ATTACHMENT D5

TOXICITY PROFILES

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D5. TOXICITY PROFILES

D5.1 INORGANIC COMPOUNDS

D5.1.1 Aluminum (CAS 007429-90-5) (RAIS)

Aluminum is a silver-white, flexible metal with a vast number of uses. It makes up about 8% of the earth's crust. The aluminum content of seawater ranges from 3 to 2,400 µg/L. Aluminum metal is used as a structural material in the construction, automotive, and aircraft industries; in the production of metal alloys; and in the electrical industry in power lines, insulated cables, and wiring. Other uses of aluminum metal include cooking utensils, decorations, fencing, highway signs, cans, food packaging, foil, and dental crowns and dentures. Aluminum powder is used in paints and fireworks, and natural aluminum minerals are used in water purification, sugar refining, and in the brewing and paper industries. Aluminum borate is used in the production of glass and ceramics, and aluminum chloride is used to make rubber, lubricants, wood preservatives, and cosmetics. Aluminum chlorohydrate is the active ingredient in antiperspirants and deodorants, while aluminum hydroxide is used as a pharmaceutical to lower plasma phosphorus levels of patients with kidney failure. Until recently, aluminum has existed in forms not available to humans and most other species; however, acid rain has increased the availability of aluminum to biological systems and has resulted in destructive effects to fish and plant species. It is unknown if humans are susceptible to this increased bioavailability. It is poorly absorbed and efficiently eliminated; however, when absorption does occur, aluminum is distributed mainly in bone, liver, testes, kidneys, and brain.

The respiratory system appears to be the primary target following inhalation exposure to aluminum. Alveolar proteinosis has been observed in guinea pigs, rats, and hamsters exposed to aluminum powders. Rats and guinea pigs exposed to aluminum chlorohydrate exhibited an increase in alveolar macrophages, increased relative lung weight, and multifocal granulomatous pneumonia. Male rats exposed to aluminum (as aluminum chloride) via gavage for six months exhibited decreased spermatozoa counts and sperm motility and testicular histological and histochemical changes. Male rats exposed to drinking water containing aluminum (as aluminum potassium sulfate) for a lifetime exhibited increases in unspecified malignant and nonmalignant tumors, and similarly exposed female mice exhibited an increased incidence of leukemia. Rats and guinea pigs exposed via inhalation to aluminum chlorohydrate developed lung granulomas, while granulomatous foci developed in similarly exposed male hamsters.

Aluminum has been placed in the U.S. Environmental Protection Agency (EPA) weight-of-evidence classification D, not classifiable as to human carcinogenicity. No slope factors, therefore, were used in this baseline human health risk assessment (BHHRA).

Chronic reference doses (RfDs) for aluminum also are available in Risk Assessment Information System (RAIS). The oral and inhalation RfDs of 1.00E+00 and 1.43E-03 mg/(kg × day), respectively, were used in the BHHRA. The gastrointestinal (GI) absorption factor is 1.0 and the corresponding absorbed dose RfD is 1.00E-01 mg/(kg × day).

D5.1.2 Antimony (CAS 007440-36-0) (RAIS)

Antimony is a naturally occurring silvery-white metal that is found in the earth's crust. Antimony ores are mined and then mixed with other metals to form antimony alloys or combined with oxygen to form antimony oxide. Little antimony is currently mined in the United States. It is brought into this country from other countries for processing; however, there are companies in the United States that produce antimony as a by-product of smelting lead and other metals. Antimony is used in lead storage batteries,

solder, sheet and pipe metal, bearings, castings, and pewter. Antimony oxide is added to textiles and plastics to prevent them from catching fire. It also is used in paints, ceramics, and fireworks, and as enamels for plastics, metal, and glass.

Metallic antimony and a few trivalent antimony compounds are the most significant regarding exposure potential and toxicity. Antimony is a common urban air pollutant, occurring at an average concentration of 0.001 $\mu g/m^3$. Exposure to antimony may occur via inhalation and by ingestion of contaminated food.

Acute oral and inhalation exposure of humans and animals to high doses of antimony or antimony-containing compounds (antimonials) may cause gastrointestinal disorders (vomiting, diarrhea), respiratory difficulties, and death at extremely high doses. Subchronic and chronic oral exposure may affect hematologic parameters. Long-term oral exposure to high doses of antimony or antimonials has been shown to adversely affect longevity in animals. Long-term occupational exposure of humans has resulted in electrocardiac disorders, respiratory disorders, and possibly increased mortality. Antimony levels for these occupational exposure evaluations ranged from 2.2 to 11.98 mg Sb/m^3. Based on limited data, occupational exposure of women to metallic antimony and several antimonials has been reported to have caused alterations in the menstrual cycle and an increased incidence of spontaneous abortions.

The Department of Health and Human Services (DHHS), the International Agency for Research on Cancer (IARC), and the EPA have not classified antimony as to its human carcinogenicity.

Chronic RfDs for antimony also are available in RAIS. The oral RfD used in the BHHRA is 4.00E-04 (mg/kg-day). The GI absorption factor is 0.15 and the corresponding absorbed dose RfD is 6.00E-05 (mg/kg-day).

D5.1.3 Arsenic (CAS 007440-38-2) (RAIS)

Arsenic is a naturally occurring element widely distributed in the earth's crust. In the environment, arsenic is combined with oxygen, chlorine, and sulfur to form inorganic arsenic compounds. Arsenic in animals and plants combines with carbon and hydrogen to form organic arsenic compounds. Inorganic arsenic compounds are used mainly to preserve wood. Organic arsenic compounds are used as pesticides, primarily on cotton plants. Arsenic cannot be destroyed in the environment. It can change its form, only. Arsenic in air either will settle to the ground or will be washed out of the air by rain. Many arsenic compounds can dissolve in water. Fish and shellfish can accumulate arsenic, but the arsenic in fish is mostly in a form that is not harmful. The toxicity of inorganic arsenic depends on its valence state and also on the physical and chemical properties of the compound in which it occurs.

Water soluble inorganic arsenic compounds are absorbed through the GI tract and lungs; distributed primarily to the liver, kidney, lung, spleen, aorta, and skin; and excreted mainly in the urine at rates as high as 80%. Symptoms of acute inorganic arsenic poisoning in humans are nausea, anorexia, vomiting, epigastric and abdominal pain, and diarrhea. Dermatitis (exfoliative erythroderma), muscle cramps, cardiac abnormalities, hepatotoxicity, bone marrow suppression and hematologic abnormalities (anemia), vascular lesions, and peripheral neuropathy (motor dysfunction, paresthesia) also have been reported. Oral doses as low as 20–60 µg/kg/day have been reported to cause toxic effects in some individuals. Severe exposures can result in acute encephalopathy, congestive heart failure, stupor, convulsions, paralysis, coma, and death. The acute lethal dose to humans has been estimated to be about 0.6 mg/kg/day.

General symptoms of chronic arsenic poisoning in humans are weakness, general debility and lassitude, loss of appetite and energy, loss of hair, hoarseness of voice, loss of weight, and mental disorders. Primary target organs are the skin (hyperpigmentation and hyperkeratosis), nervous system (peripheral

neuropathy), and vascular system. Anemia, leukopenia, hepatomegaly, and portal hypertension also have been reported. In addition, possible reproductive effects include a high male to female birth ratio.

Epidemiological studies have revealed an association between arsenic concentrations in drinking water and increased incidences of skin cancers, as well as cancers of the liver, bladder, respiratory, and GI tracts. Occupational exposure studies have shown a clear correlation between exposure to arsenic and lung cancer mortality. Several studies have shown that inorganic arsenic can increase the risk of lung cancer, skin cancer, bladder cancer, liver cancer, kidney cancer, and prostate cancer. The World Health Organization, the DHHS, and the EPA have determined that inorganic arsenic is a human carcinogen and is classified A, human carcinogen.

Cancer slope factors for arsenic are available from EPA's IRIS. The values used in the BHHRA are 1.50E+00, 1.51E+01, and 1.50 E+00 $[mg/(kg \times day)]^{-1}$ for the oral, inhalation, and dermal exposure routes, respectively. The slope factor for the dermal exposure route was calculated by assuming a GI absorption factor of 1.0.

Chronic RfDs for arsenic also are available in RAIS. The oral and dermal values used in the BHHRA were 3.00E-04 mg/(kg × day) for both. The dermal RfD was calculated by assuming a GI absorption factor of 1.0.

D5.1.4 Cadmium (CAS 007440-43-9) (RAIS)

Cadmium is a naturally occurring metal that is used in various chemical forms in metallurgical and other industrial processes, and in the production of pigments. Environmental exposure can occur via the diet and drinking water (ATSDR 1989).

Cadmium is absorbed more efficiently by the lungs (30 to 60%) than by the gastrointestinal tract, the latter being a saturable process (Nordberg et al., 1985). Cadmium is transported in the blood and widely distributed in the body but accumulates primarily in the liver and kidneys (Goyer 1991). Cadmium burden (especially in the kidneys and liver) tends to increase in a linear fashion up to about 50 or 60 years of age after which the body burden remains somewhat constant. Metabolic transformations of cadmium are limited to its binding to protein and nonprotein sulfhydryl groups, and various macromolecules, such as metallothionein, which is especially important in the kidneys and liver (ATSDR 1989). Cadmium is excreted primarily in the urine.

Acute oral exposure to 20–30 g has caused fatalities in humans. Exposure to lower amounts may cause gastrointestinal irritation, vomiting, abdominal pain, and diarrhea (ATSDR 1989). An asymptomatic period of one-half to one hour may precede the onset of clinical signs. Oral LD_{50} values in animals range from 63 to 1125 mg/kg, depending on the cadmium compound (USAF 1990). Longer term exposure to cadmium primarily affects the kidneys, resulting in tubular proteinosis although other conditions such as "itai-itai" disease may involve the skeletal system. Cadmium involvement in hypertension is not fully understood (Goyer 1991).

