2. RELEVANCE TO PUBLIC HEALTH

2.1 BACKGROUND AND ENVIRONMENTAL EXPOSURES TO CESIUM IN THE UNITED STATES

Naturally-occurring cesium exists as the stable isotope (^{133}Cs) in the earth's crust at an average concentration of about 1 ppm in granites and 4 ppm in sedimentary rocks. The most important source of commercial cesium is the mineral pollucite, which usually contains about 5–32% Cs_2O by weight. The largest deposits of pollucite are located in Manitoba, Canada and account for about two-thirds of the world's known supply. Cesium has very low mobility in soil surfaces. Clay minerals and soils rich in exchangeable potassium adsorb cesium by binding the cations to interlayer positions of the clay particles. The low hydration energy of cesium cations is primarily responsible for their selective sorption and fixation by clays, which can result in limited uptake of cesium by grass and plant material. Continental dust and soil erosion are the main emission sources of naturally-occurring cesium that is present in the environment. As a result of human activities, however, cesium is released into the environment globally in small amounts. Cesium has also been detected in the fly ash of hazardous waste incinerators and coal burning power plants. Cesium is deposited on plants and trees by wet and dry deposition and can be absorbed into the flora through its foliage. The deposited cesium can make its way to soil through litter decomposition. Due to its low relative abundance, limited use in industry, and relatively low level of toxicity observed in animal studies, exposure to stable cesium is not considered to be a significant public health concern.

Radioactive isotopes of cesium (^{134}Cs and ^{137}Cs) are formed during nuclear fission, in commercial applications such as the generation of electricity at nuclear power plants. However, high levels of ^{134}Cs and ^{137}Cs have been released to the environment, as a result of atmospheric nuclear weapons testing (which has been discontinued for many years) or underground weapons testing and the accident at the Chernobyl, Ukraine nuclear reactor site in 1986. Once released, these radioactive cesium isotopes persist in the environment, with the potential for adverse health effects. Following release to the atmosphere, radioactive cesium can travel thousands of miles before settling to earth, and is removed by wet and dry deposition. Radioactive cesium can also be released to soil or water in liquid effluents from spent fuel and fuel reprocessing plants.

The total amount of ^{137}Cs released from weapons testing through 1980 was estimated as $2.6x10^7$ Ci ($9.6x10^{17}$ Bq), 76% of which was released in the northern hemisphere and 24% in the southern hemisphere.

The accident at the Chernobyl nuclear power plant resulted in the release of an estimated $5.4x10^5$ Ci ($2.0x10^{16}$ Bq) of ^{134}Cs and $1.1x10^6$ Ci ($4.0x10^{16}$ Bq) of ^{137}Cs into the atmosphere over Europe (see Agency for Toxic Substances and Disease Registry 1999 for details of other accidental releases). Routine activities at nuclear power plants and fuel-reprocessing stations also release ^{137}Cs and ^{134}Cs to the environment on a regular basis, but these are at such levels as to be considered insignificant.

Since the half-life for some radioactive isotopes of cesium is long (the half-life of ^{137}Cs is about 30 years and the half-life of ^{134}Cs is about 2 years), the general population is exposed to ^{137}Cs and ^{134}Cs for long periods of time after it is released from a nuclear accident or weapons test, with the greatest exposure occurring near the source. Although inhalation and dermal exposure is possible, oral ingestion of contaminated food items is the greatest source of internal exposure for both naturally-occurring and radioactive cesium. Workers employed in the mining and milling of pollucite ores and the production of cesium compounds are exposed to cesium through oral, dermal, and inhalation routes. Similar routes of exposure to ^{137}Cs and ^{134}Cs are experienced by workers employed in the nuclear industry. External exposure to beta and gamma radiation can also occur for workers employed in the nuclear industry as well as for the general population following an accidental release or weapons test.

As discussed in Appendix A, the average annual effective dose of ionizing radiation (including ^{134}Cs and ^{137}Cs) from anthropogenic sources to the U.S. population is very small in comparison to natural sources.

2.2 SUMMARY OF HEALTH EFFECTS

Information regarding health effects in humans that can be associated with exposure to higher-than-normal levels of stable cesium is restricted to an account of decreased appetite, nausea, and diarrhea in a man who repeatedly ingested experimental amounts of cesium chloride and reports of prolonged QT syndrome and associated cardiac arrhythmias in patients who ingested cesium chloride as a component of homeopathic remedies.

Exposure to radioisotopes of cesium is of much greater human health concern. Energy released by radioactive isotopes can result in significant damage to living cells. Both ^{134}Cs and ^{137}Cs emit beta

particles and gamma rays, which may ionize molecules within cells penetrated by these emissions and result in tissue damage and disruption of cellular function. The most important exposure routes for radioisotopes of cesium are external exposure to the radiation released by the radioisotopes and ingestion of radioactive cesium-contaminated food sources. Inhalation and dermal exposure routes may also present a health hazard. The hazards of external exposure to ^{134}Cs and ^{137}Cs are similar to those of other gamma- and beta-emitting radionuclides.

Radiation absorbed doses are expressed in terms of the amount of energy absorbed per unit mass, in units called rad or gray (Gy) (see Appendix D and Agency for Toxic Substances and Disease Registry 1999 for a complete description of principles of ionizing radiation). Generally, acute radiation doses below 15 rad (0.15 Gy) do not result in observable adverse health effects. At doses in the range of 15–50 rad (0.15–0.5 Gy), subclinical responses such as chromosomal breaks and transient changes in formed elements of the blood may be seen in sensitive individuals. Symptoms of acute radiation syndrome are observed at radiation doses above 50 rad (0.5 Gy), characterized by transient hematopoietic manifestations, nausea and vomiting, and moderate leukopenia at doses near 100 rad (1 Gy), progressing through more serious hematopoietic symptoms, clinical signs, and gastrointestinal symptoms with increasing dose (100–800 rad or 1–8 Gy), and usually death in persons receiving total doses ≥1,000 rad (10 Gy). Other health effects from acute or continued exposure to ionizing radiation may include reproductive, developmental, and latent cancer effects.

Signs and symptoms of acute toxicity from external and internal exposure to high levels of radiation from ^{134}Cs or ^{137}Cs are typical of those observed in cases of high exposure to ionizing radiation in general. Depending on the radiation dose, symptoms may include those typical of acute radiation syndrome (vomiting, nausea, and diarrhea), skin and ocular lesions, neurological signs, chromosomal abnormalities, compromised immune function, and death.

Acute or repeated exposure of humans or animals to ionizing radiation (from radioisotopes of cesium or other radioactive elements) may result in reduced male fertility, abnormal neurological development following exposure during critical stages of fetal development, and genotoxic effects such as increased frequencies of chromosomal aberrations, T-lymphocyte point mutations, dominant lethal mutations, and reciprocal translocations.

Due to the ionizing properties of radionuclides such as ^{134}Cs and ^{137}Cs, increased cancer risk would be expected among exposed individuals. However, studies of increased cancer risk specifically associated

with exposure of humans to radioactive cesium isotopes were not located. The only documented reports of health effects in humans exposed to cesium as the source of radiation are derived from accidental exposure to a ^{137}Cs source in 1987 in Goiânia, Brazil, and during 1996 and 1997 in Russia. Long-term cancer studies on exposed individuals have not been completed to date.

Animal studies indicate increased risk of cancer following external or internal exposure to relatively high doses of radiation from ^{137}Cs sources. Increased lifetime risk of mammary tumors was noted in female rats acutely exposed to whole-body radiation. Intravenous injection of ^{137}Cs (as cesium chloride) in dogs resulted in long-term increased risk of all cancers combined in males, and all cancers combined (excluding mammary cancer) in females.

Immunological and Lymphoreticular Effects. Humans who were accidentally exposed externally and internally to ^{137}Cs that resulted in estimated radiation absorbed doses of 100–700 rad (1–7 Gy), exhibited severe bone marrow depression. Similar effects were seen in dogs exposed to ^{137}Cs by intravenous injection, resulting in estimated bone marrow doses of 700–2,400 rad (7–24 Gy).

Reproductive Effects. Exposure to radioisotopes of cesium may result in reduced fertility in males, as evidenced by reduced concentrations of spermatozoa in men who had been exposed externally and internally to ^{137}CsCl approximately 1 month prior to testing. Reduced fertility, including sterility, was reported in male mice exposed to gamma radiation from ^{137}Cs either by total-body external radiation, which resulted in a total radiation dose of 300 rad (3 Gy) over a 19.5-day exposure period, or by single or repeated oral dosing, which resulted in estimated total testicular radiation doses of 300–385 rad (3–3.85 Gy), measured at 5 weeks post-treatment. No significant reduction in male fertility was seen from total testicular radiation doses in the range of 10–100 rad (0.1–1 Gy). Persistent germinal epithelium damage and azoospermia were reported in all long-term surviving dogs that had been administered ^{137}Cs (as cesium chloride) by intravenous injection at activity levels resulting in long-term total whole-body doses ranging from 742 to 1,640 rad (7.42–16.40 Gy).

Developmental Effects. Developmental effects such as reduced post-natal body weight, impaired motor activity, morphological changes in the brain, reduced head size, and retarded odontogenesis and palatal closure have been reported in rats that had been exposed to radioactive cesium sources (^{137}Cs) *in utero* via whole-body external exposure of dams; effects were of largest magnitude when exposure occurred around gestational day 15. Reported developmental effects in similarly-exposed mice included significantly decreased brain weight and increased aggressive behavior. Atomic bomb survivors of

Hiroshima and Nagasaki, exposed to high levels of ionizing radiation *in utero* during weeks 8–15 or 16–25 post-ovulation, exhibited later signs of impaired cognitive function. Radiation-induced developmental effects would be expected in humans or animals exposed to similar levels of ionizing radiation from any ionizing radiation source, including a radiocesium source. Resulting adverse health effects would be due to the external, penetrating gamma radiation, not cesium *per se*.

Neurological Effects. Excess exposure to stable cesium appears to result in central nervous system effects. A man who voluntarily ingested cesium chloride daily for 36 days reported neurological signs that included feelings of euphoria, heightened sense perception, and tingling sensations within 15 minutes of dosing, in the absence of apparent adverse mental or motor skills. In animal studies, administration of cesium chloride has been reported to trigger stimulant and depressant central nervous system responses.

Since radioisotopes of cesium such as ^{134}Cs and ^{137}Cs emit beta particles and gamma rays capable of ionizing cells, acute radiation doses >3,000 rad (30 Gy) in humans would be expected to result in symptoms indicative of central nervous system syndrome that include immediate onset of violent nausea and vomiting, diarrhea, irrational behavior, circulatory system collapse, and neuromuscular incoordination, followed by convulsions, coma, and death within 48 hours (see Agency for Toxic Substances and Disease Registry 1999 for more detailed information on health effects from exposure to ionizing radiation).

Cancer. Studies that assess the risk of cesium-induced cancer are restricted to radioactive isotopes, not stable cesium. No human studies were located in which cancer incidence was specifically associated with exposure to radioisotopes of cesium. Due to the nature of ionizing radiation in general, carcinogenic effects similar to those observed in Japanese survivors of the 1945 atomic bombing incidents might be expected among individuals acutely exposed to high levels of radiation from a radioactive cesium source (see Agency for Toxic Substances and Disease Registry 1999 for a detailed discussion of the carcinogenic effects of ionizing radiation). However, it is unlikely that levels of ionizing radiation as high as those experienced by the survivors of the atomic bombing incidents would be experienced by individuals who might be exposed to a radiocesium source. Exceptions are reports of accidental human exposures to radioactive cesium sources in Goiânia, Brazil, in 1987 and Lilo, Georgia (Russia) in 1996 and 1997. However, the incidents are too recent for meaningful carcinogenicity data. The EPA Office of Radiation and Indoor Air (ORIA) has classified all radionuclides, including radioisotopes of cesium, as known human carcinogens.

Animal studies indicate increased risk of cancer following external or internal exposure to relatively high doses of radiation from ^{137}Cs sources. Increased lifetime risk of mammary tumors was noted in female rats acutely exposed to whole-body radiation. There were no significant differences between age groups irradiated at 8, 12, 16, 22, or 36 weeks of age, but irradiation at 64 weeks yielded fewer carcinomas than unirradiated controls. In lifetime studies of dogs administered single intravenous doses of ^{137}CsCl, which resulted in average initial body burdens ranging from 36.4 to 147 MBq/kg (1 to 4 mCi/kg), benign and malignant neoplasms were found in a variety of tissues and organs, with no apparent single target organ of toxicity.

2.3 MINIMAL RISK LEVELS

Inhalation MRLs

No acute-, intermediate-, or chronic-duration inhalation MRLs were derived for cesium due to the lack of suitable human or animal data regarding health effects following inhalation exposure to stable or radioactive cesium. Available information, considered relevant to inhalation exposure, is limited to two studies of dogs intravenously administered ^{137}CsCl (Nikula et al. 1995, 1996; Redman et al. 1972). Adverse health effects included depressed blood factors, severe bone marrow depression, germinal cell damage, early death, and increased incidences of benign and malignant neoplasms in a variety of tissues and organs. Striking similarities in the biokinetics, observed in laboratory animals exposed to ^{137}CsCl via either parenteral injection or inhalation or oral routes, indicate that adverse health effects might be common to all three routes of exposure (Boecker et al. 1969a; Melo et al. 1996, 1997; Nikula et al. 1995, 1996). However, extrapolation of data across exposure routes was not considered to be a valid basis for the derivation of inhalation MRLs.

Oral MRLs

No acute-, intermediate-, or chronic-duration oral MRLs were derived for stable cesium due to the lack of suitable human or animal data regarding health effects following oral exposure to stable or radioactive cesium. Reports of health effects following oral exposure to stable cesium are limited. Daily ingestion of approximately 68 mg Cs/kg (as cesium chloride) for up to 36 days resulted in decreased appetite, nausea, and diarrhea, as well as neurological signs within 15 minutes following ingestion (Neulieb 1984). Prolonged QT syndrome and associated cardiac arrhythmias were reported in patients who ingested cesium chloride as a component of homeopathic remedies (Bangh et al. 2001; Harik et al. 2002; Saliba et al. 2001). Animal studies regarding oral exposure to stable cesium are limited to LD_{50} studies that

indicate relatively low toxicity for stable cesium compounds (Ghosh et al. 1990; Johnson et al. 1975; Khosid 1967). Information regarding human exposure to radioactive cesium is inadequate because no human data were available on health effects from oral exposure to radioactive cesium. Oral data regarding health effects in animals exposed to radioactive cesium are restricted to a single study in which only reproductive and genotoxic end points were reported (Ramaiya et al. 1994).

Due to striking similarities in the biokinetics, observed in laboratory animals exposed to ^{137}CsCl via either parenteral injection or inhalation or oral routes, it has been suggested that adverse health effects might be common to all three routes of exposure (Boecker et al. 1969a; Melo et al. 1996, 1997; Nikula et al. 1995, 1996). Depressed blood factors, severe bone marrow depression, germinal cell damage, early death, and increased incidences of benign and malignant neoplasms in a variety of tissues and organs were observed in dogs intravenously administered ^{137}CsCl (Nikula et al. 1995, 1996; Redman et al. 1972). However, extrapolation of data across exposure routes was not considered to be a valid basis for the derivation of oral MRLs.

MRLs for External Exposure to Cesium Isotopes

Two MRLs have been derived for ionizing radiation (Agency for Toxic Substances and Disease Registry 1999) and are applicable to external exposure to radioisotopes of cesium:

- An MRL of 400 mrem (4.0 mSv) has been derived for acute-duration external exposure to ionizing radiation (14 days or less).

The acute MRL is based on results of a study by Schull et al. (1988) in which neurological effects of radiation, measured by intelligence test scores, were evaluated in children 10–11 years of age who had been exposed at critical stages of fetal development (gestation weeks 8–15) during the atomic bombing of Hiroshima and Nagasaki. When IQ scores were regressed on radiation dose estimates, IQ diminished linearly with increasing dose, resulting in an estimated decrease in IQ score of approximately 25 points per 100 rad (100 rem in dose equivalent) or 0.25 points/rem (25 points/Sv). To derive the MRL of 400 mrem (4.0 mSv), the Agency for Toxic Substances and Disease Registry (1999) divided the dose associated with a predicted change of 0.25 IQ points (1 rem) by an uncertainty factor of 3 (for human variability/sensitive population). The Agency for Toxic Substances and Disease Registry (1999) noted that a change in IQ points of 0.25 is less than the reported difference of 0.3 IQ points between separated and unseparated identical twins (Burt 1966).

The NRC set a radiation exposure limit of 500 mrem (5 mSv) for pregnant working women over the full gestational period (USNRC 1991). For the critical gestational period of 8–15 weeks, ATSDR believes that the acute MRL of 400 mrem (4 mSv) is consistent with the NRC limit and could be applied to either acute (0–14-day) or intermediate (15–365-day) exposure periods.

- An MRL of 100 mrem/year (1.0 mSv/year) above background has been derived for chronic-duration external exposure to ionizing radiation (365 days or more).

The MRL is based on the BEIR V (1990) report that the average annual effective ionizing radiation dose to the U.S. population is 360 mrem/year (3.6 mSv/year) from all background sources of radiation (earth, cosmic rays, building materials, etc.), a dose not expected to produce adverse health effects. This dose is obtained mainly by naturally-occurring radiation from external sources, medical uses of radiation, and radiation from consumer products. An uncertainty factor of 3 (for human variability) was applied to the NOAEL.