high in ^{226}Ra for extended periods or ingested ^{226}Ra incorporated in food (ICRP, 1993). Normal elderly human subjects that ingested mock radium dial paint containing ^{224}Ra absorbed approximately 20 percent of ingested radium as an average (Maletskos *et al*., 1966, 1969). In a study in which an adult human male took 0.05 mg radium by mouth on two occasions, an estimated 25 to 35 percent of the ingested amount remained in the body at 5-6 days (Siel, 1915). In rats, fasting for 18 hours increased absorption of radium in young adult males (Taylor, 1962). For radium, the ICRP adopted a gut to blood transfer factor value (f_1) of 0.2 for adults (ICRP, 1993).

There is considerable evidence of elevated gastrointestinal absorption of the alkaline earth elements by both laboratory animals and humans during periods of rapid growth, but there is relatively little radium-specific information (ICRP, 1993). Scientists report results that suggest that dietary ^{226}Ra is transferred to the bone at a higher rate during periods of rapid growth than during adulthood or periods of slow growth (Muth and Globel, 1983). Taylor *et al*. (1962) estimated that radium absorption in suckling rats was 79 percent, and absorption in young adult and old rats was 11 percent and 3 percent, respectively. Data from a beagle study suggest considerably greater radium absorption in immature individuals (Della Rosa *et al*., 1967). Because of this information and information from other alkaline earth elements, particularly strontium, the ICRP recommend f_1 values of 0.6 for infants and 0.3 for ages 1-15 (ICRP, 1993).

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, 2000). 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 absorption to the blood occurs only in the small intestine.

Absorption of radium after inhalation exposure has also been reported. Marinelli *et al.* (1953) found radium deposited both in the lungs and the skeleton of individuals who were exposed to radium following the accidental rupture of capsules containing radium sulfate (presumed to be primarily ^{226}radium). However, it is not clear if the radium that entered the systemic circulation was due to inhalation of the material or due to the coughing up of inhaled radium followed by ingestion.

Metabolism

Radium is an element and cannot be metabolized (ASTDR, 1990). Radium salts that are deposited in a biological system will dissociate based on their solubility in that media. Over time, the radium cation will decay.

Distribution

The ICRP summarized the extensive literature on the distribution and retention of radium in adult humans (ICRP, 1993). Briefly, radium absorbed to blood from the GI tract or lungs follows the behavior of calcium, although the rate of movement between plasma, bone, and soft tissue, and excretion rates differs between radium and calcium. Following oral exposure, a large fraction (about 80 percent) of absorbed radium leaves the blood and passes into the intestines, and is excreted with the feces (ASTDR, 1990). Secretion into the GI tract is much greater for humans than laboratory animals. Radium deposits in the bone substantially more than in the soft tissue. Much of the radium deposited in the bone is returned to the plasma within a few weeks, but a fraction (initially around 16 percent) is retained and moves out of the bone more slowly, probably due to bone remodeling (ASTDR, 1990). In mature humans, skeletal retention of radium may decrease to less than 10 percent of injected levels after a month. After 25 years, skeletal retention decreases to about 1 percent. Limited data on humans suggests that soft tissue radium may represent about 20 percent of the total radium body burden during the first several weeks after exposure but represents a much smaller fraction after a longer time.

A limited amount of information on the biokinetics of radium in immature humans is available (ICRP, 1993). These data are supplemented with age-specific data from laboratory animals. The ICRP used data from beagles combined with the human information to make estimates of the distribution and retention of radium in children (ICRP, 1993). These data indicate that radium is retained to a greater degree in children because the skeleton is growing. The radium burden in bone acquired during periods of growth tends to remain higher than the burden acquired by mature bone. Both deposition and removal of radium appear to be greater in areas of bone undergoing rapid remodeling. Greater deposition in the young skeleton causes less systemic radium available for excretion and soft tissue uptake.

Excretion

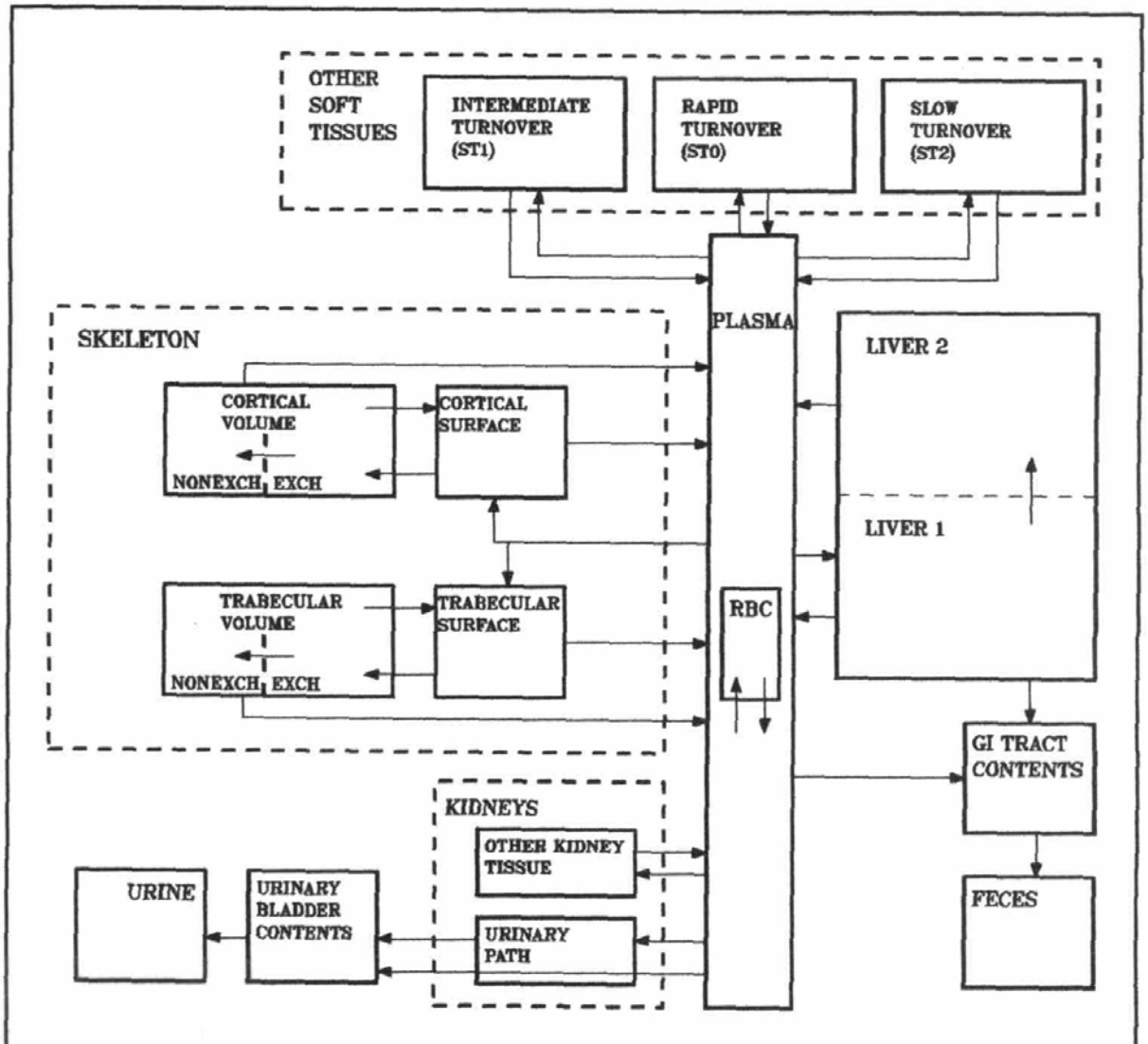
Excretion of radium from the human body occurs in two phases following oral, inhaled, or injected exposures (ASTDR, 1990). For all routes, the majority of the excretion is through feces. Maletskos *et al*. (1966, 1969) found approximately 80 percent of ingested radium was rapidly eliminated through the feces. In the second phase, most of the remaining 20 percent was excreted more slowly in the feces. Fecal to urinary ratios were reported to be 30-to-1 for intravenous exposure and 10-to-1 for subcutaneous exposure (Maletskos *et al*., 1966, 1969).

The radium systemic biokinetic model is described in ICRP Publication 67 (1993). It 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. Figure 1 shows a schematic of the systemic model. Table 6 summarizes the age-specific transfer and excretion rates, and f_1 values used by the ICRP.

Table 6. Selected Age Specific Transfer Rates (day^{-1}) for the ICRP's Radium Biokinetic Model (ICRP, 1993)

	AGE					
	3 mo	**1 y**	**5 y**	**10 y**	**15 y**	**Adult**
Plasma to urinary bladder	0.202	0.444	0.488	0.355	0.210	0.606
Plasma to upper large intestine	7.26	16.0	17.43	12.78	7.55	21.79
Plasma to trabecular bone surface	10.5	6.3	6.22	9.88	14.45	9.72
Plasma to cortical bone surface	42.0	25.2	21.78	29.32	37.35	7.78
Plasma to liver	0.117	0.257	0.280	0.205	0.121	0.350
Plasma to soft tissue 0	7.56	16.63	18.14	13.31	7.86	22.68
Plasma to soft tissue 1	2.33	5.13	5.60	4.11	2.43	7.00
Bone surface to plasma	0.578	0.578	0.578	0.578	0.578	0.578
Bone surface to bone volume exchange	0.116	0.116	0.116	0.116	0.116	0.116
Trabecular and cortical bone volume to plasma	0.00822	0.00822	0.00822	0.00822	0.00822	0.00822
Soft tissue 0 to plasma	2.52	5.54	6.05	4.44	2.62	7.56
Soft tissue 1 to plasma	0.693	0.693	0.693	0.693	0.693	0.693
F_1	0.6	0.3	0.3	0.3	0.3	0.2

Figure 1. ICRP's Radium Systemic Biokinetic Model



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.

Mechanism of Action

Upon internalization of either radionuclide (^{226}Ra and ^{228}Ra), the decay process for both radionuclides releases enough energy to produce ionizations and excitations of molecules in their path. However, radium absorbed to blood from the GI-tract or lungs follows the behavior of calcium and is primarily deposited in bone. The radium burden in bone acquired during periods of growth tends to remain higher than the burden acquired by mature bone. Both deposition and removal of radium appear to be greater in areas of bone undergoing rapid remodeling.

Although the two radionuclides have similar distribution and absorption characteristics, the energy released during decay is distinct. Radium-226 has a higher energy and the emission products travel a larger distance than radium-228. These differences lead to differences in toxic potency for the two radionuclides.

In general, radiation ionizes cellular atoms and molecules (i.e., DNA) via direct or indirect actions. Direct ionization of DNA involves partial or complete energy transfer to one or more electrons on the molecule while indirect pathways may involve formation of toxic products such as free radicals, hydrogen peroxide, hydroperoxy radicals that can diffuse from the site of formation and interact with their surroundings (ASTDR, 1999). An ionizing event may have several outcomes: no damage if the ionized molecule reforms immediately; damage is repaired with no clinical effects; or the alterations lead to a wide range of biological responses including carcinogenic and non-carcinogenic endpoints (ATSDR, 1999).

TOXICOLOGY

Toxicological Effects in Animals and Plants

In general, the acute adverse effects of radium are believed to be a consequence of the radiation emitted from the radionuclide itself and its progeny. Because there is already a considerable amount of information on the acute effects of radiation on humans derived from studies on the effects of the atomic bomb survivors and therapeutic uses of radiation, the effects observed following exposure to radium and its progeny are described in more detail in the Toxicological Effects in Humans section of this document. The experimental animal studies conducted with radium do not duplicate the human effects. The experimental animal studies have instead concentrated on radium's most sensitive endpoint, cancer (ATSDR, 1990). Animal studies include acute and chronic exposures in dogs and rodents. The adverse effects include death, hematological, bone and kidney damage, immunological and developmental effects, and cancer.

Acute Toxicity

In 1914, Proescher and Almquest (ASTDR, 1990) observed fatalities within 7 to 10 days in mice injected with radium (presumably radium-226) at 2,000 to 4,000 μCi/kg. No other information was provided. Larkin (1930) reported decreased body weights,

hematological changes, marked degenerative changes in bone marrow and spleen, and damage to liver, kidney, and thymus gland in rabbits exposed to 15 and 200 mg of radium. Death occurred within 18 days of treatment, averaging 17 days after the start of exposure.

Similar findings were reported by Whitman (1933), who reported decreased white blood cells and decreased body weights in Wistar rats exposed to highly filtered gamma rays from radium. Rats were exposed to 6 g or less of radium filtered through 1 mm platinum, 1 mm brass, 16 mm lead, and 5 mm celluloid. Exposure times varied from 0.5 minute to 17 hours (hr) in geometrical progression. The lethal exposure to radium with filters was between three hr and six hr.

Other investigators have also reported hematological effects in mice (Schoeters and Vanderborght, 1981; Schoeters *et al*., 1983) and ocular effects in dogs following injections of ^{226}radium (Taylor *et al*., 1972). In mice, a depression of hemopoietic cells was reported following intraperitoneal injections of 17,820 or 22,320 μCi/kg (660,000 or 827,00 kBq/kg). Taylor *et al*. (1972) reported loss of pigment and melanosis and intraocular melanoma formation in dogs following intravenous administration of radium-226 at doses of 0.062 to1.1 μCi/kg (2.3 to 41 kBq/kg).

Subchronic Toxicity

Because there is already a considerable amount of information on the subchronic effects of radiation on humans derived from studies on the effects of the therapeutic uses of radiation and dial painters, the subchronic effects observed following exposure to radium and its progeny are described in more detail in the Subchronic Toxicity section of the Toxicological Effects in Humans portion of this document.

Genetic Toxicity

No studies were located regarding genotoxic effects of radium in animals. However, three reports were found in which the genotoxicity of radium is described. The data are reported in the Genotoxicity section of the Toxicological Effects in Humans. In addition, it should be noted that ATSDR considers ionizing radiation a mutagen (ATSDR, 1997).

Developmental and Reproductive Toxicity

Whitman (1933) reported reproductive and developmental effects in Wistar rats exposed to highly filtered gamma rays from radium. Rats were exposed to 6 g or less of radium filtered through 1 mm platinum, 1 mm brass, 16 mm lead, and 5 mm celluloid. Exposure times varied from 0.5 minute to 17 hr in geometrical progression. Radiation exposure of immature females caused delayed opening of the vagina. In the progeny of the rats exposed 30 minutes or more, seven abnormalities (absence or reduced size of eye, shortened tail) occurred in 160 offspring. With rats exposed 20 minutes or less, one abnormal rat occurred in 91 offspring. In 300 offspring of normal controls, one abnormal rat occurred.

Immunotoxicity

No studies were located regarding immunotoxicological effects of radium in animals.

Neurotoxicity

No studies were located regarding neurotoxic effects of radium in animals.

Chronic Toxicity and Carcinogenicity

Most studies with experimental animals (primarily Beagle dogs) following injection of radium have investigated effects on bone, due to the preferential accumulation and long-term retention of radium in the skeleton. Scientists demonstrated these effects with ^{224}Ra, ^{226}Ra 26 and ^{228}Ra. Effects on bone shortly after injection include changes in bone structure (Jee *et al*., 1969; Momeni *et al*., 1976) or hematopoiesis (Schoeters and Vanderborght, 1981). Doses used in these studies varied from 2.3 kBq/kg to above 24,800 kBq/kg. When animals are followed for a considerably longer portion of their lifetimes, bone sarcomas were found in all species tested (ATSDR, 1990; Raabe *et al*., 1981; Humphreys *et al.*, 1985; Mays *et al*., 1987). Studies also report tumors after a single injection of radium (Taylor, 1983; Kofranek *et al*., 1985). Leukemias or lymphomas have been reported following injection, but the occurrence peaks at low doses (8-16 kBq of ^{224}Ra), lower than the doses (64 kBq of ^{224}Ra) that cause osteosarcomas (Humphreys *et al.*, 1985; Muller *et al*., 1988). The results of the animal studies confirm the association of bone necrosis and bone sarcomas with radium exposures in humans, and provide support for an approximately linear relationship between dose and the incidence of bone cancer (Wrenn *et al.*, 1985; Mays *et al*., 1987).

Toxicological Effects in Humans

The principal data concerning human effects of exposure to radium come from epidemiological studies of workers, mainly women, employed as radium dial painters. The luminizing industry used radium-containing paint to make watch dials with numerals that would glow in the dark. Prior to the mid-1920s, little attention was paid to limiting radium exposure of workers. A common practice was sharpening the tip of the paint-laden brush by twisting it in the corner of the mouth, which led to considerable ingestion of paint among many workers. Occupational exposure in the dial industry continued after 1930 but at substantially lower levels.

Acute Toxicity

No studies were located regarding the acute toxicological effects of radium in humans. Many of the effects described in the literature as the result to radium exposure occur due to long-term exposures. In some cases, although the exposure may have been acute, the reported effects observed were considered long-term due to the long half-life of the

radionuclides and poor elimination of the biologically active radionuclide (ATSDR, 1997).

Subchronic Toxicity

Keane *et al*. (1983) investigated bone changes in young radium dial workers (median age of 18 years) compared to matching controls with no radium exposure. The subjects in this study ingested radium over a very short time period (about a year). Because of the dosimetry of radium (preferential concentration in the bone and long-term radioactive decay), the effects of the ingested amount are thought to be relatively independent of the time-course of exposure (U.S. EPA, 1991). They expressed radium exposure as intake to blood in μCi of ^{226}Ra and ^{228}Ra. Bone changes expressed as foci of necrosis were evaluated by examination of x-ray radiographs of exposed and control women. Keane *et al*. (1983) found that below 10 μCi intake of either isotope for a period of 1.39 or 1.12 years (mean duration of radium intake for ^{226}Ra and ^{228}Ra, respectively), the severity and frequency of bone changes was not statistically different between the exposed and control groups. They also found that below 100 μCi total intake, all changes were mild. Since radiographs are not sensitive to histological changes in bone, and Keane *et al*. (1983) did not investigate possible effects on bone growth, healing, or homeostasis. The U.S. EPA considers the detected lesions to be an adverse effect (U.S. EPA, 1991).

The U.S. EPA used the Keane *et al*. (1983) study to calculate a non-cancer No Observed Adverse Effect Level (NOAEL). Keane *et al*. (1983) found that bone changes were not significantly different from the controls below a total intake to the blood of 10 μCi of either ^{226}Ra or ^{228}Ra. In agreement with the U.S. EPA, OEHHA used 10 μCi as the initial NOAEL to calculate the final NOAEL. In order to derive a NOAEL in units of μCi/kg–day, OEHHA assumed that bone necrosis was a function of radium intake adjusted for body weight and duration of radium intake. For ^{226}Ra, the derived NOAEL would be 3.37×10^{-4} μCi/kg-day [10 μCi/(60 kg x 496 days)]. In the case of ^{228}Ra, the derived NOAEL would be 4.08×10^{-4} μCi/kg-day. These derived NOAELs were used to calculate the health-protective concentration.

Mays *et al*. (1985) briefly discussed non-malignant disease observed at increased incidence in patients injected with ^{224}Ra. These diseases included benign bone growths, severe growth retardation in children, tooth breakage, kidney and liver disease, and cataracts. No dose-response information was given for these effects, but the average injected dose was approximately 300 μCi.

Genetic Toxicity

Three studies show that radium causes mutagenic effects in humans. Muller *et al*. (1966) examined bone marrow cells from 5 controls and 16 individuals exposed to ^{226}Ra and/or Sr-90. Exposed individuals had significantly greater incidence of aneuploid cells and cells with chromosomal aberrations. Boyd *et al*. (1966) found a significantly greater incidence of chromosomal aberrations in the chromosomes of peripheral lymphocytes of 62 radium dial painters containing radium ranging from non-measurable to 0.56

microcurie of ^{226}Ra, compared to 57 control individuals. This incidence was also dose related. Hoegerman *et al*. (1973) found a weak positive correlation between radium body burden and the frequency of chromosomal aberrations in 19 dial painters with similar body burdens.

Developmental and Reproductive Toxicity

Two studies on radium dial painters suggest possible reproductive and developmental effects. Polednak (1980) investigated the fertility of female radium dial painters with measured radium body burdens. He found that the live birth rate was significantly lower for women with ovarian doses above 20 rem compared to doses below 20 rem. This decrease was complicated by the fact that confounding factors like contraceptive practices were not accounted for or controlled. Sharpe (1974) reported the case histories of 42 workers in the radium dial industry. His comparison showed a decreased number of children born to women exposed to radium. He also reported birth defects for a child born to one woman exposed to radium. The number of cases, however, was too small to attribute these effects to radium exposure.

Immunotoxicity

No studies were located regarding immunotoxicity effects of radium in humans.

Neurotoxicity

No studies were located regarding neurotoxicity effects of radium in humans.

Chronic Toxicity

Fatal cases of jaw necrosis and aplastic anemia among women employed as dial painters were an early indication of the hazards associated with ^{226}Ra and ^{228}Ra ingestion (Martland, 1931). From 1922 to 1928, 12 deaths occurred due to these causes among dial painters and chemists employed in the dial painting industry in New Jersey. Keane *et al.* (1983) adequately characterized a dose-response relationship in humans for bone necrosis. In addition, other non-cancer effects in humans have been reported with higher doses of radium exposure (Rundo *et al*., 1986). Rundo *et al.* (1986) estimated that the lowest total intake level of radium associated with a malignancy was 60 μCi or 1.03 μCi/kg based on women of 58 kg body weight.

Carcinogenicity

Scientists have long recognized that two types of cancer with very low spontaneous rates, bone sarcomas and head sarcomas, were elevated in exposed dial workers (U.S. EPA, 1991). Our discussion focuses on studies that made quantitative evaluations of the incidence of tumors as a function of ingested dose.

Rundo *et al*. (1986) reported the rate of bone and head sarcomas to be significantly higher for radium dial painters. They identified a total of 64 bone sarcomas and 24 head sarcomas in a cohort of 4,032 radium dial painters compared to matched controls.

Rowland *et al*. (1978) evaluated a cohort of almost 800 female dial workers. They found 38 bone sarcomas and 17 head sarcomas with incidence rates ranging from about 1 to 37 sarcomas per 1,000 person years at risk. The highest incidence was above 1,000 μCi ^{226}Ra + 2.5 μCi ^{228}Ra. No sarcomas were found in the groups exposed to less than 100 μCi ^{226}Ra. Spontaneous incidence rates for these two types of sarcomas are less than one case for a cohort of this size.

In a later study of a subgroup of dial painters, Rowland *et al*. (1983) reported bone sarcoma rates as high as 46 sarcomas per 1,000 person years at risk. They observed the higher rates between 500 and 2500 μCi of ^{226}Ra intake.

Rowland *et al*. (1978) concluded that a microcurie of ^{228}Ra was about two times as effective at producing bone sarcomas as a microcurie of ^{226}Ra. In addition, they demonstrated that the incidence of head carcinomas was associated only with ^{226}Ra exposure, not with exposure to ^{228}Ra. The National Academy of Sciences (NAS) explained this association by the accumulation of radon gas in the mastoid air cells and paranasal sinuses (NAS, 1988). Both ^{226}Ra and ^{228}Ra have radon decay products, but the half-life of ^{220}Rn, the progeny of ^{228}Ra, is only about 50 seconds, too short for substantial diffusion to air cells in the skull to take place.

No conclusive evidence has been found for statistically significant increases in cancer other than bone sarcomas and head carcinomas in dial painters (U.S. EPA, 1991). Marginal increases in breast cancer, multiple myeloma, and leukemia have been noted. The lack of increased leukemia incidence is unexpected, because the accumulation of radium in the bone would be expected to provide substantial irradiation to potentially leukemogenic cells (Mays *et al*., 1985). Possible explanations for the lack of increased leukemia incidence may be non-uniformity of irradiation, lethality in target cells, low frequency of target cells in irradiated regions, or an overestimation of leukemia risk coefficients (U.S. EPA, 1991).

Petersen *et al*. (1966) studied mortality statistics of almost one million people in rural communities of Iowa and Illinois who had an average of 4.7 pCi/L of ^{226}Ra in their drinking water. Compared to controls, fatalities from bone malignancies were marginally elevated.

Bean *et al*. (1982) studied residents of small communities in Iowa and found increased incidence for four cancers. This increase was correlated with increasing radium content in the water supplies. These cancers included bladder and lung cancer in males, and breast and lung cancer in females. These findings are weakened by the facts that correlations with indoor radon levels could not be ruled out, and these cancers were not observed in dial painters (NAS, 1988).

Lyman *et al*. (1985) investigated the correlation between radium content of groundwater and leukemia incidence in Florida. They found a small but consistent excess of leukemia in high-exposure areas, but no evidence of a dose-response. The rank correlation coefficients of 0.56 and 0.45 were observed between the radium contamination level and

the incidence of total leukemia and acute myeloid leukemia, respectively. Again, the significance of these results is questioned because increased incidence of leukemia has not been observed in dial painters (U.S. EPA, 1991).

DOSE-RESPONSE ASSESSMENT

Noncarcinogenic Effects

OEHHA found that the only health effect of radium ingestion with an adequately characterized dose-response relationship in humans was bone necrosis, in a study by Keane *et al*. (1983). Other non-cancer effects in humans have been reported at higher doses (Rundo *et al*., 1986). The U.S. EPA also considers agents emitting ionizing radiation to be mutagens and teratogens. Several other studies have confirmed that radium causes bone necrosis using animal studies (Taylor *et al*., 1976; Jee *et al*., 1969; and Momeni *et al*., 1976). The NOAELs derived from the Keane *et al*. (1983) study were based on the assumption that bone necrosis was a function of radium intake adjusted for body weight and duration of radium intake. With these assumptions, the derived NOAELS used in our calculations of the health-protective concentration were 3.37×10^{-4} μCi/kg-day (337 pCi/kg-day) for ^{226}Ra and 4.08×10^{-4} μCi/kg-day (408 pCi/kg-day) for ^{228}Ra. See calculations below.

Carcinogenic Effects

The U.S. EPA classifies all emitters of ionizing radiation as Group A carcinogens based on sufficient epidemiological evidence (U.S. EPA, 1999). There is strong human evidence that the ingestion of ^{226}Ra and ^{228}Ra caused bone and head cancers in radium dial painters (Mays *et al*., 1985; NAS, 1988). Patients injected with known amounts of ^{224}Ra had increased risk of developing bone sarcomas (NAS, 1988). The dose-response from both the dial painters and the injected patients was linear (NAS, 1988). In 1994 the U.S. EPA estimated the radiogenic cancer risks from ionizing radiation and calculated the overall mortality and morbidity risk to be about 5.1×10^{-4} and 7.6×10^{-4} per rad, respectively (U.S. EPA, 1994).

More recently, the U.S. EPA developed carcinogenic potencies or risk coefficients for almost all radionuclides including ^{226}Ra and ^{228}Ra. These risk coefficients are listed in U.S. EPA's Federal Guidance Report No. 13 (U.S. EPA, 1999). These 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 at each age (from the first step) are used to convert the calculated absorbed dose rates to lifetime cancer risks for 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 divided 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 it 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 ^{226}Ra and ^{228}Ra are listed in Table 7 below for the water ingestion exposure route (U.S. EPA, 1999) in both units of Bq^{-1} and pCi^{-1}.

Table 7. Drinking Water Risk Coefficients for ^{226}Ra and ^{228}Ra

Radionuclide	Risk Coefficient [1] (Bq^{-1})		Risk Coefficient [2] (pCi^{-1})	
	Mortality	Morbidity	Mortality	Morbidity
^{226}Ra	5.32×10^{-9}	7.75×10^{-9}	1.97×10^{-10}	2.87×10^{-10}
^{228}Ra	2.00×10^{-8}	2.81×10^{-8}	7.40×10^{-10}	1.04×10^{-9}

[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 reflects 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, as reported by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) (UNSCEAR, 1994; NCRP, 2001).

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 a hormesis interpretation of the radiation epidemiological literature. They conclude 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 in 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 carcinogens or non-carcinogens 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

Non-carcinogenic effects due to radium have been characterized since 1922. Fatal cases of jaw necrosis and aplastic anemia among women employed as dial painters were reported by Martland (1931). Keane *et al.* (1983) characterized the dose-response relationship in humans for bone necrosis following radium exposure. Furthermore, bone necrosis has also been reported to occur in animals following exposure to radium (Taylor *et al.*, 1976; Jee *et al.*, 1969; and Momeni *et al.*, 1976). The NOAELs based on the Keane *et al*. (1983) study were used to calculate the proposed health-protective concentrations below for radium–226 and radium–228. An uncertainty factor of 3 was applied in the calculation to correct for less than lifetime exposure since the data were obtained from individuals exposed for less than 2 years. In addition, an uncertainty factor of 3 was used to account for interindividual variability in the diverse California population. A larger uncertainty factor was not used for interindividual variability since the data were obtained from a population whose median age was 18 years; already a sensitive population for bone necrosis. We calculated the public-health protective concentration (C) for non-carcinogenic endpoints using the equation:

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

where:

NOAEL	=	derived No Observable Adverse Effect Levels are 337 pCi/kg-day ^{226}Ra and 408 pCi/kg-day for ^{228}Ra;
BW	=	adult body weight of 70 kg, or 10 kg for a child;
RSC	=	relative source contribution of 0.5, based on the estimated contribution from foods compared to drinking water;
UF	=	combined uncertainty factor (3 to account for individual differences in sensitivity to radium toxicity and 3 for non-lifetime exposure, multiplied to equal 10 based on the convention that the two values of 3 each represent half of 10 on a logarithmic scale);
WC	=	drinking water ingestion rate for an adult of 2 L/day and a child of 1 L/day.

For a child, the calculated health-protective concentration for the two radionuclides would be as follows:

$$C = \frac{337 \text{ pCi/kg-day} \times 10 \text{ kg} \times 0.5}{10 \times 1 \text{ L/day}} = 170 \text{ pCi/L for } ^{226}Ra$$

$$C = \frac{408 \text{ pCi/kg-day} \times 10 \text{ kg} \times 0.5}{10 \times 1 \text{ L/day}} = 200 \text{ pCi/L for } ^{228}Ra$$

For an adult, the calculated health-protective concentration for the two radionuclides would be as follows:

$$C = \frac{337 \text{ pCi/kg-day} \times 70 \text{ kg} \times 0.5}{10 \times 2 \text{ L/day}} = 590 \text{ pCi/L for } ^{226}Ra$$

$$C = \frac{408 \text{ pCi/kg-day} \times 70 \text{ kg} \times 0.5}{10 \times 2 \text{ L/day}} = 710 \text{ pCi/L for } ^{228}Ra$$

Table 8 lists the calculated health-protective concentrations (C) for the two radionuclides and ages, based on non-cancer effects. Additionally, the public health protective concentrations are expressed in pg/L for comparative purposes. This value is obtained by dividing the calculated health-protective concentration in μCi/L by the specific activity

for each radionuclide (i.e., 0.988 pCi/pg and 275 pCi/pg for ^{226}Ra and ^{228}Ra, respectively).

Table 8. Health-Protective Concentrations for Non-cancer Effects of ^{226}Ra and ^{228}Ra

Radionuclide	Health Protective Concentrations			
	Child		Adult	
	pCi/L	pg/L	pCi/L	pg/L
^{226}Ra	170	170	590	600
^{228}Ra	200	0.75	710	2.6

We conclude that appropriate concentrations to protect against non-cancer effects of these isotopes are 200 pCi/L of either isotope, corresponding to 200 pg/L of ^{226}Ra and 1 pg/L of ^{228}Ra (all values rounded to one significant figure). These public health protective concentrations are much higher than the one derived below for cancer. Therefore the drinking water concentration proposed below to protect against carcinogenic effects is also protective against non-cancer chronic toxicity.

Carcinogenic Effects

There is strong human evidence that ingestion of ^{226}Ra and ^{228}Ra caused bone and head cancers in radium dial painters (Mays *et al*., 1985; NAS, 1988). Patients injected with known amounts of ^{224}Ra had increased risk of developing bone sarcomas (NAS, 1988). The dose-response from both dial painters and injected patients was linear (NAS, 1988). The U.S. EPA developed carcinogenic potencies or risk coefficients for almost all radionuclides, including ^{226}Ra and ^{228}Ra. The risk coefficients for ^{226}Ra and ^{228}Ra are listed in Table 7 and are based on the findings of the U.S. EPA′s Federal Guidance Report No. 13 (U.S. EPA, 1999). For calculating the health-protective concentration for ^{226}Ra and ^{228}Ra, the morbidity risk coefficients were used in our calculations. The morbidity risk coefficient is an estimate of the average total risk of experiencing a radiogenic cancer, whether or not the cancer is fatal. We calculated the drinking water concentration corresponding to a *de minimis* cancer morbidity risk (1 in 1 million) using the following equation for each radionuclide.

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

where:

R = *de minimis* cancer risk of one in a million;

EP = exposure period of 70 years (25,568 days);

CRC = morbidity cancer risk coefficients (pCi^{-1}) $^{226}Ra = 2.87 \times 10^{-10}$, $^{228}Ra = 1.04 \times 10^{-9}$;

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

The health-protective concentration of ^{226}Ra is therefore calculated as:

$$C = \frac{10^{-6}}{25{,}568 \text{ d} \times 2.87 \times 10^{-10} \text{ pCi}^{-1} \times 2 \text{ L/d}} = 0.068 \text{ pCi/L}$$

The health-protective concentration of ^{228}Ra is calculated as:

$$C = \frac{10^{-6}}{25{,}568 \text{ d} \times 1.04 \times 10^{-9} \text{ pCi}^{-1} \times 2 \text{ L/d}} = 0.019 \text{ pCi/L}$$

Because the cancer values are much lower and more health-protective than the non-cancer values, the PHG is proposed to be set at the health-protective values for the cancer endpoint. These values, 0.068 pCi/L for ^{226}Ra and 0.019 pCi/L for ^{228}Ra, correspond to a 1 in one million upper-bound lifetime cancer morbidity risk for each of the isotopes. At these radioactivity levels in water, individuals, including sensitive subpopulations, should also be protected against the non-cancer effects of the isotopes.

RISK CHARACTERIZATION

The primary sources of uncertainty in the development of the PHG for radium-226 and radium-228 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 of the risk assessment of radium, including the mode of action, inter- and intra-species extrapolation, and relative source contribution (RSC). A substantial body of information exists on the carcinogenic effects of radionuclides, including radium, on human subjects. U.S. EPA as well as other entities have developed and are perfecting models to estimate human body exposures to radionuclides, which have also added to the certainty of the estimations.

The proposed PHGs for radium-226 and radium-228 are 0.068 and 0.019 pCi/L, respectively. These estimated protective health concentrations were calculated based on the carcinogenic potencies of 2.87×10^{-10} and 1.04×10^{-9} per pCi, respectively, developed by U.S. EPA (1998). In calculating the proposed PHG, a *de minimis* theoretical excess individual cancer risk level of 10^{-6} was assumed. The corresponding levels for lifetime cancer risks of 10^{-5} or 10^{-4} are 0.68 pCi/L and 6.8 pCi/L, respectively, for radium 226. For radium-228, the corresponding levels for lifetime cancer risks of 10^{-5} or 10^{-4} are 0.19 pCi/L and 1.9 pCi/L, respectively.

No additional assumptions are needed with respect to the use of RSCs for radium. The U.S. EPA's risk value is specific for water ingestion of radium.

OTHER REGULATORY STANDARDS

As early as 1928, both the international and U.S. radiation protection community 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 9 summarizes the international and national guidelines and standards pertinent to human exposure to ionizing radiation and Radium-226. 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 Radium-226 in drinking water (Table 10).

The federal government has regulated the levels of ^{226}Ra and ^{228}Ra in community water supplies since the mid-1970s. The U.S. EPA promulgated Maximum Contaminant Levels (MCLs) for radium and other radionuclides in community water supplies in their 1976 National Interim Primary Drinking Water Regulation (U.S. EPA, 1976). The combined MCL for ^{226}Ra and ^{228}Ra is 5 pCi/L.

Table 9. Relevant Radiation Protection Guidelines and Regulations (from ATSDR 2001)

Agency	Description	Guideline or Regulation
ICRP	**Guideline** dose for the protection of the general public	100 mrem/year
NCRP	**Guideline** dose for the protection of 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 the general public	100 mrem/year (10 CFR 20.1301)
NRC	**Regulation** for the protection of the general public – Low-level Radioactive Waste Disposal Facilities	25 mrem/year (10 CFR 61)
NRC	**Regulation** for the protection of the general public- Decommissioned Facilities	25 mrem/year (10 CFR 20)
U.S. EPA	**Regulation**. Maximum Contaminant Level in community water systems Radium-226, Radium-228, and alpha particle: Beta particle and photon activity:	5 pCi/L (40 CFR 141.15) 0.004 mrem/year (40 CFR 141.16)
DOT	**Regulation** for transport in normally occupied space.	2 mrem/hour (49 CFR 173)

*- CFR – Code of Federal Regulations

In 1991, the U.S. EPA proposed new MCLs for ^{226}Ra and ^{228}Ra 8 at 20 pCi/L each based on newer dosimetry (U.S. EPA, 1991). They based the MCLs on a 4 mrem/year effective dose equivalent using the RADRISK Computer Code and 2 L/day drinking water rate. The proposed rule was never implemented.

In 2000, the U.S. EPA finalized their rule for drinking water (U.S. EPA, 2000, 2002). For ^{226}Ra and ^{228}Ra the MCL remains at 5 pCi/L (combined) because updated dosimetry and risk levels yielded similar concentrations (U.S. EPA, 2004a). This MCL is scheduled for review in the next 2 to 3 years for risk management issues.

California adopted the U.S. EPA MCL of 5 pCi/L for the combined radionuclides in 1997, and this MCL is still in force (DHS, 2004d).

Table 10. State Regulations for Radium-226 in Drinking Water (ATSDR, 2001)

State or Territory	Standard (pCi/L)
Alabama, Alaska, California, Colorado, Connecticut, Florida, Iowa, Indiana, Rhode Island, Utah	5
New York, Puerto Rico, Washington, Wyoming	3

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