Inhalation exposure to cadmium and cadmium compounds may result in effects including headache, chest pains, muscular weakness, pulmonary edema, and death (USAF 1990). The 1-minute and 10-minute lethal concentration of cadmium for humans has been estimated to be about 2,500 and 250 mg/m^3, respectively (Barrett et al. 1947; Beton et al. 1966). An 8-hour TWA (time-weighted-average) exposure level of 5 mg/m^3 has been estimated for lethal effects of inhalation exposure to cadmium, and exposure to 1 mg/m^3 is considered to be immediately dangerous to human health (Friberg 1950). Renal toxicity (tubular proteinosis) also may result from inhalation exposure to cadmium (Goyer 1991).

Chronic oral RfDs of 5E-4 and 1E-3 mg/kg/day have been established for cadmium exposure via drinking water and food, respectively (EPA 1991). Both values reflect incorporation of an uncertainty factor of 10. The RfDs are based on an extensive database regarding toxicokinetics and toxicity in both humans and animals, the critical effect being renal tubular proteinuria. Confidence in the RfD and data base is high.

Inhalation RfC values currently are not available.

The target organ for cadmium toxicity via oral exposure is the kidney (Goyer 1991). For inhalation exposure, both the lungs and kidneys are target organs for cadmium-induced toxicity (ATSDR 1989; Goyer 1991).

There is limited evidence from epidemiologic studies for cadmium-related respiratory tract cancer (ATSDR 1989). An inhalation unit risk of 1.8E-3 $(\mu g/m^3)^{-1}$ and an inhalation slope factor of 6.1E+0 $(mg/kg/day)^{-1}$ are based on respiratory tract cancer associated with occupational exposure (EPA 1985). Based on limited evidence from multiple occupational exposure studies and adequate animal data, cadmium is placed in weight-of-evidence group B1, probable human carcinogen.

D5.1.5 Cobalt

Cobalt is a naturally-occurring element that has properties similar to those of iron and nickel. It has an atomic number of 27. There is only one stable isotope of cobalt, which has an atomic mass number of 59; however, there are many unstable or radioactive isotopes, two of which are commercially important, Co-60 and Co-57. All isotopes of cobalt behave the same chemically and will therefore have the same chemical behavior in the environment and the same chemical effects on the human body.

Small amounts of cobalt occur in natural forms in most rocks, soil, water, plants, and animals, typically in small amounts. Cobalt also is found in meteorites. Elemental cobalt is a hard, silvery grey metal. However, cobalt usually is found in the environment combined with other elements such as oxygen, sulfur, and arsenic. Small amounts of these chemical compounds can be found in rocks, soil, plants, and animals. A biochemically important cobalt compound is vitamin B12 or cyanocobalamin. Vitamin B12 is essential for good health in animals and humans.

Cobalt metal usually is mixed with other metals to form alloys, which are harder or more resistant to wear and corrosion. These alloys are used in a number of military and industrial applications such as aircraft engines, magnets, and grinding and cutting tools. They are also used in artificial hip and knee joints. Cobalt compounds are used as colorants in glass, ceramics, and paints, as catalysts, and as paint driers. Cobalt colorants have a characteristic blue color; however, not all cobalt compounds are blue. Cobalt compounds are also used as trace element additives in agriculture and medicine.

Cobalt has both beneficial and harmful effects on human health. Cobalt is beneficial for humans because it is part of vitamin B12, which is essential to maintain human health. Cobalt (0.16–1.0 mg cobalt/kg of body weight) has also been used as a treatment for anemia, including in pregnant women, because it causes red blood cells to be produced. Cobalt also increases red blood cell production in healthy people, but only at very high exposure levels. Cobalt is also essential for the health of various animals, such as cattle and sheep. Exposure of humans and animals to levels of cobalt normally found in the environment is not harmful.

Too much cobalt can cause harmful health effects. Workers who breathed air containing 0.038 mg cobalt/m^3 (about 100,000 times the concentration normally found in ambient air) for 6 hours had trouble breathing. Serious effects on the lungs, including asthma, pneumonia, and wheezing, have been found in people exposed to 0.005 mg cobalt/m^3 while working with hard metal, a cobalt-tungsten carbide alloy.

People exposed to 0.007 mg cobalt/m^3 at work have also developed allergies to cobalt that resulted in asthma and skin rashes.

Nonradioactive cobalt has not been found to cause cancer in humans or in animals following exposure in the food or water. Cancer has been shown, however, in animals who breathed cobalt or when cobalt was placed directly into the muscle or under the skin. Based on the animal data, the International Agency for Research on Cancer (IARC) has determined that cobalt is possibly carcinogenic to humans.

Much of our knowledge of cobalt toxicity is based on animal studies. Cobalt is essential for the growth and development of certain animals, such as cows and sheep. Short-term exposure of rats to high levels of cobalt in the air results in death and lung damage. Longer-term exposure of rats, guinea pigs, hamsters, and pigs to lower levels of cobalt in the air results in lung damage and an increase in red blood cells. Short-term exposure of rats to high levels of cobalt in the food or drinking water results in effects on the blood, liver, kidneys, and heart. Longer-term exposure of rats, mice, and guinea pigs to lower levels of cobalt in the food or drinking water results in effects on the same tissues (heart, liver, kidneys, and blood) as well as the testes, and also causes effects on behavior. Sores were seen on the skin of guinea pigs following skin contact with cobalt for 18 days. Generally, cobalt compounds that dissolve easily in water are more harmful than those that are hard to dissolve in water.

Cancer slope factors for cobalt used in the BHHRA are 3.15E+01 $[mg/(kg \times day)]^{-1}$ for the inhalation exposure routes, respectively. Chronic RfDs for cobalt used in the BHHRA were 3.00E-04 mg/(kg × day) for both oral and absorbed doses. The dermal RfD was calculated by assuming a GI absorption factor of 1.0.

D5.1.6 Copper (CAS 007440-50-8) (RAIS)

Copper is a reddish metal that occurs naturally in the environment in plants and animals. Copper is an essential element for all living things including humans. Copper is extensively mined in the United States and is used to make wire, sheet metal, pipes, and pennies. It also is used in farming to treat some plant diseases; in water treatment; and to preserve wood, leather, and fabrics. Also, because of its high electrical and thermal conductivity and other properties such as malleability, metallic copper is widely used in the manufacture of electrical equipment.

Copper is an essential trace element that is widely distributed in animal and plant tissues. Copper is necessary for good health and can be absorbed by the oral, inhalation, and dermal routes of exposure. Very large doses, however, can be harmful. In humans, ingestion of gram quantities of copper salts may cause GI, hepatic, and renal effects with symptoms such as severe abdominal pain, vomiting, diarrhea, hemolysis, hepatic necrosis, hematuria, proteinuria, hypotension, tachycardia, convulsions, coma, and death. Acute inhalation exposure to copper dust or fumes at concentrations of 0.075-0.12 mg Cu/m3 may cause metal fume fever with symptoms such as cough, chills, and muscle ache. Skin contact with copper can result in an allergic reaction, usually skin irritation or a skin rash.

No suitable bioassays or epidemiological studies are available to assess the carcinogenicity of copper. EPA, therefore, has placed copper in weight-of-evidence group D, not classifiable as to human carcinogenicity. No slope factors, therefore, were used in this BHHRA.

The chronic RfDs for the oral and dermal routes of exposure from RAIS was used in the BHHRA. The oral and dermal RfDs used were 4.00E-02 (mg/kg-day), for both. The GI absorption factor used was 1.0.

D5.1.7 Iron (CAS 007439-89-6)

Iron is one of the most abundant metals in the environment and is used in many industrial processes. It is an essential element in the human diet. More than 80% of the iron present in the body is involved in the support of red blood cell production. In addition, it is also an essential component of myoglobin and various enzymes. Iron deficiency is the most common cause of anemia (Goodman and Gilman 1985). Exposure to excessive levels of iron may cause GI damage and dysfunction and enlargement of the liver and pancreas (Goodman and Gilman 1985).

Iron has not been classified by EPA with regard to cancer weight-of-evidence. No slope factors were used in this BHHRA.

Chronic RfDs also have not been released by EPA in IRIS or HEAST; however, oral and dermal RfDs of 7.00E-01 mg/(kg × day), for both, were used in the BHHRA based on a provisional value from NCEA. The GI absorption factor used was 1.0.

D5.1.8 Manganese (CAS 007439-96-5) (RAIS)

Manganese is a silver-colored, naturally occurring metal that is found in many types of rocks and makes up about 0.10% of the earth's crust. Manganese is not found alone, but combines with other substances such as oxygen, sulfur, or chlorine. Manganese also can be combined with carbon to make organic manganese compounds, including pesticides (e.g., maneb or mancozeb) and methylcyclopentadienyl manganese tricarbonyl, a fuel additive in some gasolines. Manganese is an essential trace element and is necessary for good health. Normal nutritional requirements of manganese are satisfied through the diet, which is the normal source of the element, with minor contributions from water and air. The National Research Council recommends a dietary allowance of 2–5 mg/day for a safe and adequate intake of manganese for an adult human. Manganese can be found in several food items, including grains, cereals, and tea.

Manganese can elicit a variety of serious toxic responses upon prolonged exposure to elevated concentrations, either orally or by inhalation. The central nervous system is the primary target. Initial symptoms are headache, insomnia, disorientation, anxiety, lethargy, and memory loss. These symptoms progress with continued exposure and eventually include motor disturbances, tremors, and difficulty in walking, symptoms similar to those seen with Parkinsonism. These motor difficulties are often irreversible. Some individuals exposed to very high levels of manganese for long periods of time at work developed mental and emotional disturbances and slow and clumsy body movements. This combination of symptoms is a disease called "manganism."

There are no human cancer data available for manganese. Manganese has been placed in the EPA weight-of-evidence classification D: not classifiable as to human carcinogenicity; therefore, no slope factors were used in this BHHRA.

The oral, inhalation, and dermal RfDs for manganese in diet from RAIS used in the BHHRA were 1.40E-01 and 1.43E-05, and 1.40E-01 mg/(kg × day), respectively. The GI absorption factor is 1.0.

D5.1.9 Mercury (CAS 007439-97-6) (RAIS)

Mercury is a naturally occurring metal which has several forms. The metallic mercury is a shiny, silver-white, odorless liquid; if heated, it is a colorless, odorless gas. Mercury combines with other elements, such as chlorine, sulfur, or oxygen, to form inorganic mercury compounds or "salts," which are usually white powders or crystals. Mercury also combines with carbon to make organic mercury compounds;

methylmercury is the most common organic mercury compound and is produced mainly by microscopic organisms in the water and soil. More mercury in the environment can increase the amounts of methylmercury that these small organisms make. Metallic mercury is used to produce chlorine gas and caustic soda and is also used in thermometers, dental fillings, electrical switches, and batteries. Mercury salts are sometimes used in skin lightening creams and as antiseptic creams and ointments.

The nervous system is very sensitive to all forms of mercury. Methylmercury and metallic mercury vapors are more harmful than other forms, because more mercury reaches the brain in these forms. Exposure to high levels of metallic, inorganic, or organic mercury can permanently damage the brain, kidneys, and developing fetus. Effects on brain functioning may result in irritability, shyness, tremors, changes in vision or hearing, and memory problems. Short-term exposure to high levels of metallic mercury vapors may cause lung damage, nausea, vomiting, diarrhea, increases in blood pressure or heart rate, skin rashes, and eye irritation.

No data were available regarding the carcinogenicity of mercury in humans or animals. EPA has placed inorganic mercury in weight-of-evidence classification D, not classifiable as to human carcinogenicity. Other forms of mercury are possible human carcinogens.

A chronic RfD for the oral route of exposure from RAIS was used in the BHHRA. The values used in the BHHRA are 3.00E-04 and 2.10E-05 (mg/kg-day) for the oral and dermal routes, respectively. The dermal RfD was calculated assuming a GI absorption factor of 7.0E-02.

D5.1.10 Molybdenum (CAS No. 007439-98-7) (RAIS)

Molybdenum (Mo) occurs naturally in various ores; the principal source being molybdenite (MoS_2) (Stokinger 1981). Molybdenum compounds are used primarily in the production of metal alloys. Molybdenum is considered an essential trace element; the provisional recommended dietary intake is 75–250 g/day for adults and older children (NRC 1989).

Water-soluble molybdenum compounds are readily taken up through the lungs and gastrointestinal tract; but insoluble compounds are not. Following absorption, molybdenum is distributed throughout the body with the highest levels generally found in the liver, kidneys, spleen, and bone (Wennig and Kirsch 1988). Limited data suggest that 25 to 50% of an oral dose is excreted in the urine, with small amounts also eliminated in the bile. Biological half-life may vary from several hours in laboratory animals to as much as several weeks in humans (Friberg and Lener 1986; Jarrell et al. 1980; Stokinger 1981; Vanoeteren et al. 1982; Venugopal and Luckey 1978).

Data documenting molybdenum toxicity in humans are limited. The physical and chemical state of the molybdenum, route of exposure, and compounding factors such as dietary copper and sulfur levels may all affect toxicity. Mild cases of molybdenosis may be clinically identifiable only by biochemical changes (e.g., increases in uric acid levels due to the role of molybdenum in the enzyme xanthine oxidase). Excessive intake of molybdenum causes a physiological copper deficiency, and conversely, in cases of inadequate dietary intake of copper, molybdenum toxicity may occur at lower exposure levels.

There is no information available on the acute or subchronic oral toxicity of molybdenum in humans. In studies conducted in a region of Armenia where levels of molybdenum in the soil are high (77 mg Mo/kg), 18% of the adults examined in one town and 31% of those in another town were found to have elevated concentrations of uric acid in the blood and urine, increased blood xanthine oxidase activity, and gout-like symptoms such as arthralgia, articular deformities, erythema, and edema (Kovalskii et al. 1961). The daily molybdenum intake was estimated to be 10–15 mg. An outbreak of genu valgum

(knock-knees) in India was attributed to an increase in Mo levels in sorghum, the main staple food of the region. The estimated daily Mo intake was 1.5 mg (Jarrell et al. 1980).

In animals, acutely toxic oral doses of molybdenum result in severe gastrointestinal irritation with diarrhea, coma, and death from cardiac failure. Oral LD_{50} values of 125 and 370 mg Mo/kg for molybdenum trioxide and ammonium molybdate, respectively, have been reported in laboratory rats (Venugopal and Luckey 1978). Subchronic and chronic oral exposures can result in gastrointestinal disturbances, growth retardation, anemia, hypothyroidism, bone and joint deformities, sterility, liver and kidney abnormalities, and death (Lloyd et al. 1976; Venugopal and Luckey 1978; Valli et al. 1969; Fairhall et al. 1945; Rana and Kumar 1980). Fatty degeneration of the liver occurred in rabbits dosed with 50 mg/kg/day for 6 months (Asmangulyan 1965) and in rats dosed with 5 mg/kg/day as ammonium molybdate for 1 year (Valjcuk and Sramko 1973). Male sterility was reported in rats fed diets containing 80 or 140 ppm Mo (Jeter and Davis 1954). Teratogenic effects have not been observed in mammals, but embryotoxic effects, including reduced weight gain, reduced skeletal ossification, nerve system demyelinization, and reduced survival of offspring have been reported (Wide 1984; Earl and Vish 1979; Schroeder and Mitchener 1971).

Information on the inhalation toxicity of molybdenum in humans following acute and subchronic exposures is not available. Studies of workers chronically exposed to Mo indicate a high incidence of weakness, fatigue, headache, irritability, lack of appetite, epigastric pain, joint and muscle pain, weight loss, red and moist skin, tremor of the hands, sweating, and dizziness (Akopajan 1964; Ecolajan 1965; Walravens et al. 1979). Elevated levels of Mo in blood plasma and urine and high levels of ceruloplasmin and uric acid in blood serum were reported for workers exposed to Mo (8-hr TWA 9.5 mg Mo/m^3) (Walravens et al. 1979). Occupational exposure to molybdenum may also result in increased serum bilirubin levels and decreased blood IgA/IgG ratios due to a rise in alpha-immunoglobulins (Avakajan 1966b; 1968). Direct pulmonary effects of chronic exposure to Mo have been reported in only one study in which 3 of 19 workers exposed to Mo and MoO_3 (1 to 19 mg/m^3) for 3–7 years were symptomatic and had X-ray findings indicative of pneumoconiosis (Mogilevskaya 1963). Adverse reproductive or developmental effects have not been observed in molybdenum workers (Metreveli et al. 1985).

In animal studies, inhalation exposures to molybdenum compounds have resulted in respiratory tract irritation, pulmonary hemorrhages, perivascular edema, and liver and kidney damage (Mogilevskaya 1963; Fairhall, et al. 1945). Other effects reported in animals include diarrhea, muscle incoordination, loss of hair, loss of weight (Fairhall et al. 1945), changes in ECG, increased arterial blood pressure, increased serum lactate dehydrogenase, increased cardiac adrenaline and noradrenaline levels (Babayan et al. 1984), and inflammation of the uterine horns with necrotic foci and endometrial atrophy (Metreveli and Daneliya 1984). Some molybdenum compounds, such as molybdenum trioxide and sodium molybdate (Na_2MoO_4) are strong eye and skin irritants; however, others, such as calcium and zinc molybdates are not primary irritants.

Subchronic and chronic Reference Concentrations (RfC) for molybdenum are not available.

Information on the oral or inhalation carcinogenicity of molybdenum compounds in humans was not available, and animal data indicate that Mo may have an inhibitory effect on esophageal (Luo et al. 1983; van Rensburg et al. 1986; Komada et al. 1990) and mammary carcinogenesis (Wei et al. 1987). However, intraperitoneal injections of MoO_3 in mice produced a significant increase in the number of lung adenomas per mouse and an insignificant increase in the number of mice bearing tumors (Stoner et al. 1976). Molybdenum is placed in EPA Group D, not classifiable as to carcinogenicity in humans (EPA 1990) and calculation of slope factors is not possible.

The chronic oral RfD for molybdenum and molybdenum compounds is 0.005 mg/kg/day, based on biochemical indices in humans (EPA 1992). The subchronic RfD is also 0.005 mg/kg/day (EPA 1992).

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D5.1.11 Nickel (CAS 007440-02-0 for Soluble Nickel Salts) (RAIS)

Nickel is a very abundant element in the environment. It is found primarily combined with oxygen (oxides) or sulfur (sulfides), found in all soils, and is emitted from volcanoes. Pure nickel is a hard, silvery-white metal that is combined with other metals to form alloys. Some of the metals that nickel can be alloyed with are iron, copper, chromium, and zinc. These alloys are used to make metal coins and jewelry and in industry. Nickel compounds also are used for nickel plating, to color ceramics, to make some batteries, and as substances known as catalysts that increase the rate of chemical reactions. Nickel and its compounds have no characteristic odor or taste. Nickel forms included in this profile are nickel carbonyl, CAS number 13463-39-3; nickel refinery dust, no CAS number; nickel subsulfide, CAS number 12035-72-2; and nickel soluble salts, no CAS number.

Nickel is required to maintain health in animals. A small amount of nickel probably is essential for humans, although a lack of nickel has not been found to affect the health of humans. The absorption of nickel is dependent on its physicochemical form, with water-soluble forms being more readily absorbed. The most common adverse health effect of nickel in humans is an allergic reaction. Humans can become sensitive to nickel when jewelry or other nickel-containing items are in direct contact with the skin. Once a person is sensitized to nickel, further contact will produce a reaction; the most common reaction is a skin rash at the site of contact. Less frequently, some humans who are sensitive to nickel have asthma attacks or other reactions following exposure to nickel in food, water, or dust. Lung effects, including chronic bronchitis and reduced lung function, have been observed in workers who breathed large amounts of nickel. Current levels of nickel in workplace air are much lower than in the past, and today few

workers show symptoms of nickel exposure. Humans who are not sensitive to it must eat very large amounts of nickel to show adverse health effects. In large doses (> 0.5 g), some forms of nickel may be acutely toxic to humans when taken orally. Workers who accidentally drank water containing very high levels of nickel (100,000 times more than in normal drinking water) had stomachaches and effects on their blood and kidneys.

Epidemiologic studies have shown that occupational inhalation exposure to nickel dust (primarily nickel subsulfide) at refineries has resulted in increased incidences of pulmonary and nasal cancer. Inhalation studies using rats also have shown nickel subsulfide or nickel carbonyl to be carcinogenic. Based on these data, the EPA has classified nickel subsulfide and nickel refinery dust in weight-of-evidence group A; human carcinogen. Based on an increased incidence of pulmonary carcinomas and malignant tumors in animals exposed to nickel carbonyl by inhalation or by intravenous injection, this compound had been placed in weight-of-evidence group B2: probable human carcinogen. EPA has not evaluated soluble salts of nickel as a class of compounds for potential human carcinogenicity. Because the form of nickel of concern to this BHHRA was soluble salts, no slope factors were used in this BHHRA.

A chronic RfD for the oral and dermal routes of exposure from RAIS was used in the BHHRA. The RfDs used in the BHHRA for the oral and dermal routes of exposure were 2.00E-02 and 8.00E-04 mg/(kg × day), respectively. The dermal route RfD was based on a GI absorption factor of 4.00E-02.

D5.1.12 Silver (CAS 97161-97-2) (RAIS)

Silver is a relatively rare metal that occurs naturally in the earth's crust and is released to the environment from various industrial sources. Human exposure to silver and silver compounds can occur orally, dermally, or by inhalation. Silver is found in most tissues, but has no known physiologic function.

In humans, accidental or intentional ingestion of large doses of silver nitrate has produced corrosive damage of the gastrointestinal tract, abdominal pain, diarrhea, vomiting, shock, convulsions, and death (EPA 1985). Respiratory irritation was noted following acute inhalation exposure to silver or silver compounds. Silver nitrate solutions are highly irritating to the skin, mucous membranes, and eyes (Stokinger 1981).

Ingestion, inhalation, or dermal absorption of silver may cause argyria, the most common indicator of long-term exposure to silver or silver compounds in humans. Argyria is a gray or blue-gray, permanent discoloration of the skin and mucous membranes that is not a toxic effect per se, but is considered cosmetically disfiguring. Chronic inhalation exposure of workers to silver oxide and silver nitrate dusts resulted in upper and lower respiratory irritation, deposition of granular silver-containing deposits in the eyes, impaired night vision, and abdominal pain (Rosenman et al. 1979). Mild allergic responses have been attributed to dermal contact with silver (ATSDR 1990).

In long-term oral studies with experimental animals, silver compounds have produced slight thickening of the basement membranes of the renal glomeruli, growth depression, shortened lifespan, and granular silver-containing deposits in skin, eyes, and internal organs (Matuk et al. 1981; Olcott 1948, 1950). Hypoactivity was seen in rats subchronically exposed to silver nitrate in drinking water (Rungby and Danscher 1984).

A Reference Dose (RfD) of 0.005 mg/kg/day for oral exposure was used in this BHHRA. The absorbed RfD used was 2.00E-04. The lowest-observed-adverse-effect level (LOAEL) of 0.014 mg/kg/day for argyria observed in patients receiving i.v. injections of silver arsphenamine was calculated by EPA (EPA 1992a,b). Data are presently insufficient to derive a Reference Concentration (RfC) for silver (EPA 1992a). The gastrointestinal absorption factor used was 4.00E-02.

Data adequate for evaluating the carcinogenicity of silver to humans or animals by ingestion, inhalation, or other routes of exposure were not found. Based on EPA guidelines, silver is placed in weight-of-evidence group D, not classifiable as to human carcinogenicity (EPA 1992a).

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D5.1.13 Thallium (CAS 007440-28-0) (RAIS)

Pure thallium is a bluish-white metal that is found in trace amounts in the earth's crust. In the past, thallium was obtained as a by-product from smelting other metals; however, it has not been produced in the United States since 1984. Currently, all the thallium is obtained from imports and from thallium reserves. In its pure form, thallium is odorless and tasteless. It can also be found combined with other substances such as bromine, chlorine, fluorine, and iodine. When it's combined, it appears colorless-to-white or yellow. The EPA has evaluated the toxicity of the following thallium compounds: thallic oxide, CAS number 1314-32-5; thallium acetate, CAS number 563-68-8; thallium carbonate, CAS number 6533-73-9; thallium chloride, CAS number 7791-12-0; thallium nitrate, CAS number 10102-45-1; thallium selenite, CAS number 12039-52-0; and thallium sulfate CAS number 7446-18-6. Thallium is

used mostly in manufacturing electronic devices, switches, and closures, primarily for the semiconductor industry. It also has limited use in the manufacture of special glass and for certain medical procedures.

Exposure to high levels of thallium can result in harmful health effects. A study on workers exposed on the job over several years reported nervous system effects, such as numbness of fingers and toes, from breathing thallium. Humans who ingested large amounts of thallium over a short time have reported vomiting, diarrhea, temporary hair loss, and effects on the nervous system, lungs, heart, liver, and kidneys as well as death. It is not known what the effects are from ingesting low levels of thallium over a long time. Birth defects were not reported in the children of mothers exposed to low levels from eating vegetables and fruits contaminated with thallium. Studies in rats, however, exposed to high levels of thallium, showed adverse developmental effects.

Data suitable for evaluating the carcinogenicity of thallium to humans or animals by ingestion, inhalation, or other routes of exposure were not found. Thallium sulfate, selenite, nitrate, chloride, carbonate, acetate, and thallic oxide have been placed in EPA's weight-of evidence Group D, not classifiable as to human carcinogenicity based on inadequate human and animal data. The DHHS and the IARC, have not classified pure thallium as to its human carcinogenicity. No studies are available in humans or animals on the carcinogenic effects of breathing, ingesting, or touching thallium.

Chronic RfDs from RAIS were available for thallium chloride. The RfDs used in the BHHRA for the oral and dermal routes of exposure is 8.00E-05 (mg/kg-day), for both. The dermal route RfD was based on a GI absorption factor of 1.00E+00.

D5.1.14 Uranium (Metal and Soluble Salts) (CAS 007440-61-1)

Uranium is a hard, silvery white amphoteric metal and is a radioactive element. In its natural state it consists of three isotopes: U-234, U-235, and U-238. More than 100 uranium minerals exist; those of commercial importance are the oxides and oxygenous salts. The processing of uranium ore generally involves extraction then leaching either by an acid or a carbonate method. In addition, the metal may be obtained from its halides by fused salt electrolysis. The primary use of natural uranium is in nuclear energy as a fuel for nuclear reactors, in plutonium production, and as feeds for gaseous diffusion plants; it is also a source of radium salts. Uranium compounds are used in staining glass, glazing ceramics, and enameling; in photographic processes; for alloying steels; and as a catalyst for chemical reactions, radiation shielding, and aircraft counterweights (Sittig 1985).

The primary route of exposure to uranium metals and salts is through dermal contact. Uranium soluble compounds act as a poison to cause kidney damage under acute exposure and pneumoconiosis or pronounced blood changes under chronic exposure conditions. Furthermore, it is difficult to separate the toxic chemical effects of uranium and its compounds from their radiation effects. The chronic radiation effects are similar to those produced by ionizing radiation. Reports now confirm that carcinogenicity is related to dose and exposure time. Cancer of the lung, osteosarcoma, and lymphoma have all been reported (Sittig 1985). An EPA weight-of-evidence classification for uranium metal was not located in the available literature. Slope factors for uranium metal also were not available for use in the BHHRA.

Chronic RfDs from RAIS were available for uranium metal (listed as uranium soluble salts). The oral and dermal RfD used in the BHHRA was 3.00E-03 mg/(kg × day), for both. A GI absorption factor of 1.00E+00 was used to derive the dermal RfD.

D5.1.15 Vanadium (CAS 007440-62-2 for metal) (RAIS)

Vanadium is a compound that occurs in nature as a white-to-gray metal and is often found as crystals. Pure vanadium has no smell and usually combines with other elements such as oxygen, sodium, sulfur, or chloride, which greatly alter toxicity. Vanadium and vanadium compounds can be found in the earth's crust and in rocks, some iron ores, and crude petroleum deposits. Vanadium is mostly combined with other metals to make special metal mixtures called alloys. Most of the vanadium used in the United States, vanadium oxide, is used to make steel for automobile parts, springs, and ball bearings. Vanadium oxide is a yellow-orange powder, dark-gray flakes, or yellow crystals. Vanadium also is mixed with iron to make important parts for aircraft engines. Small amounts of vanadium are used in making rubber, plastics, ceramics, and other chemicals.

Exposure to high levels of vanadium can cause harmful health effects. Vanadium compounds are poorly absorbed through the digestive system (0.5–2% of dietary amount), but slightly more readily absorbed through the lungs (20–25%). The major effects from breathing high levels of vanadium are on the lungs, throat, and eyes. Workers who breathed it for short and long periods sometimes had lung irritation, coughing, wheezing, chest pain, runny nose, and a sore throat. These effects stopped soon when removed from the contaminated air. Similar effects have been observed in animal studies. No other significant health effects of vanadium have been found in humans. The health effects in humans of ingesting vanadium are not known. Animals that ingested very large doses have died. Lower, but still high, levels of vanadium in the water of pregnant animals resulted in minor birth defects. Some animals that breathed or ingested vanadium over a long term had minor kidney and liver changes.

There is no evidence that any vanadium compound is carcinogenic; however, very few adequate studies are available for evaluation. No increase in tumors was noted in a long-term animal study where the animals were exposed to vanadium in the drinking water. The DHHS, the IARC, and EPA have not classified vanadium as to its human carcinogenicity.

Chronic RfDs from RAIS were available for vanadium. The RfDs used in the BHHRA for the oral and dermal routes of exposure were 7.00E-05 and 1.820E-06 mg/(kg × day), respectively. The dermal route RfD was based on a GI absorption factor of 2.60E-02.

D5.2 ORGANIC COMPOUNDS

D5.2.1 Total PCBs (High Risk) (RAIS)

PCBs are inert, thermally and physically stable, and have dielectric properties. In the environment, the behavior of PCB mixtures is directly correlated to the degree of chlorination. They have been used in closed systems such as heat transfer liquids, hydraulic fluids and lubricants, and in open systems such as plasticizers, surface coatings, inks, adhesives, pesticide extenders, and for microencapsulation of dyes for carbonless duplicating papers. Aroclor is strongly sorbed to soil and remains immobile when leached with water; however, the mixture is highly mobile in the presence of organic solvents. PCBs are resistant to chemical degradation by oxidation or hydrolysis. PCBs have high bioconcentration factors and tend to accumulate in the fat of fish, birds, mammals, and humans.

PCBs are absorbed after oral, inhalation, or dermal exposure and are stored in adipose tissue. The major route of PCB excretion is in the urine and feces; however, more important is the elimination in human milk. Accidental human poisonings and data from occupational exposure to PCBs suggest initial dermal and mucosal disturbances followed by systemic effects that may manifest themselves several years post-exposure. Initial effects are enlargement and hypersecretion of the Meibomian gland of the eye, swelling

of the eyelids, pigmentation of the fingernails and mucous membranes, fatigue, and nausea. These effects were followed by hyperkeratosis, darkening of the skin, acneiform eruptions, edema of the arms and legs, neurological symptoms, such as headache and limb numbness, and liver disturbance.

Data are suggestive but not conclusive concerning the carcinogenicity of PCBs in humans; however, hepatocellular carcinomas in three strains of rats and two strains of mice have led the EPA to classify PCBs as group B2, probable human carcinogen.

Cancer slope factors for the total class of PCBs (based on high risk) are available from RAIS. The slope factors used in the BHHRA for the oral, inhalation, and dermal exposure routes are 2.00E+00, 2.20E+00, and 2.00E+00 $[mg/(kg \times day)]^{-1}$, respectively. The slope factor for the dermal exposure route was calculated by assuming a GI absorption factor of 90%.

Chronic RfDs for PCB-1254 are available from RAIS. This RfD was used for calculating noncarcinogenic hazard for Total PCBs. The value used in the BHHRA for the oral, and dermal routes was 2.00E-05 mg/(kg × day) for both. The dermal RfD was derived using a GI absorption factor of 90%.

D5.2.2 Total PAHs

Total PAHs are evaluated in this BRA by weighting the concentration of each PAH to convert it to benzo(a) pyrene equivalents as described in the 2001 Risk Methods Document and then evaluating the sum of the concentrations based on the toxicity of benzo(a)pyrene. The PAHs included in this calculation for the PAH class are benzo(a)pyrene, benzo(a)anthracene, benzo(b)fluoranthene, benzo(k)fluoranthene, chrysene, dibenzo(a,h)anthracene, and indeno(1,2,3-c,d)pyrene.

Benzo[a]pyrene is one of many chemicals known as PAHs. It exists as yellowish plates and needles. Benzo[a]pyrene is practically insoluble in water but is soluble in benzene, toluene, xylene and sparingly soluble in alcohol and methanol. No current commercial production or use of benzo[a]pyrene is known. It occurs ubiquitously in products of incomplete combustion and in fossil fuels. It has been identified in surface water, tap water, rain water, groundwater, waste water, and sewage sludge. Benzo[a]pyrene is primarily released to the air and removed from the atmosphere by photochemical oxidation and dry deposition to land or water. Biodegradation is the most important transformation process in soil or sediment.

No data are available on the systemic (noncarcinogenic) effects of benzo[a]pyrene in humans. Benzo[a]pyrene is readily absorbed following inhalation, oral, and dermal routes of administration. Following inhalation exposure, benzo[a]pyrene is rapidly distributed to several tissues in rats. The metabolism of benzo[a]pyrene is complex and includes the formation of a proposed ultimate carcinogen, benzo[a]pyrene 7,8 diol-9,10-epoxide. Dietary administration of doses as low as 10 mg/kg during gestation caused reduced fertility and reproductive capacity in mice offspring, and treatment by gavage with 120 mg/kg/day during gestation caused stillbirths, resorptions, and malformations.

Numerous epidemiologic studies have shown a clear association between exposure to various mixtures of PAHs containing benzo[a]pyrene (e.g., coke oven emissions, roofing tar emissions, and cigarette smoke) and increased risk of lung cancer and other tumors. Each of the mixtures also contained other potentially carcinogenic PAHs; therefore, it is not possible to evaluate the contribution of benzo[a]pyrene to the carcinogenicity of these mixtures. Based on United States EPA guidelines, benzo[a]pyrene was assigned to weight-of-evidence group B2, probable human carcinogen.

Cancer slope factors for benzo[a]pyrene are available from RAIS, and are described in the section on that chemical, as are other constants used for specific PAHs.

D5.2.3 Total Dioxins/Furans

Dioxins and furans are a structurally related group of compounds based on the aromatic chemicals dibenzo-dioxin or dibenzofuran, with each base compound having arrays of chlorine atoms covalently linked to specific carbon atoms on the ring. The large number of possibilities that exist for the degree of chlorine substitution and its positioning define the structural integrity of each component. Of the 75 different isomers (congeners) of each base compound that are thought to exist, by far the most extensively studied is 2,3,7,8-tetrachlorodibenzo-dioxin (2,3,7,8-TCDD) (CASRN 1746-0 1-6). However, to this point, EPA has published an IRIS record for (mixtures of) hexachlorodibenzo-dioxins (HxCDD) (CASRN 19408-74-3) only, a group of compounds assigned to the B2 weight-of-evidence category for carcinogenicity, based on inadequate evidence in human beings, but adequate evidence of this capacity in laboratory animals (EPA 2000). Thus, the IRIS compilers derived an oral carcinogenic slope factor of 6.2E+03 $(mg/kg\text{-}day)^{-1}$ for the mixture, based on a dose-dependent increase in tumor formation in the livers of Osborne-Mendel rats and B6C3F1 mice (EPA 2000; NTP 1980).

In general, a dichotomy exists between the marked toxicity/carcinogenicity of the compounds in laboratory animals and their less-well characterized and possibly Jess severe toxicity in human beings. Thus, as in the case of HxCDD, the dioxins and furans as a whole are known to have profound tumorigenic effects in some strains of laboratory animals, often at very low doses. By contrast, the compounds harmful effects in human beings appear to be much less clear-cut, as suggested by the outcome of a number of well-documented environmental pollution incidents in which specific population subgroups were accidentally exposed. For example, persons exposed to dioxin as a result of a chemical plant explosion at Seveso, Italy, in 1974 developed chloracne and lipid disorders for the most part, but they displayed few overt signs of reproductive disorders or tumor formation. By contrast, when 2,3,7,8-TCDD was sprayed in large quantities on forests in Vietnam as a contaminant of the defoliant, Agent Orange [containing the herbicide, 2,4,5-trichlorophenoxyacetic acid (2,4,5-T)], considerable anecdotal and accumulating case-control data attest to the harmful and potentially carcinogenic effects of the compound in human beings.

As discussed in the Hazardous Substances Data Bank (HSDB 2000) 2,3,7,8-TCDD has at various times been tested for utility as a· component of flame-proofing materials and as an insecticide and fungicide, though without finding a commercial application. Environmentally, they appear ubiquitously as a product of the incomplete pyrolysis of organic material (combustion emissions). In an industrial setting, the compounds are formed as a byproduct of bleaching wood pulp and are routinely discharged to water bodies from paper mills.

In recent years, EPA has published extensive multi-volume reassessments of both the exposure and toxicity of the dioxins, particularly 2,3,7,8-TCDD. The series of monographs on the potential human health impacts of the compounds has the primary aim of evaluating the discrepancy between their carcinogenicity in laboratory animals and the much weaker evidence for this association in human beings (EPA 1994) The reassessment builds on a large body of evidence that covers the spectrum of relevant findings on the toxicological, toxicokinetic, biochemical, and epidemiological effects of the compounds. Recent insights into the molecular biology of dioxin-subcellular interactions have helped to forge the link between empirical observations of toxicity in animal and human receptors and potentially etiologically important tumorigenic interactions with one or more target genes. Thus, in general terms, the scheme envisions dioxins as one of a general class of compounds (including other environmentally important compounds such as the PCBs) that can enter tissues and bind to the Ah receptor, thereby forming a complex that has deoxyribonucleic acid (DNA)-binding capability. Such an interaction could presumably alter gene expression, with consequent modulation of m-RNA regulation and protein synthesis. Early cellular responses are thought to involve the stimulation of cell growth, with later events characterized by irreversible changes to tissue components.

Perhaps the most important finding to emerge from EPA's reassessment of the human health impacts of the dioxins is that, in EPA's opinion, the epidemiological data support the evidence of carcinogenicity in laboratory anima1s (EPA1994). Also endorsed in the report was the application of the concept of toxic equivalency to the dioxins/furans, in which the carcinogenicity/toxicity of different (and possibly less well characterized) congeners could be compared to that of a "benchmark" compound such as 2,3,7,8-TCDD. Based on the totality of the evidence, the Agency considered that a carcinogenic risk of one in a million (l.0E-06) was equivalent to a daily dose of 0.01 pg TEQ/kg-day, while noting that, because of the ubiquitous nature of the compounds in the environment, background exposure to these compounds is likely to be up to I 00-times greater than this level.

This risk assessment has used oral and inhalation carcinogenic slope factors for 2,3,7,8-TCDD of 1.5E+05 $(mg/kg\text{-}day)^{-1}$ (EPA 1997), with TEFs for the other congeners as listed in Exhibit 1.22. No toxicity values are available for the noncarcinogenic effects of the compounds.

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D5.2.4 Pentachlorophenol (CAS 87-86-5)

Pentachlorophenol, a man-made organic biocide, is often contaminated with other toxic organic chemicals such as chlorinated phenols, dioxins, and dibenzofurans (Williams 1982; U.S. Air Force 1989; ATSDR 1992).

Pentachlorophenol is readily absorbed following oral or inhalation exposure and is widely and rapidly distributed throughout the body (Wagner et al. 1991; ATSDR 1992; Jorens and Schepens 1993). Human and animal studies have provided evidence indicating that pentachlorophenol is metabolized to various conjugated metabolites. Both the parent compound and the conjugates are excreted in the urine (Braun et al. 1979).

Assessing the potential toxicity of technical (commercial) grade pentachlorophenol is complicated by the presence of the toxic impurities that are usually present, and the effects resulting from occupational exposure are often difficult to attribute to a specific route of exposure (Jorens and Schepens 1993). The effects in humans following acute oral exposure include increased heart and respiratory rates, elevated temperature, increased basal metabolic rate, and death (29 and 401 mg/kg) (RTECS 1989).

Human fatalities and toxic effects including tachycardia, jaundice, and other hematologic alterations have been reported for acute and subchronic occupational (e.g., sawmill workers, herbicide sprayers) inhalation exposures to pentachlorophenol. Upper respiratory tract inflammation and bronchitis were reported for sawmill workers chronically exposed to pentachlorophenol (Baader and Bauer 1951; Menon et al. 1958; ATSDR 1992). However, dose-terms for these exposures were not available, and concurrent exposures to other chemicals make definitive assessments impossible.

Data regarding the dermal exposure of humans to pentachlorophenol are anecdotal or equivocal, lack dose terms, and are compromised by concurrent exposures to other chemicals including the known contaminants in technical-grade pentachlorophenol. Acute exposure to 0.4% pentachlorophenol produced localized irritation (Bevenue et al. 1967), and subchronic exposures have caused chloracne (Baader and Bauer 1951; O'Malley et al. 1990) and possibly renal damage (ATSDR 1992). Dermal lesions including pemphigus and chronic urticaria have been reported for humans chronically exposed to pentachlorophenol-treated wood (Lambert et al. 1986). There currently are no definitive data regarding reproductive toxicity in humans exposed to pentachlorophenol.

Acute oral exposure of animals to pentachlorophenol affects the liver, kidneys, cardiovascular system, and the peripheral and central nervous system. Oral LD_{50} values for laboratory animals range from 27 to 230 mg/kg (Borzelleca et al. 1985; U.S. Air Force 1989; ATSDR 1992). Definitive data regarding the effects of subchronic or chronic oral exposure of humans to pentachlorophenol are not available. However, subchronic exposure (1 to 8 months) of rats to pentachlorophenol at doses ranging from 5 to 40 mg/kg/day has produced cardiovascular, hematotoxic, renal, hepatic, and immunologic responses (Schwetz et al. 1974, 1978; U.S. Air Force 1989; ATSDR 1992). Evidence of reproductive/developmental toxicity (increased resorptions, embryolethality, embryotoxicity, and teratogenicity) also has been observed in rats given pentachlorophenol during gestation (Larsen et al. 1974, 1976; Schwetz et al. 1978).

Because the most significant acute toxic effect of pentachlorophenol is elevated metabolism, a specific target organ or tissue is difficult to identify. However, for subchronic and chronic exposures, toxicity data indicate that the liver, kidney, and cardiovascular system are targets for some of the toxic effects of pentachlorophenol.

Both the chronic and subchronic RfDs for pentachlorophenol are 3.00E-02 mg/kg/day based on a NOAEL of 3 mg/kg/day and a LOAEL of 10 mg/kg/day for histopathologic findings in the liver and kidneys of rats given pentachlorophenol in the diet for 2 years (EPA 1994; Schwetz et al. 1978).

The RfC for pentachlorophenol is under review (EPA 1994a).

Based upon increased incidences of hepatocellular adenomas and carcinomas, adrenal medulla pheochromocytomas, malignant pheochromocytomas, and hemangiosarcomas/hemangiomas in mice, pentachlorophenol is classified by the EPA as a probable human carcinogen (Weight-of-evidence Category B2) and has an oral slope factor of 1.2E-01 $(mg/kg/day)^{-1}$ and an oral unit risk of 3.0E-06 $(g/L)^{-1}$ (EPA 1994). The potential carcinogenicity of pentachlorophenol following inhalation exposure has not been evaluated.

D5.3 RADIONUCLIDES

Radionuclides are unstable atoms of chemical elements that will emit charged particles or energy or both to achieve a more stable state. These charged particles are termed “alpha and beta radiation”; energy is termed “neutral gamma rays.” Interaction of these charged particles (and gamma rays) with matter will

produce ionization events, or radiation, which may cause living cell tissue damage. Because the deposition of energy by ionizing radiation is a random process, sufficient energy may be deposited (in a critical volume) within a cell and result in cell modification or death. In addition, ionizing radiation has sufficient energy that interactions with matter will produce an ejected electron and a positively charged ion (known as free radicals) that are highly reactive and may combine with other elements, or compounds within a cell, to produce toxins or otherwise disrupt the overall chemical balance of the cell. These free radicals also can react with deoxyribonucleic acid (DNA), causing genetic damage, cancer induction, or even cell death.

Radionuclides are characterized by the type and energy level of the radiation emitted. Radiation emissions fall into two major categories: particulate (electrons, alpha particles, beta particles, and protons) or electromagnetic radiation (gamma and X-rays). Therefore, all radionuclides are classified by the EPA as Group A carcinogens based on their property of emitting ionizing radiation and on the extensive weight-of-evidence provided by epidemiological studies of humans with cancers induced by high doses of radiation. Alpha particles are emitted at a characteristic energy level for differing radionuclides. The alpha particle has a charge of +2 and a comparably large size. Alpha particles have the ability to react (and/or ionize) with other molecules, but they have very little penetrating power and lack the ability to pass through a piece of paper or human skin. However, alpha-emitting radionuclides are of concern when there is a potential for inhalation or ingestion of the radionuclide. Alpha particles are directly ionizing and deposit their energy in dense concentrations [termed high linear energy transfer (LET)], resulting in short paths of highly localized ionization reactions. The probability of cell damage increases as a result of the increase in ionization events occurring in smaller areas; this also may be the reason for increased cancer incidence caused by inhalation of radon gas. In addition, the cancer incidence in smokers may be directly attributed to the naturally occurring alpha emitter, polonium-210, in common tobacco products.

Beta emissions generally refer to beta negative particle emissions. Radionuclides with an excess of neutrons achieve stability by beta decay. Beta radiation, like alpha radiation, is directly ionizing but, unlike alpha activity, beta particles deposit their energy along a longer track length (low LET), resulting in more space between ionization events. Beta-emitting radionuclides can cause injury to the skin and superficial body tissue, but are most destructive when inhaled or ingested. Many beta emitters are similar chemically to naturally occurring essential nutrients and will, therefore, tend to accumulate in certain specific tissues. For example, strontium-90 is chemically similar to calcium and, as a result, accumulates in the bones, where it causes continuous exposure. The health effects of beta particle emissions depend upon the target organ. Those seeking the bones would cause a prolonged exposure to the bone marrow and affect blood cell formation, possibly resulting in leukemia, other blood disorders, or bone cancers. Those seeking the liver would result in liver diseases or cancer, while those seeking the thyroid would cause thyroid and metabolic disorders. In addition, beta radiation may lead to damage of genetic material (DNA), causing hereditary defects.

Gamma emissions are the energy that has been released from transformations of the atomic nucleus. Gamma emitters and x-rays behave similarly, but differ in their origin: gamma emissions originate in nuclear transformations, and x-rays result from changes in the orbiting electron structure. Radionuclides that emit gamma radiation can induce internal and external effects. Gamma rays have high penetrating ability in living tissue and are capable of reaching all internal body organs. Without such sufficient shielding as lead, concrete, or steel, gamma radiation can penetrate the body from the outside and does not require ingestion or inhalation to penetrate sensitive organs. Gamma rays are characterized as low-LET radiation, as is beta radiation; however, the behavior of beta radiation differs from that of gamma radiation in that beta particles deposit most of their energy in the medium through which they pass, while gamma rays often escape the medium because of higher energies, thereby creating difficulties in determining actual internal exposure. For this reason, direct whole-body measurements are necessary to detect gamma radiation, while urine/fecal analyses are usually effective in detecting beta radiation.

People receive gamma radiation continuously from naturally occurring radioactive decay processes going on in the earth's surface, from radiation naturally occurring inside their bodies, from the atmosphere as fallout from nuclear testing or explosions, and from space or cosmic sources. Cesium-137 (from nuclear fallout) decays to barium-137, the highest contributor to fallout-induced gamma radiation. Beta radiation from the soil is a less penetrating form of radiation, but has many contributing sources. Potassium-40, Cs-137, lead-214, and bismuth-214 are among the most common environmental beta emitters. Tritium is also a beta emitter but contributes little to the soil beta radiation because of the low energy of its emission and its low concentration in the atmosphere. Alpha radiation also is emitted by the soil, but is not measurable more than a few centimeters from the ground surface. The majority of alpha emissions are attributable to radon-222 and radon-220 and their decay products. This contributes to what is called background exposure to radiation.

The general health effects of radiation can be divided into stochastic (related to dose) and nonstochastic (not related to dose) effects. The risk of development of cancer from exposure to radiation is a stochastic effect. Examples of nonstochastic effects include acute radiation syndrome and cataract formation, which occur only at high levels of exposures.

Radiation can damage cells in different ways. It can cause damage to DNA within the cell, and the cell either may not be able to recover from this type of damage or may survive but function abnormally. If an abnormally functioning cell divides and reproduces, a tumor or mutation in the tissue may develop. The rapidly dividing cells that line the intestines and stomach and the blood cells in bone marrow are extremely sensitive to this damage. Organ damage results from the damage caused to the individual cells. This type of damage has been reported with doses of 10 to 500 rads (0.1 to 5.0 gray, in SI units). Acute radiation sickness is seen only after doses of > 50 rads 0.5 gray), which is a dose rate usually achieved only in a nuclear accident.

When the radiation-damaged cells are reproductive cells, genetic damage can occur in the offspring of the person exposed. The developing fetus is especially sensitive to radiation. The type of malformation that may occur is related to the stage of fetal development and the cells that are differentiating at the time of exposure. Radiation damage to children exposed in the womb is related to the dose the pregnant mother receives. Mental retardation is a possible effect of fetal radiation exposure.

The most widely studied population that has had known exposure to radiation is the atomic bomb survivors of Hiroshima and Nagasaki, Japan. Data indicate an increase in the rate of leukemia and cancers in this population. However, the rate at which cancer incidence is significantly affected by low radiation exposures, such as results of exposure to natural background and industrially contaminated sites, is still undergoing study and is uncertain. In studies conducted to determine the rate of cancer and leukemia increase, as well as genetic defects, several radionuclides must be considered.

D5.3.1 Americium-241 (CAS 014596-10-2) (EPA)

Americium is a man-made metal produced when plutonium atoms absorb neutrons in nuclear reactors and in nuclear weapons detonations. Americium has several different isotopes, all of which are radioactive. The most important isotope is Am-241. Americium is a silver-white, crystalline metal that is solid under normal conditions. All isotopes of americium are radioactive. Am-241 primarily emits alpha particles, but also emits gamma rays. A mixture of Am-241 and beryllium emits neutrons. Americium-241 has a half-life of 432.7 years.

People may be directly exposed to gamma radiation from Am-241 by walking on contaminated land. They may also be exposed to both alpha and gamma radiation by breathing in americium contaminated dust or drinking contaminated water. Because Am-241 was widely dispersed globally during the testing

of nuclear weapons, only very minute amounts of it are found in the soil, plants, and water. Living near a weapons testing or production facility may increase your chance of exposure to Am-241. People who live or work near a contaminated site, such as a former weapons production facility, may ingest Am-241 with food and water, or may inhale it as part of resuspended dust.

Once in the body, Am-241 tends to concentrate in the bone, liver, and muscle. It can stay in the body for decades and continue to expose the surrounding tissues to radiation, and increase your risk of developing cancer.

When inhaled, some Am-241 remains in the lungs, depending upon the particle size and the chemical form of the americium compound. The chemical forms that dissolve easily may pass into the bloodstream from the lungs. The chemical forms that dissolve less easily tend to remain in the lungs, or are coughed up through the lung's natural defense system, and swallowed. From the stomach swallowed americium may dissolve and pass into the bloodstream. However, undissolved material passes from the body through the feces. Am-241 poses a significant risk if ingested (swallowed) or inhaled. It can stay in the body for decades and continue to expose the surrounding tissues to both alpha and gamma radiation, increasing the risk of developing cancer.

Oral, inhalation and external exposure cancer slope factors used in the BHHRA Am-241 are 9.10E-11 risk/pCi, 2.81E-08 risk/pCi and 2.76E-08 risk/yr per pCi/g soil, respectively. A dermal cancer slope factor was not calculated because this route of exposure is not evaluated in the BHHRA. Oral and inhalation RfDs are available in EPA’s IRIS.

D5.3.2 Cesium-137 (EPA)

Radioactive Cs-137 is produced when uranium and plutonium absorb neutrons and undergo fission. Examples of the uses of this process are nuclear reactors and nuclear weapons. The splitting of uranium and plutonium in fission creates numerous fission products. Cs-137 is one of the more well-known fission products. Cesium, as well as Cs-137, is a soft, malleable, silvery white metal. Cesium is one of only three metals that is a liquid near room temperature (83°F). The half-life of Cs-137 is 30 years.

People may also be exposed from contaminated sites: Walking on Cs-137 contaminated soil could result in external exposure to gamma radiation. Leaving the contaminated area would prevent additional exposure. Coming in contact with waste materials at contaminated sites could also result in external exposure to gamma radiation. Leaving the area would also end the exposure. If Cs-137 contaminated soil becomes air-borne as dust, breathing the dust would result in internal exposure. Because the radiation emitting material is then in the body, leaving the site would not end the exposure. Drinking Cs-137 contaminated water, also would place the Cs-137 inside the body, where it would expose living tissue to gamma and beta radiation.

People may ingest Cs-137 with food and water, or may inhale it as dust. If Cs-137 enters the body, it is distributed fairly uniformly throughout the body's soft tissues, resulting in exposure of those tissues. Slightly higher concentrations of the metal are found in muscle, while slightly lower concentrations are found in bone and fat. Compared to some other radionuclides, Cs-137 remains in the body for a relatively short time. It is eliminated through the urine. Exposure to Cs-137 also may be external (that is, exposure to its gamma radiation from outside the body).

Like all radionuclides, exposure to radiation from Cs-137 results in increased risk of cancer. Everyone is exposed to very small amounts of Cs-137 in soil and water as a result of atmospheric fallout. Exposure to waste materials, from contaminated sites, or from nuclear accidents can result in cancer risks much higher than typical environmental exposures.

If exposures are very high, serious burns, and even death, can result. Instances of such exposure are very rare. One example of a high-exposure situation would be the mishandling a strong industrial Cs-137 source. The magnitude of the health risk depends on exposure conditions. These include such factors as strength of the source, length of exposure, distance from the source, and whether there was shielding between you and the source (such as metal plating).

Oral, inhalation and external exposure cancer slope factors used in the BHHRA for Cs-137 are 5.85E-14 risk/pCi, 4.11E-14 risk/pCi and risk/yr per pCi/g soil, respectively. A dermal cancer slope factor was not calculated because this route of exposure is not evaluated in the BHHRA. Oral and inhalation RfDs are available in EPA's IRIS.

D5.3.3 Neptunium-237 (CAS 013994-20-2)

Specific literary information for Np-237 is limited. However, available literature states that during neutron bombardment, Np-237 breaks down to Pu-238 , which produces small masses of high capacity energy that is useful for satellites and spacecraft (Moskalev et al. 1979).

The most common route of Np-237 exposure is inhalation of aerosols. According to studies conducted on rats, acute effects include injury to the liver and kidney and circulation disorders. Long-term effects include osteosarcomas and lung cancer. Extremely high doses cause immediate or premature death by destruction of the lungs (Moskalev et al. 1979).

Oral, inhalation, and external exposure cancer slope factors used in the BHHRA for Np-237 are 6.74E-11 risk/pCi, 1.77E-08 risk/pCi, and 7.97E-07 [(risk × g)/(pCi × yr)], respectively. The slope factors for Np-237 include ingrowth of short-lived degradation products. A dermal cancer slope factor was not calculated because this route of exposure is not considered significant for radionuclides and is not evaluated in the BHHRA. Oral, dermal, and inhalation RfDs are not available for this element; therefore, systemic toxicity due to exposure to Np-237 is not quantified in the BHHRA.

D5.3.4 Plutonium-239 (CAS 015117-48-3) (EPA)

Plutonium is created from uranium in nuclear reactors. When U-238 absorbs a neutron, it becomes U-239 which ultimately decays to Pu-239. Different isotopes of uranium and different combinations of neutron absorptions and radioactive decay create different isotopes of plutonium.

Plutonium is a silvery-grey metal that becomes yellowish when exposed to air. It is solid under normal conditions, and is chemically reactive. Plutonium has at least 15 different isotopes, all of which are radioactive. The most common ones are Pu-238, Pu-239, and Pu-240. Pu-238 has a half-life of 87.7 years. Pu-239 has a half-life of 24,100, and Pu-240 has a half-life 6,560 years. The isotope Pu-238 gives off useable heat, because of its radioactivity.

Pu-239 is used to make nuclear weapons. For example, the bomb dropped on Nagasaki, Japan, in 1945, contained Pu-239. The plutonium in the bomb undergoes fission in an arrangement that assures enormous energy generation and destructive potential.

All isotopes of plutonium undergo radioactive decay. As plutonium decays, it releases radiation and forms other radioactive isotopes. For example, Pu-238 emits an alpha particle and becomes U-234; Pu-239 emits an alpha particle and becomes U-235. This process happens slowly since the half-lives of plutonium isotopes tend to be relatively long; Pu-238 has a half-life of 87.7 years; Pu-239 has a half-life is 24,100 years, and Pu-240 has a half-life of 6,560 years. The decay process continues until a stable, nonradioactive element is formed.

People who live near nuclear weapons production or testing sites may have increased exposure to plutonium, primarily through particles in the air, but possibly from water as well. Plants growing in contaminated soil can absorb small amounts of plutonium.

People may inhale plutonium as a contaminant in dust. It also can be ingested with food or water. Most people have extremely low ingestion and inhalation of plutonium. However, people who live near government weapons production or testing facilities may have increased exposure. Plutonium exposure external to the body poses very little health risk.

The stomach does not absorb plutonium very well, and most plutonium swallowed with food or water passes from the body through the feces. When inhaled, plutonium can remain in the lungs depending upon its particle size and how well the particular chemical form dissolves. The chemical forms that dissolve less easily may lodge in the lungs or move out with phlegm, and either be swallowed or spit out. But, the lungs may absorb chemical forms that dissolve more easily and pass them into the bloodstream.

Once in the bloodstream, plutonium moves throughout the body and into the bones, liver, or other body organs. Plutonium that reaches body organs generally stays in the body for decades and continues to expose the surrounding tissue to radiation.

External exposure to plutonium poses very little health risk, since plutonium isotopes emit alpha radiation, and almost no beta or gamma radiation. In contrast, internal exposure to plutonium is an extremely serious health hazard. It generally stays in the body for decades, exposing organs and tissues to radiation, and increasing the risk of cancer. Plutonium is also a toxic metal, and may cause damage to the kidneys.

Oral, inhalation and external exposure cancer slope factors used in the BHHRA for Pu-239 are 3.33E-08 risk/pCi, 1.21E-10 risk/pCi and 2.00E-10 risk/yr per pCi/g soil, respectively. A dermal cancer slope factor was not calculated because this route of exposure is not evaluated in the BHHRA.

D5.3.5 Protactinium-231

Protactinium (Pa) is a malleable, shiny, silver-gray radioactive metal that does not tarnish rapidly in air. It has a density greater than that of lead and occurs in nature in very low concentrations as a decay product of uranium. There are three naturally occurring isotopes, with Pa-231 being the most abundant (ANL 2005). Pa-231 is a decay product of U-235 decays by emitting an alpha particle with a half-life of 33,000 years.

Oral, inhalation, and external exposure cancer slope factors used in the BHHRA for Pa-231 are 2.98E-10 risk/pCi, 7.62E-08 risk/pCi, and 1.27E-07 [(risk × g)/(pCi × yr)], respectively. A dermal cancer slope factor was not calculated because this route of exposure is considered to be insignificant for radionuclides and is not evaluated in the BHHRA. Oral, dermal, and inhalation RfDs are unavailable for this element. Therefore, systemic toxicity is not quantified in the BHHRA.

D5.3.6 Radium-228

Radium (Ra) is an alkali-earth metal that was extensively used in the past as an ingredient of luminescent paints for instrument dials, watches, and similar self-illuminating instrumentation. It also occurs naturally as a daughter product of the naturally occurring radioactive material uranium decay chain.

Pure metallic radium is brilliant white when freshly prepared, but blackens on exposure to air, probably due to formation of the nitride. It exhibits luminescence, as do its salts, and it decomposes in water and is somewhat more volatile than barium. Radium imparts a carmine red color to a flame. Radium is extremely scarce but found in uranium ores such as pitchblende at slightly more than 1 g in 10 tons of ore. It can be separated on a small scale by the electrolysis of molten radium chloride, $RaCl_2$. This was first achieved using a mercury cathode, which gave a radium amalgam. The metal was subsequently isolated by distillation.

All isotopes of radium are radioactive. Radium emits alpha, beta, and gamma rays and produces neutrons when mixed with beryllium. Inhalation, injection, or external exposure to radium can cause cancer. Radium is over a million times more radioactive than the same mass of uranium.

Oral, inhalation, and external exposure cancer slope factors used in the BHHRA for Ra-228 are 1.98E-09 risk/pCi, 4.37E-08 risk/pCi, and 4.04E-06 [(risk × g)/(pCi × yr)], respectively. A dermal cancer slope factor was not calculated because this route of exposure is considered to be insignificant for radionuclides and is not evaluated in the BHHRA. Oral, dermal, and inhalation RfDs are unavailable for this element. Therefore, systemic toxicity is not quantified in the BHHRA.

D5.3.7 Technetium-99 (CAS 014133-76-7) (EPA)

Technetium (Tc) is a radioactive element that occurs in a number of isotopic forms. Technetium is found in some extraterrestrial material (i.e., stars); however, no appreciable amounts have been found in nature due to the relatively short half-lives of its radioactive isotopes (Kutegov et al. 1968). While no isotopes of technetium are stable, the existence of three technetium isotopes is well established. Two common forms of technetium, Tc-97 and Tc-98, have half-lives of 2.6×10^6 and 1.5×10^6 years, respectively. The third isotope, Tc-99, has a half-life of 2.12×10^5 years. None, however, possesses a half-life sufficiently long to allow technetium to occur naturally (Boyd 1959). Technetium is made artificially for industrial use, and natural technetium, particularly Tc-99, has been identified and isolated from the spontaneous fission of uranium, as well as other fissionable material or via the irradiation of molybdenum (Venugopal and Luckey 1978; Clarke and Podbielski 1988).

Technetium is an emitter of beta particles of low specific activity (Boyd 1959). It does not release nuclear energy at a rate sufficient to make the element attractive for the conventional applications of radioactivity (Boyd 1959). Tc-99 is the only long-lived isotope that is readily available and is the isotope on which most of the chemistry of technetium is based. Although gamma radiation has not been associated with Tc-99, the secondary X-rays may become important with larger amounts of the element.

Oral, inhalation, and external exposure cancer slope factors used in the BHHRA for Tc-99 are 2.75E-12 risk/pCi, 1.41E-11 risk/pCi, and 8.14E-11 ([risk × g]/[pCi × yr]), respectively. A dermal cancer slope factor was not calculated because this route of exposure is not evaluated in the BHHRA. Oral, dermal, and inhalation RfDs are not available for this element; therefore, systemic toxicity due to exposure to Tc-99 is not quantified in the BHHRA.

D5.3.8 Thorium (CAS 014274-82-9 for Thorium-228, CAS 014269-63-7 for Thorium-230, and CAS 007440-29-1 for Thorium-232, EPA and ATSDR)

Thorium (Th) is a soft, silvery white metal. Pure thorium will remain shiny for months in air, but if it contains impurities, it tarnishes to black when exposed to air. When heated, thorium oxide glows bright white, a property that makes it useful in lantern mantles. It dissolves slowly in water. Th-232 has a half-life of 14 billion (14×10^9) years, and decays by alpha emission, with accompanying gamma radiation. Th-232 is the top of a long decay series that contains key radionuclides such as Ra-228, its

direct decay product, and Rn-220. Two other isotopes of thorium, which can be significant in the environment, are Th-230 and Th-228. Both belong to other decay series. They also decay by alpha emission, with accompanying gamma radiation, and have half-lives of 75,400 years and 1.9 years, respectively. Only a small portion of naturally occurring thorium exists as Th-230. More than 99% of natural thorium exists in the form of Th-232. Th-230 breaks down into two parts—a small part called "alpha" radiation and a large part called the decay product. The decay product also is not stable and continues to break down through a series of decay products until a stable product is formed. During these decay processes, radioactive substances are produced. These include radium and radon. These substances give off radiation, including alpha and beta particles, and gamma radiation. The half-life for Th-230 is 75,400 years.

Small amounts of thorium are present in all rocks, soil, water, plants, and animals. Soil contains an average of about 6 parts of thorium per million parts of soil (6 ppm). Where high concentrations occur in rock, thorium may be mined and refined, producing waste products such as mill tailings. If not properly controlled, wind and water can introduce the tailings into the wider environment. Commercial and federal facilities that have processed thorium also may have released thorium to the air, water, or soil. Man-made thorium isotopes are rare and almost never enter the environment.

Since thorium is naturally present in the environment, people are exposed to tiny amounts in air, food, and water. The amounts usually are very small and pose little health hazard. Thorium is also present in many consumer products such as ceramic glazes, lantern mantles, and welding rods. People who live near a facility that mines or mills thorium or manufactures products with thorium may receive higher exposures. Also, people who work with thorium in various industries may receive higher exposures.

People may inhale contaminated dust, or swallow thorium with food or water. Living near a thorium-contaminated site or working in an industry where thorium is used increases the chance of exposure to thorium.

If inhaled as dust, some thorium may remain in the lungs for long periods of time, depending on the chemical form. If ingested, thorium typically leaves the body through feces and urine within several days. The small amount of thorium left in the body will enter the bloodstream and be deposited in the bones where it may remain for many years. There is some evidence that the body may absorb thorium through the skin, but that would not likely be the primary means of entry.

The principal concern from low to moderate level exposure to ionizing radiation is increased risk of cancer. Studies have shown that inhaling thorium dust causes an increased risk of developing lung cancer and cancer of the pancreas. