PUBLIC HEALTH GOALS FOR CHEMICALS IN DRINKING WATER

TRITIUM

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Public Health Goal for

TRITIUM

in Drinking Water

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PREFACE

Drinking Water Public Health Goal
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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 TRITIUM (H-3) IN DRINKING WATER

SUMMARY

The Office of Environmental Health Hazard Assessment (OEHHA) hereby establishes a Public Health Goal (PHG) of 400 pCi/L for tritium in drinking water. Tritium is a radioactive compound that decays to produce beta particle emissions, with a half-life of 12.35 years. The PHG is based on the known carcinogenic effects of radiation observed in humans. In 1999, the 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 state-of-the-art methods and models that take into account many factors, including age, gender, and competing causes of death, and can 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 tritium. OEHHA followed general risk assessment practices, and used risk coefficients recommended in Federal Guidance Report 13 to estimate health-protective levels for tritium. The calculation of the PHG level applies the risk coefficient for tritium to a lifetime of exposure to 2 L/day of water and incorporates a *de minimis* excess individual cancer risk level of 10^{-6} (one in one million) from exposure to tritium to estimate the health-protective value of 400 pCi/L. Lifetime risks of 10^{-4} and 10^{-5} would correspond to tritium activity levels of 40,000 pCi/L and 4,000 pCi/L, respectively.

A non-cancer public-health protective concentration was estimated, based on changes in lifespan and hematopoietic tissues in chronic mouse studies cited in Balonov *et al.* (1993). Using a combined uncertainty factor (UF) of 100, which includes factors of 10 for intra- and interspecies extrapolation, a health-protective concentration for children is estimated to be 6×10^7 pCi/L, and for adults is estimated to be 2.1×10^8 pCi/L. Because these levels are much higher than the risk estimates based on potential cancer effects, a health-protective concentration based on cancer effects is assumed to protect against all non-cancer health effects. This concentration is also judged to be health-protective for all groups, including potential sensitive subpopulations.

The federal maximum contaminant level (MCL) for tritium in drinking water is 20,000 pCi/L, based on a radiation exposure level judged to be acceptable of one mrem/yr for this specific contaminant. The California MCL is also 20,000 pCi/L.

INTRODUCTION

This PHG technical support document provides information on health effects from tritium (^3H) 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 can be used to 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.

Elements that contain unstable nuclei are said to be radioactive or are called radionuclides. To achieve a more stable energy state, radioactive nuclei or radionuclides spontaneously emit one or more alpha or beta particles, followed in some cases by the emission of x-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} disintegrations per second. For drinking water, the common representation of activity is the picocurie (pCi), which is equal to 10^{-12} Ci. Another representation of radioactivity is the becquerel (Bq), which is one disintegration per second.

When radioactive atoms release their energy either through particles or electromagnetic radiation (photons), these in turn interact with other atoms or matter, particularly to knock out electrons from 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 ergs) deposited in one gram of matter or tissue. In International Units, grays (Gy) are used for characterizing absorbed dose, representing one joule/kg of energy deposited and is equivalent to 100 rads.

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 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, tritium, is a naturally occurring radioactive isotope of hydrogen. At the atomic level, it consists of one proton and one electron (the basic structure of hydrogen), plus two neutrons. Tritium is ubiquitous in the environment because it is formed by cosmic radiation impinging on the atmosphere, resulting in a small amount of tritium in most environmental media including drinking water. It is also formed during the process of nuclear fission, which occurs in a nuclear reactor or an atomic explosion. Tritium decays with a half-life of 12.35 years to helium (^{3}He) and emits a beta particle in the decay process. Tritium was introduced into the atmosphere worldwide from the testing of nuclear weapons, although its levels have decreased greatly since the end of

atmospheric testing by the U.S., Great Britain, and the USSR in 1963, by France in 1974, and by China in 1980.

The federal government has regulated the levels of tritium in community water supplies since the mid-1970s. The U.S. EPA promulgated MCLs for tritium 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 defined as the concentration in water that yielded 4 mrem/year to the total body or any given internal organ. For tritium the U.S. EPA set a separate MCL of 20,000 pCi/L (740 Bq/L) which yields 1 mrem/year to the total body.

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 (ede). The proposed rule was never implemented.

In 2000, the U.S. EPA finalized their rule for drinking water. For tritium the MCL remains at 20,000 pCi/L because updated dosimetry and risk levels yielded similar concentrations. This MCL is planned to be reviewed in the next 2 to 3 years for risk management issues. The California MCL for tritium is also 20,000 pCi/L (CCR, 2002). Other agencies have developed health protective levels for tritium.

Other agencies have developed differing health protective levels for radionuclides and provide equivocal guidance for setting a tritium 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 nonthreshold 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 tritium and to derive an appropriate health-protective PHG for tritium in drinking water.

CHEMICAL PROFILE

Chemical Identity

Tritium (H-3) is both a naturally-occurring and man-made radioactive isotope of hydrogen, consisting of a nucleus containing one proton and 2 neutrons plus an orbital electron, for a combined atomic weight of three. The most common form of hydrogen, with an atomic weight of 1.0, is also known as protium; the form with one neutron, with an atomic weight of 2.0, is known as deuterium. Tritium decays with a half-life of 12.35 years to helium-3 (which contains two protons, two electrons, and one neutron, and also has an atomic weight of 3.0). Tritium emits a beta particle (an energetic electron) plus a neutrino in the decay process. The energy of the tritium-emitted beta particles (maximum, 0.018 MeV) is quite weak, compared to the range of beta particle energies (^{32}P maximum, 1.7 MeV), but is sufficient to produce ionizations and excitations of molecules in their path. The average range of these beta particles in water is less than 1 μm (NCRP, 1979). Because of the low energy and short range of the beta particles,

tritium does not pose an external radiation hazard; the radiation is not sufficiently energetic to pass through skin. However, tritium is readily taken into the body, presenting an internal radiation hazard. Table 1 summarizes some of the more important characteristics of tritium.

Table 1. Characteristics of Tritium

Properties	**Value**
Atomic number	1
Atomic mass	3
Half-life	12.35 year
Decay constant	0.056 per year
Characteristics of its beta particles	
Average energy	5.685 keV
Average track length	0.56 μm (water)
Maximum energy	18.60 keV
Maximum track length	6.0 μm (water)
Maximum track length	5 mm (air)
Effective biological half-life in humans	10 days
Specific activity	9.7×10^3 Ci/g (3.59×10^{14} Bq/g)

Physical and Chemical Properties

Because tritium is an isotope of hydrogen, its chemical properties and its distribution in nature are essentially the same as hydrogen (protium). A very large majority of the environmental tritium is in the form of water (NCRP, 1979). As such, the dispersal of tritium into the environment is governed by the same processes that control the transport and distribution of ordinary water. Thus, tritiated water (normally consisting of one protium atom, one tritium, and one oxygen, or HTO) follows the same pathways as natural water in the environment, and in plants, animals, and humans.

A small exception occurs when tritiated water passes across a liquid-gas phase boundary. Because of the difference in mass between H_2O and tritiated water (18 vs 20), the vapor pressure of tritiated water is reduced to 90 to 92 percent that of normal water (Horton, 1971). This lower vapor pressure of HTO slightly favors the surface evaporation of natural water.

In transpiring plants with leaves having large surface areas, tritium levels may exceed environmental levels through the preferential transpiration of non-tritiated water from the surface of leaves to the atmosphere. Under extreme conditions of low humidity, as may occur in the desert, the tritium content in plants may be increased by as much as a factor

of three over the specific activity of the environmental soil water (NCRP, 1979). The potential for bioconcentration in plants in more temperate climates is small. In fact, in mammals, the specific activity of tritium in body water and tissue is slightly lower than that in drinking water and food (NCRP, 1979).

Production and Uses

Consumer products containing tritium include luminous dials, signs, and navigational instruments, and electronic devices filled with tritium gas. The total number of consumer items is difficult to assess, but it is estimated that about one percent of the processed activity in consumer items is lost to the atmosphere during fabrication and ten percent is released through waste disposal (incineration) of such consumer items. Environmental releases from consumer products are estimated in tens of thousands of curies per year.

Tritium production facilities produce tritium by neutron bombardment of lithium in a nuclear reactor. Releases of tritium from production facilities are mostly in gaseous form and quantities may reach several hundred thousand curies per year from a single facility. NCRP (1979) estimated that about 2.7 million curies (10^{17} Bq) of tritium had been produced for consumer products.

Sources

Natural production of tritium occurs when cosmic rays from outer space interact with atoms of oxygen and nitrogen in the upper layers of our atmosphere. The total world inventory of naturally produced tritium from cosmic ray production is estimated at 70 million curies (2.6×10^{18} Bq) (NCRP, 1979). Based on the loss of tritium through radioactive decay, it can be readily calculated that the natural production rate is approximately 4 million curies (1.4×10^{17} Bq) per year. Nearly all of this tritium is present as water.

Nuclear weapons testing produced tritium by both ternary fission and neutron activation. The tritium inventory of atmospheric weapons testing reached a maximum in 1963. This inventory has now been reduced to about 400 million curies (1.4×10^{19} Bq).

Nuclear power stations also produce tritium by fission and neutron activation. Because of the differences in water chemistry among various nuclear power plant designs, production rates vary. Heavy water reactors, which use deuterium as coolant and moderator, produce hundreds to thousands times greater quantities of tritium than boiling water or pressurized water reactors. Typical values of tritium production are about 12 curies (4.4×10^{11} Bq) per billion watts of electricity for boiling water reactors and about 800 curies (2.96×10^{13} Bq) per billion watts of electricity produced for pressurized water reactors (Luykx, 1986).

ENVIRONMENTAL OCCURRENCE AND HUMAN EXPOSURE

Tritium is ubiquitous, but environmental levels are low. These levels have been declining since the early 1960s when most of the atmospheric testing of nuclear weapons

ceased. Human exposure to tritium can result from consumption of food, drinking water, or the inhalation of water vapor and hydrogen gas. Food and drinking water are the largest sources of exposure.

Air

Atmospheric levels of tritium have been declining since the cessation of atmospheric nuclear weapons testing. Okada and Momoshima (1993) reported the results of six years of tritium air monitoring in Japan. They showed that tritium levels in hydrogen, water vapor and methane per cubic meter of air are all on the same order of magnitude, ranging from 13 to 47 mBq/m^3 (0.4 to 1.3 pCi/m^3). Table 2 summarizes the findings.

Table 2. Tritium in Air at Fukuoka City, Japan, from 1984 to 1990

Chemical Form	**Tritium Concentration (mBq/m^3 of air)**
Water vapor	19-23
Hydrogen gas	33-47
Methane	13-15

Air concentrations of tritium were found to be higher, close to a source of tritium. Atmospheric concentrations of tritium averaged from 24 Bq/m^3 close to the release stack of Lawrence Berkeley National Laboratory's (LBL) Tritium Labeling Facility, to 3.3 Bq/m^3 a distance away from the facility (McKone and Brand, 1997).

Soil

Tritium levels in soil vary widely and depend on anthropogenic activities. Measured soil and sediment samples around and offsite of the LBL Tritium Labeling Facility averaged 3 Bq/kg (81 pCi/kg). The average tritium soil concentration weighted by volume from 11 Department of Energy (DOE) contaminated sites was 3600 pCi/g (133 Bq) (SC&A, 1995), based on the data in Table 3.

Table 3. Tritium Levels in Soil at 11 DOE Facilities (from SC&A, 1995)

Facility	Weighted Tritium Concentration (pCi/g)	Soil Volume (ft^3)
Argonne National Lab	-	-
Brookhaven National Lab	2.99	1.9×10^6
Hanford Reservation	9.9	7.9×10^5
Idaho National Engineering Lab	25,000	130
Oak Ridge Gaseous Diffusion Plant	-	-
Los Alamos National Lab	-	-
Lawrence Livermore National Lab	-	-
Rocky Flats Plant	-	-
Sandia National Lab	-	-
Savannah River Site	65,000	3.4×10^5
Y-12 Plant	-	-

Water

Okada and Momoshima (1993) report tritium levels in various types of Japanese environmental water. These levels are summarized in Table 4.

Table 4. Tritium in Japanese Waters

Samples	Tritium Concentration (Bq/L)
Precipitation	0.1 – 3.4
Groundwater	0* – 10.7
River Water	1.9
Coastal Sea	0.4 – 1.1
Ocean	0* – 0.6

* not detected

Water concentrations of tritium were found to be higher located close to a source of tritium. Tritium concentrations were reported for rain and surface water at the Lawrence Berkeley National Laboratory's (LBL) Tritium Labeling Facility (currently inactive) for 1995. Rainwater fluctuated between 0 and 290 Bq/L (0 to 7,800 pCi/L) depending on the distance away from the facility (McKone and Brand, 1997). Similarly, tritium in surface water ranged from 10 to 100 Bq/L (270 to 2,700 pCi/L).

The U.S. EPA's Environmental Radiation Ambient Monitoring System (ERAMS) measures water samples for tritium at numerous sites around the country. The U.S. EPA established the ERAMS in 1973. It is a quarterly monitoring program made up of a

nationwide network of sampling stations for air, surface water, drinking water, and milk. There are 78 sampling stations in the drinking water program covering 42 states, including two locations in California, Los Angeles and Berkeley. For the period of July to September 2003, the reported concentrations for the two California sites ranged from below the level of quantification to 84 pCi/L (3.7 Bq/L) (U.S. EPA, 2003).

The State of California has monitored public drinking water supply wells from 1994 to 2001 for various radioactive contaminants including tritium. Tritium was not found to exceed the MCL of 20,000 pCi/L at any source during that period (DHS, 2002).

Food

Tritium has been measured in various foods. Table 5 summarizes the measured levels. The tritium levels are usually reported as tritium present in food water. Okada and Momoshima (1993) estimated the amount of tritium intake through food to be about 4.2 Bq/day (114 pCi/day) for a family of 5-6 eating breakfast, lunch and dinner.

Table 5. Tritium Levels in Various Foods

Food	Tritium, pCi/L (Bq/L)	Reference
Rice	68 (2.5)	Okada and Momoshima (1993)
Green Vegetable	30 (1)	Okada and Momoshima (1993)
Other Vegetable	27 (1)	Okada and Momoshima (1993)
Fish/Clams	13 (0.5)	Okada and Momoshima (1993)
Milk/Dairy	54 (2)	Okada and Momoshima (1993)
Meats	35 (1)	Okada and Momoshima (1993)
Eggs	46 (2)	Okada and Momoshima (1993)
Fruit	300 (11)	PNL (2002a)
Wine	100-300 (3.7-11)	PNL (2002a)
Milk	0-260 (0-9.6)	PNL (2002b)

METABOLISM AND PHARMACOKINETICS

In this country, 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). We used the metabolic and pharmacokinetic information in these ICRP documents to summarize what is known about the absorption, distribution and excretion of tritium.

Tritium may be released in the environment in three main chemical forms: tritium gas, tritiated water, and organic compounds of tritium. In the environment, tritium gas is converted to tritiated water, so the ICRP considers the metabolism of tritiated water and organically bound tritium separately (ICRP, 1989).

Absorption

Water ingested into the body is almost completely absorbed from the gut into the blood and then eventually reabsorbed by the kidneys and excreted via the urinary tract. For tritiated water the ICRP considers the adsorption of tritium from the gut into the blood to be complete and instantaneous (ICRP, 1979, 1989). The gut to blood transfer factor (f_1) that they recommend for all ages is 1.0. The NCRP (1979) reported that ingested tritiated water is almost completely absorbed from the GI-tract and quickly appears in the venous blood. Within minutes, it can be found in varying concentrations in the various organ fluids and tissues of the body.

When organic compounds containing tritium are ingested, a considerable fraction is broken down in the gastrointestinal tract, producing tritiated water. Organic compounds of tritium may also be catabolized after they have crossed the gut (ICRP, 1979). In rodents, more than 90 percent of tritiated thymidine is broken down in the gastrointestinal tract (Lambert and Clifton, 1968). In the GI-tract, foodstuffs containing organically bound tritium will undergo digestion to yield smaller molecules, which are readily absorbed. A small portion of the tritium will probably be present in indigestible fibers and will not be absorbed. However, the ICRP (1989) assumes that the non-absorbable fraction of organically bound tritium represents a very small portion of the dietary organic tritium, so they assigned an f_1 value of 1.0 to tritium in organic molecules.

Distribution and Metabolism

Ingested tritiated water mixes rapidly and completely with total body water after its entry into the blood (ICRP, 1989). A fraction of the tritium then becomes organically bound, and its retention depends on the metabolic activity of the various tissues. For example, the ICRP (1989) states that the retention of bound tritium in liver and intestine is shorter than that in the brain and skin.

A two-compartment model describes the whole-body retention of tritium taken in by adults and children as tritiated water. The first compartment is the body water compartment that contains 97 percent of the total tritium. The second compartment represents the tritium incorporated into organic compounds. This compartment represents 3 percent of the total tritium and is based on the fact that animal studies suggest that 1-5 percent of the tritiated water entering the blood becomes organically bound (ICRP, 1989). The equation below describes the whole body retention for tritium intake as water. Table 6 summarizes ICRP's biokinetic parameters for this equation.

$$\text{Retention} = A\, e^{-0.693t/T1} + B\, e^{-0.693t/T2}$$

In this equation, A represents the fraction in the body water compartment and B, the organically bound compartment.

Table 6. Biokinetic Data for Tritiated Water (ICRP, 1989)

Age	Distribution (percent) Total Body		Biological Half-time (day)	
	Body Water Compartment A	**Organically Bound Compartment B**	**Compartment A (*T1*)**	**Compartment B (*T2*)**
3 months	97	3	3.0	8.0
1 year	97	3	3.5	15
5 years	97	3	4.6	19
10 years	97	3	5.7	26
15 years	97	3	7.9	32
Adult	97	3	10.0	40.0

Following the absorption into the blood, organically bound tritium will be incorporated into the body tissues to an extent that will depend on the metabolic activity of the individual tissue and on the specific chemical form. Studies in animals fed various forms of organically bound tritium have shown that relatively higher concentrations of tritium occur in the liver, kidney, and small intestine; lower concentrations occur in fat, muscle, and brain (ICRP, 1989). Due to the strength of the bond between certain atoms, tritium attached to oxygen, sulfur, nitrogen, or phosphorous is in general readily exchangeable with hydrogen from the body water pool. However, tritium bound to carbon will normally be released only through enzyme-mediated breakdown of the molecule in which the carbon is situated due to strength of the carbon-hydrogen bond (Smith, 1986). The breakdown rate may be rapid for small organic molecules or very slow for carbon-bound tritium incorporated into structural proteins or phospholipids.

Total fractional incorporation into major tissues may be expected to range from 9 to 45 percent (ICRP, 1989). The ICRP conservatively assumes that 50 percent of the ingested organically bound tritium is incorporated by carbon-hydrogen bonding in the tissues and that its metabolic turnover will follow that of carbon. The remaining 50 percent will have the same metabolic behavior as tritiated water. ICRP uses the same retention equation above for organically bound tritium with the specific parameters in Table 7.

Table 7. Biokinetic Data for Organically Bound Tritium (ICRP, 1989)

Age	Distribution (percent) Total Body		Biological Half-time (days)	
	Body Water Compartment A	Organically Bound Compartment B	Compartment A (*T1*)	Compartment B (*T2*)
3 months	50	50	3.0	8.0
1 year	50	50	3.5	15
5 years	50	50	4.6	19
10 years	50	50	5.7	26
15 years	50	50	7.9	32
Adult	50	50	10.0	40.0

Excretion

In 310 individuals who had been chronically exposed to tritium gas and whose urine contained more than 20 μCi (74 kBq) of tritium per liter, the biological half-life ranged from 4 to 18 days with an average of 9.5 days. There was no correlation between the amount of tritium assimilated and the biological half-life. The half-life was inversely correlated with age (Butler and LeRoy, 1964).

In two chronically-exposed tritium dial painters, Moghissi *et al.* (1971) reported effective half-lives for tritium of two separate tritium pools ranging from 21 to 26 days for the first pool and 280 to 550 days for the second pool of tritium. Jones and Lambert (1964) also reported biological half-lives for tritium in chronically exposed tritium dial painters of 12.1 to 13.4 days.

Acute exposure gives the best estimate of the short-term half-life values in body water. These exposures are not complicated by the heavily loaded, organically-bound tritium pools that can develop in protracted exposures. Data from several acute exposure studies suggest that one tritium pool is in the form of free body water with half-lives ranging from 6 to 18 days. The retention curves suggest the existence of two additional pools with half-lives that range from 21 to 30 days and from 250 to 550 days. The shorter pool represents the existence of a labile organic pool, and the other pool represents tritium more tightly bound to organic substances (NCRP, 1979).

TOXICOLOGY

Tritium toxicity can be largely understood based on the pharmacokinetics of tritium. Tritium, as tritiated water (HTO), enters the body and distributes widely through all water containing compartments without concentrating in any one site. Tritium then readily exchanges with hydrogen in many body molecules, including ribonucleotides, proteins and others, thereby being in the position to impart its energy upon critical molecules. For example, tritium incorporated into DNA may result in beta particle radiation altering chromosomes, allowing for the induction of cancer. In addition, the degradation product

of a substituted tritium in DNA, ^{3}He, might cause replacement of bases and can impart a point mutation in lower organisms (Balonov *et al*., 1993). However, there are factors mitigating the effects of tritium on the organisms as well. As easily as tritium is exchanged into biological molecules, it can as easily be exchanged out, averting damage and obviating repair mechanisms. Tritium has a relatively short radiological half-life of about 12 years, a low ionization energy and short track length of energy deposition. Largely due to these factors, tritium has not been reported to be associated with significant toxicity in humans except under unusual or extreme exposures.

Toxicological Effects in Animals

Acute Toxicity

Wang *et al*. (1999) studied the induction of apoptosis by tritium exposure in brain sections of embryos and newborn mice (C57BL/6J). They gave 481.8 kBq/g of body weight (13 μCi/g) of tritiated water to pregnant mice by a single intraperitoneal injection. They estimated that the cumulative absorbed dose to the offspring *in utero* was about 1 Gy (100 rad). Apoptosis is a cell's suicide response resulting from the activation of specific genes that terminate the life of an affected cell. An increase in apoptotic cells was observed in the neural tube of embryos from one day after injection to one week after birth. In an earlier study under the same experimental conditions, Wang and Zhou (1993) observed a significant decrease in the number of neuron dendrites in the postnatal cerebrum layer.

Subchronic Toxicity

Balonov *et al*. (1993) reported on several studies which evaluated the effect of tritium on bone marrow-related parameters in mice and rats. Under continuous ingestion of tritiated water at a dose of 370 kBq/g-day (10 μCi/g-day), the number of rat erythropoietic precursor cells in all life stages was reduced to 50 to 60 percent of the control. In continuously dosed CBA mice, morphologically unrecognizable cell-precursor bone marrow cell populations (undifferentiated stem cell line) decreased relative to control populations to nearly 50 percent of control at 5 days at 370 kBq/g-day, decreasing to about 25 percent of controls at 30 days, and recovering back to 50 percent in 90 days. Changes to granulocytopoiesis were less pronounced than that of erythrocytopoiesis. Based on the pronounced effect on the number of cells at an intake rate of 370 kBq/g-day, a NOAEL of 37 kBq/g-day can be determined. Converting to picocuries and kilogram body weight (37kBq/g-day x 1 pCi/0.37 Bq), the NOAEL is calculated as 1.0 x 10^{9} pCi/kg-day (1 mCi/kg-day).

Cahill and colleagues (1975a,b) exposed female Sprague-Dawley rats to 1,10, 50 or 100 μCi/mL (37, 370, 1850, or 3700 kBq/mL) of HTO in body water during gestation. The study population consisted of 145 pregnant rats distributed as follows: controls (36), 1 μCi (24), 10 μCi (26), 50 μCi (23), 100 μCi (36). The rats first received an intraperitoneal injection of tritiated water to achieve the desired concentrations in body water before administering the dose through drinking water. After weaning, the dams

were housed and maintain until their natural death, upon which autopsies were performed for neoplasms. Although an increase in mammary fibroadenomas was noted for the two higher doses, the authors felt that the significance of this data was marginal due to the small number of tumors observed. The overall incidence was within the range of the historical control population. Life spans were also reduced at the two higher doses (22 percent at 100 μCi/mL). Female offspring (Cahill *et al.* (1975b) exposed to the two higher doses were sterile, but had a lower incidence of overall tumors than controls. Both female and male offspring had reduced life spans at the highest dose.

Genetic Toxicity

Balonov *et al*. (1993) reported damage to the DNA in Wistar rats given tritiated water. Continuous ingestion of tritiated water (37 to 1850 kBq/g per day) resulted in damage to the DNA of hematopoietic tissue only in animals given the highest dose. DNA damage was assessed by measuring changes in double and single stranded DNA. In single injection experiments, the percent increase of non-reconstructed breaks in mouse DNA was dose dependent from 11 to 33 MBq tritium/g of body mass (0.3 to 9 mCi/g). Increased DNA damage was observed at all dose levels. Based on DNA damage observed in hematopoietic tissues, a NOAEL for this effect would be 370 kBq/g-d ($1.37x10^{10}$ pCi/kg-d) based on the continuous exposure study.

Tritium effects on mouse chromosomes in developing oocytes were studied by Mailes *et al.* (1987). Fifty Hale-Stoner Brookhaven mice females were maintained on 0, 3.0, 7.5, 15.0, or 30.0 μCi/mL (111, 259, 555, or 1110 kBq/mL) from three to seven weeks of age. Ovulation was induced, ovaries were excised, and oocytes were extracted. No evidence was found for dose–related increases in chromosomal aberrations.

Carsten *et al*. (1989) evaluated dominant lethal mutations in Hale-Stoner-Brookhaven mice maintained with water containing 0, 0.3, 1.0, or 3.0 μCi/mL (0, 11, 37, or 111 kBq/mL) of HTO. Effects were demonstrated only at 1.0 and 3.0 μCi/mL of HTO. Another study reported (Carsten *et al.,* 1989) tritium exposure effects upon rates of sister chromatid exchanges and micronuclei evaluations for animals exposed to 0.0, 3.0, 7.5, 15.0, or 30 μCi/mL (0,111, 277.5, 555, or 1,110 kBq/mL). Sister-chromatid exchanges trended higher for treated groups, but no dose-response relationship could be determined. The number of sister-chromatid exchanges remained constant throughout life, while the number in control groups decreased. Micronuclei numbers increased in 15 and 30 μCi/mL groups.

Developmental and Reproductive Toxicity

The effect of tritium exposure upon developing oocytes was studied by Dobson and Kwan (1976). Four treatment groups of ten Swiss-Webster mice were injected on the day of fertilization with 0.73, 2.20, 4.35, or 6.57 μCi of treated water in order to achieve a targeted dose of 1, 3, 6, 9 μCi/mL of HTO in body water. They then were exposed by drinking water to 1.53, 4.59, 9.18, or 13.76 μCi/ mL HTO to maintain the desired body water concentration up to 14 days after birth. The ovaries were then removed and oocytes were counted. Significant dose-related reductions were noted in primary oocyte

counts at all dose levels. At the lowest dose the reduction was 30 percent of the controls (effective concentration of 0.97 μCi/mL).

Cahill and Yuile (1970) studied the effects 1, 10, 20, 50, or 100 μCi/mL (37, 370, 740, 1850, 37,000 kBq/mL) of tritium in body water upon Sprague-Dawley rats exposed *in utero.* Groups of females (10-20 per group) were first mated and then injected with HTO to immediately achieve the desired HTO body concentration. Rats were maintained by exposure to HTO in drinking water throughout pregnancy. The concentration in the drinking water was usually 30 percent higher than the level sought for in the body water to compensate for dilution and other loss of activity. Stunting of the offspring was noted for groups treated at 20 μCi/mL and higher ($p<0.05$). Litter size was reduced only at the higher dose ($p<0.05$). Decreases in testicular weight were noted ($p<0.05$) at doses of 10 μCi/mL and greater.

Groups of 30 Sprague-Dawley rats were exposed constantly to tritium-containing drinking water from conception to the delivery of the F_2 generation (Laskey *et al.*, 1973). The targeted doses were 0.01, 0.1, 1.0, or 10 μCi/mL (0.37, 3.7, 37, or 370 kBq/mL) of HTO in body water (estimated by measuring urine activity), which corresponded to whole body dose rates of approximately 3-3000 mrads per day. Statistically significant reported effects were: 30 percent reduction in the testes weight of F_1 males at 10 μCi/mL, decreased litter size and increased resorption rate at 10 μCi/mL, and decreased body weights and relative brain weights at 1 and 10 μCi/mL. No instances of malformations were reported.

Kashiwabara *et al*. (2003) reported on the effects of a one-time injection of tritiated water into six-week old male mice at doses of 23.2, 46.3 or 92.5 MBq/animal (about 28, 56 and 108 μCi/animal) upon the male reproductive organs. Three strains of mice were used, C3H/HeNCrj, C57BL/6NCrj and F_1 Crj:B6C3F1, with 6-10 animals/ group. Animals were evaluated on day 30. A dose–dependant reduction in testis weights was noted for all three groups, and significant changes were noted for two out of three groups at the lowest dose. Vacuolization of seminiferous tubules and decreases in their size were significant at the lowest dose and the effects generally increased in a dose-related fashion. At the highest dose, spermatids and spermatocytes were largely absent in the testes.

Another experiment to evaluate the effects of tritium administered *in utero* to mice was conducted by Lambert and Phipps (1977). They exposed groups of pregnant SAS/4 mice to 1.8, 11, 16, or 30 μCi/mL (66.6, 407, 592 or 1,110 kBq/mL) of water containing HTO from the first day of pregnancy to delivery. Offspring were sacrificed 14 days later to recover ovaries. The concentration of tritium in body water reached equilibrium in four days and was about 65 percent of that of drinking water. The two higher doses led to an apparent reduction in the number of oocytes.

In a multigenerational study (Laskey *et al.,* 1980), Sprague-Dawley rats (10 per group) were given concentrations of 0.13, 1.3, or 13 μCi/mL (4.81, 48.1, or 481 kBq/mL) HTO to drink in order to achieve concentration of 0.1, 1.0, or 10 μCi/mL (3.7, 37, or 370 kBq/mL) of body water. Dosing commenced from conception and continued until delivery of the F_2 generation. The majority of effects were significant ($p<0.05$) only at the highest dose, 12 μCi/mL. These included decreased size of litters, sperm counts, and testes weights, and increased levels of FSH-F_1 and LH-F_1. Using a NOAEL of 1.3

μCi/mL of water, a dose can be estimated, assuming female Sprague-Dawley rats weighed 338 gm and consumed 0.045 L/day chronically (U.S. EPA, 1988), as 0.17×10^9 pCi/kg.

Satow *et al*. (1989) evaluated the effects of tritium on germ cells and fertility in ICR mice. Tritiated water, in doses of 46, 92, 184, or 276 μCi/10 g body weight, was injected once into the abdominal cavity of newborn female mice at age 14 days. Two weeks later, after 99 percent of the tritium was excreted, the ovaries were removed and the surviving oocytes were counted. Satow *et al*. (1989) also measured reproductive capacity in a separate group of female mice undergoing the same exposure conditions. After the two-week clearance period, the mice were mated four times during their lifetime, and the number of offspring was counted. Oocyte survival decreased with increasing dose. There was no statistically significant reduction for the two lower dose levels (46 and 92 μCi/10 g). The results of the reproductive capacity experiments showed significant reductions in the number of offspring for the 184 and 276 μCi/10 g exposure levels. These reductions ranged from about 20 to 60 percent.

Although there is a large volume of data on the sensitivity of female oocytes to the lethal effects of tritium, this information may not be very relevant in predicting human response. Mouse oocytes are estimated to be 30-40-fold more sensitive to the radiolethality produced by tritium and other radioactive sources than human oocytes (Straume and Carsten, 1993).

Chronic Toxicity

Carsten *et al*. (1989) maintained groups of 20 of each sex of Hale-Stoner Brookhaven mice for a lifetime on plain tap water, equivalent gamma exposure, or HTO drinking water at an activity level of 3 μCi/mL. No differences in survival were noted among the different groups. Thus, 3 μCi/mL is the NOAEL for HTO. Assuming ingestion of drinking water of 8 mL/day and an average body weight of 35 g, the estimated NOAEL for this study is 6.85×10^8 pCi/kg (based on 3,000 μCi/L x 8 mL/day / 0.035 kg).

Balonov *et al*. (1993) evaluated the nonstochastic parameter of average life-span shortening for random-bred rats given 3.7 to 370 kBq/g tritium in water/day. At 3.7 kBq/g-day, lifespan increased by 12 percent over that of controls. At 37 kBq/g-day, the lifespans of the treated and control groups were identical, and at 192 and 370 kBq/g-day, HTO-treated groups had decreased life spans compared to controls by 18 and 33 percent, respectively. Thus, a NOAEL can be identified as 37 kBq/g-day (1.4×10^6 pCi/kg-day).

Carcinogenicity

Balonov *et al*. (1993) reported the results of lifetime exposure studies on rats. Random-bred Wistar rats were given tritiated water at levels from 3.7 to 370 kBq/g (0.1 to 10 μCi/g) per day throughout their lifetime. There were 140 animals in the control group and 200 for the experimental groups. This resulted in the following lifetime doses: 0.24, 2.0, 12.5, and 25.3 Gy (24, 200, 1,250, and 2,530 rad). Total frequency of malignant tumors was measured at death. Leukemia, cancer of the lung and mammary glands, skin cancer, and osteosarcomas correlated positively with dose. Lymphosarcomas correlated

negatively with dose. The frequency of total malignancies exceeded the control levels on the average by a factor of about two, but did not depend on the amount of ingested tritium.

Weanling C57Bl mice were either injected with 1 μCi/ml (37 kBq/mL) of tritiated water or were given that concentration to drink for a lifetime (Mewissen *et al.* 1987). Two additional groups of rats were exposed *in utero* when their mothers were given these doses either by injection or by drinking water. Overall, the incidence of lymphocytic leukemia was significantly increased in both sexes ($p<0.05$) in all treatment groups over controls, but this was not always the case for the incidence of reticuloendothelial tumors. In general, there was no difference in tumorigenic response between animals injected and those given drinking water. Both tumor types occur at a high rate in this particular mouse strain.

Mewissen and colleagues (1999) conducted a more recent study with the same strain of mice using a protocol similar to that above. In one group newborn mice received one injection of 1 μCi/mL (37 kBq/mL) of tritiated water, in another group newborns received that same concentration in drinking water, and finally, weanling rats received the same concentration in water. Incidence rates of lymphocytic leukemia were significantly elevated in the dosed populations, but no significant elevation of reticulum cell tumors was noted with dosing.

Yin and colleagues (2002) recently investigated the tumorigenicity of tritiated water on male and female C3H/HeN Crj mice. Male and female 12-day old pups (groups of 24-28) were injected with 0.23, 0.92, or 3.70 MBq/mouse (6.2, 26.7, 99.9 μCi/mouse) and watched only up to 14 months, so as to preclude the observance of excessive numbers of spontaneous tumors. Consistent with other reports noted above, there was a decrease in average life spans at the highest dose. Liver tumors in males were significantly increased in a dose-related manner as follows: controls, 10 percent; 0.23 MBq, 51.8 percent; 0.92 MBq, 68 percent; and 3.70 MBq, 91.7 percent. For females, no increase in liver tumors was noted, but there was an elevated, but not significant increase in ovarian tumors.

Toxicological Effects in Humans

Noncarcinogenic Effects

There have been several anecdotal accounts of death from tritium exposure in humans (NCRP, 1979). In some, death is caused by the destruction of bone marrow cells after incorporating tritium. The estimated doses were very high - over several thousand rem (NCRP, 1979). No dose-response inferences should be made from these studies.

A woman was accidentally exposed to tritiated gas that escaped from glass capillary tubes (Lloyd *et al.*, 1998). She incorporated about 35 GBq (1 Ci) of tritiated water. After several hours of delay, treatment was initiated to reduce the exposure by enhanced fluid intakes and forced diuresis. She was followed for chromosomal aberrations for 11 years. The authors monitored the number of dicentric chromosomes found in lymphocytes, and found that they have fallen over the years with a half-time of 3.3 years. No other significant clinical abnormalities were noted.

Effects on other common toxicological endpoints in humans (i.e., neurotoxicological, reproductive/developmental, or immunological effects) have not been documented.

Carcinogenic Effects

We found no epidemiological studies of tritium causing cancer in humans. It appears unlikely that tritium in the environment from present sources would produce detectable effects (NCRP, 1979). The carcinogenicity of tritium must be inferred from the amount of ionizing energy absorbed by human tissue from its beta particle emission.

DOSE-RESPONSE ASSESSMENT

Noncarcinogenic Effects

Several studies are available in which both short-term and long-term effects of tritium were evaluated in experimental animals, that are potentially useful for risk assessment. However, the difficulty lies in dose extrapolation. The NOAELs and LOAELs from the animal toxicity studies described above for which doses could be estimated are summarized in Table 8. The table shows that the NOAEL for hemopoietic effects, reproductive and organ weights decreases, and shortening of lifespan occurred in the range of $10^8 – 10^9$ pCi/kg-day from mostly longer term and multigenerational exposure studies.

Laskey and colleagues (1980) gave Sprague-Dawley rats (10 per group) 0.13, 1.3, or 13 μCi/mL (4.81, 48.1, or 481 kBq/mL) HTO to drink in order to achieve the concentrations of 0.1, 1.0, or 10 μCi/mL (3.7, 37, or 370 kBq/mL) of body water. Dosing commenced from conception and continued until delivery of the F_2 generation. Effects were noted at the highest dose, 13 μCi/mL, which included decreased size of litters, sperm counts, and testes weights, and increased levels of FSH-F_1 and LH-F_1. Using a NOAEL of 1.3 μCi/mL of water, a dose can be estimated as 0.17×10^9 pCi/kg, assuming female Sprague-Dawley rats weigh 338 g and consume 0.045 L/day of water chronically (U.S. EPA, 1988).

Carsten *et al*. (1989) summarized the results of several studies of the effects of tritium on mice. Mice maintained for a lifetime drinking either normal tap water or HTO at 3 μCi/mL showed no effect of HTO upon their lifespan, compared with controls. Carsten *et al*. also reported somatic and genotoxic effects upon exposure that were non-dose-related: sister-chromatid elevations over controls for concentrations of 3.0 to 30 μCi/mL. They observed a slight reduction in bone marrow stem cells at concentrations of HTO in water of 10 μCi/mL, although the cellularity of the bone marrow remained constant. Overall, the biological significance of these findings is not clear. No life-shortening effects were observed at 6.85×10^8 pCi/kg-day (2.53×10^7 Bq/kg-d), which would be the NOAEL.

Table 8. NOAEL and LOAEL Summary

Exposure or Effect	Doses (pCi/kg-day)	NOAEL (pCi/kg-day)	LOAEL (pCi/kg-day)	Comment	Reference
Survival - mice	6.86×10^8	6.86×10^8		Assumed daily water intake of 8 mL/day and average weight of 0.035 kg	Carsten *et al*., 1989
Hemopoietic effects	10^8 to 10^{10}	10^9	10^{10}	Rats and mice	Balonov *et al*., 1993
Survival - rats	10^8 to 10^{10}	10^9	5.2×10^9	6 month exposure	Balonov *et al*., 1993
Reproductive effects - rats	1.7×10^7 –1.7×10^9	1.7×10^8	1.7×10^9	2 generations of dosing	Laskey *et al.*, 1980

Balonov *et al*. (1993) reported the results of several studies evaluating tritium toxicity in mice given a range of doses from 3.7 to 370 kBq/g-day (0.1 to 10 μCi/g-day). A tritium-induced dose-dependent decrease of hematopoietic cells in mice was noted with continuous ingestion of tritiated water at a dose of 370 kBq/g-day. The number of erythropoietic cells in all life stages was reduced to 50 to 60 percent of the control. This effect was noted in one stem cell colony, $CFU_{s\text{-}I1}$ as early as five days after the start of dosing, and increased in magnitude with further dosing to day 60. The reduction of number of cells at an intake rate of 3.7 or 37 kBq/g-day was less and there was no clear dose-dependence. In another study, shortening of average lifespan was seen at the same dose. Changes to DNA in hematopoietic tissue were noted at doses above 37 kBq/g-day (10^9 pCi/kg-day)). Regardless of whether by chronic or short-term dosing, the most sensitive NOAEL would be about 10^9 pCi/kg-day.

Carcinogenic Effects

For tritium, the experimental evidence for carcinogenicity is rather weak. Many animal studies show no increased incidences of tumors over controls, or the evidence is debatable. To optimize the possibility to observe tritium induced tumors, investigators have focused their efforts by administering tritium *in utero* or shortly after birth, yet this approach did not always result in increased tumor incidence. Life-span shortening seen at high doses of tritium described by Balonov *et al.* (1993) and Cahill *et al.* (1975) were associated with decreased tumor incidence when compared with lower doses of tritium exposure. Apparently, animals were not dying from tumors associated with tritium exposure.

We found no human data that specifically address the carcinogenic effects of tritium. There is a wealth of human cancer information on ionizing radiation in general. Hence, 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). It should be noted that radionuclides as a class are listed under California's Proposition 65 as Known to the State to Cause Cancer (listing date: July 1, 1989).

More recently, the U.S. EPA developed carcinogenic potencies or risk coefficients for almost all radionuclides including tritium. 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:

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.
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 acute intake of a unit of radionuclide activity. Six ages are used: 100 days and 1, 5, 10, 15, and 20-25 years.
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 acute intake of one unit of activity at each age x_i.
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.
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 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. In addition, 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 tritium are listed in Table 9 below for the water ingestion exposure route in units of Bq^{-1} and pCi^{-1}. The coefficients are for tritiated water, as this would be the most likely chemical form in drinking water. The U.S. EPA lists cancer risk coefficients for organically bound tritium, but this form is more relevant for food ingestion where some fraction of the tritium would be in organic compounds and an additional part in an organic matrix.

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 (UNSCEAR, 1994; NCRP, 2001).

Table 9. Drinking Water Risk Coefficients for Tritium

Radionuclide	**Risk Coefficient [1] (Bq^{-1})**		**Risk Coefficient [2] (pCi^{-1})**	
	Mortality	Morbidity	Mortality	Morbidity
^{3}H	$9.44x10^{-13}$	$1.37x10^{-12}$	$3.49x10^{-14}$	$5.07x10^{-14}$

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

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 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 with regard to the type of DNA damage that induces adaptive responses.

Extensive data from animal experiments with other radionuclides 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 studies described by Balonov *et al*. (1993), however, indicate a potential adaptive response to the effects of low levels of tritium resulting in increased lifespan

over controls. The National Council on Radiation Protection and Measurements (NCRP, 2001) reviewed the most recent epidemiological evidence and reported that there is no strong support for a hormesis interpretation of the radiation epidemiological literature. Their conclusion was 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

Noncarcinogenic Effects

Balonov *et al*. (1993) was selected as the critical study to be used to derive a noncarcinogenic, health-based risk value for tritium exposure by the drinking water route. Balonov *et al.* (1993) compiled the most extensive discussion of long-term tritium studies. They report on several studies in rats and mice given a range of doses of 3.7 to 370 kBq/g-day. In one study in mice, a tritium-induced dose-dependent decrease of hematopoietic cells was noted under continuous ingestion of tritiated water at a dose of 370 kBq/g-day. The number of erythropoietic cells in all life stages was reduced to 50 to 60 percent of the control. This effect was noted five days after the start of dosing. The authors reported no reduction in the number of cells at an intake rate of 37 kBq/g-day. In another study, shortening of average lifespan was seen at the same dose. Changes to DNA in hematopoietic tissues were noted at doses above 37 kBq/g-day (10^9 pCi/kg-day). Regardless of whether dosing was short-term or chronic, Balonov *et al.* (1993) results define the most sensitive LOAEL with the highest NOAEL for tritium when compared with other candidate studies for risk assessment. Thus, the NOAEL for risk assessment is selected as10^9 pCi/kg-day.

Estimation of relative source contribution for tritium for non-cancer effects is based on a release scenario, because current exposure levels are far below levels of concern for non-cancer effects. Tritium is likely to be released into the environment by spillage into the waters or release into the air of a facility producing or using tritium. Releases of tritium into the air would eventually go to surface water. Tritium would follow irrigation water to plants, then to dairy and meat products. Thus exposures could be comprised of an acute inhalation dose, a short-term exposure in drinking water, then a longer-term exposure from plant and animal uptake, as the tritium moves through the ecosystem. The ratio of exposure from these different sources would depend on the circumstances of a particular release event. It seems to us that drinking water would provide the greatest contribution of tritium to human exposure, but the potential contribution from food and air would also be significant for likely release scenarios. For our purposes, a relative source contribution of 60 percent will be assumed for drinking water.

Thus using the NOAEL of 10^9 pCi/kg-day, the public-health protective concentration (C) for noncarcinogenic endpoints can be calculated using the equation below:

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

where,

C	=	health protective concentration in pCi/L;
NOAEL	=	No Observed Adverse Effect Level (10^9 pCi/kg-day);
BW	=	body weight in kg, usually 10 kg for a child or 70 kg for an adult;
RSC	=	relative source contribution of water to total exposure to the contaminant (estimated as 0.6 for this analysis);
UF	=	combined uncertainty factors, which may include factors of 10 for intraspecies extrapolation, for human variability, for a subchronic to chronic extrapolation, or other aspects of uncertainty;
IR	=	drinking water ingestion rate, a default of 1 L/day for a child and 2 L/day for an adult.

a combined UF of 100 is chosen, which includes factors of 10 for intra- and interspecies extrapolation. Thus a non-cancer health-protective concentration for a 10-kg infant (1 year old) can be estimated as:

$$C = \frac{10^9 \text{ pCi/kg-d} \times 10 \text{ kg} \times 0.6}{100 \times 1 \text{ L/day}} = 6 \times 10^7 \text{ pCi/L}$$

For an adult (chronic) exposure,

$$C = \frac{10^9 \text{ pCi/kg-d} \times 70 \text{ kg} \times 0.6}{100 \times 2 \text{ L/day}} = 2.1 \times 10^8 \text{ pCi/L}$$

As shown, the infant and adult health protective concentrations (C) for tritium based on non-cancer endpoints from the long-term tritium studies described by Balonov *et al*. (1993) would be 6×10^7 pCi/L and 2.1×10^8 pCi/L, respectively.

Carcinogenic Effects

The U.S. EPA (1999) has determined a cancer coefficient for tritium of 5.07×10^{-14}/pCi using the DCAL model dose estimates and modeling the response with the linearized multistage model. The health-protective concentration, C (in pCi/L), for tritium in drinking water, corresponding to a *de minimis* cancer morbidity risk of one in a million, is 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 (5.07×10^{-14}/pCi);

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

Thus,

$$C = \frac{1 \times 10^{-6}}{25{,}568 \text{ d} \times 5.07 \times 10^{-14}/\text{pCi} \times 2 \text{ L/d}} = 387 \text{ pCi/L} = 400 \text{ pCi/L (rounded)}$$

The drinking water concentration of tritium resulting in an estimated 1 in a million lifetime cancer morbidity risk is 400 pCi /L. This calculated health-protective concentration based on carcinogenic risks is lower and more health-protective than the concentrations developed for noncarcinogenic effects of 6×10^7 pCi/L and 2.1×10^8 pCi/L, for infants and adults, respectively. Therefore, the PHG has been set at 400 pCi/L, based on cancer risk.

RISK CHARACTERIZATION

The primary sources of uncertainty in the development of the PHG for tritium in drinking water include some of the general issues of uncertainty in any risk assessment, particularly dose-response modeling and estimation of exposures. In the case of tritium, in view of its weak evidence for carcinogenicity based on animal studies and no human information, it is to assume that tritium is a human carcinogen solely on its radioactive properties. A substantial body of information exists on the carcinogenic effects of radionuclides on human subjects. Thus, U.S. EPA feels it is appropriate to consider all radionuclides as potential carcinogens. U.S. EPA and other entities have developed and are perfecting models to estimate human body exposures to radionuclides; the recent reassessment decreases the uncertainty of the estimations.

The PHG for tritium of 400 pCi /L was based on the carcinogenic potency of 5.07×10^{-14} per pCi developed by U.S. EPA (1999) and an assumed *de minimis* excess individual cancer risk level of 10^{-6}. The corresponding tritium concentrations in water for cancer risks of 10^{-5} or 10^{-4} are 4,000 pCi/L and 40,000 pCi/L, respectively. No additional assumptions are needed with respect to the use of an RSC for tritium. The U.S. EPA's risk value is specific for the intake of tritium from drinking water only.

A non-cancer public health-protective concentration is provided for perspective, although this value is so large, compared to the cancer-based value, that it is largely irrelevant for public health protection. Also, the derivation of this value from the endpoints of changes in lifespan and hematopoietic tissues in the chronic mouse study reported by Balonov *et al.* (1993) must be considered highly uncertain. The estimation of a relative source

contribution of 0.6 is similarly uncertain, but values anywhere within the default range of 0.2 to 0.8 are unlikely to be of public health significance.

The federal MCL of 20,000 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 was applied to all beta/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 current tritium MCL of 20,000 pCi/L falls within the U.S. EPA risk goal range of 10^{-4} to 10^{-6} for radionuclides (U.S. EPA, 2000).

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 10 summarizes the international and national guidelines and standards pertinent to human exposure to ionizing radiation and tritium. These include the guidelines from the ICRP and NCRP, relevant federal standards from the NRC, U.S. EPA, and the DOT. Almost all state regulations and guidance incorporate the U.S. EPA MCL.

The U.S. EPA promulgated Maximum Contaminant Levels (MCLs) for tritium 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 tritium, U.S. EPA set a separate MCL of 20,000 pCi/L because the gross beta screening methodology does not account for tritium. Tritium as water vapor is lost in the analysis.

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 tritium the MCL remains at 20,000 pCi/L because updated dosimetry and risk levels yielded similar concentrations. This MCL is scheduled to be reviewed in the next two to three years for risk management issues.

Table 10. Relevant Radiation Protection Guidelines and Regulations

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	tritium 20,000 pCi/L (40 CFR 141)
DOT	**Regulation** for transport in normally occupied space.	2 mrem/hour (49 CFR 173)

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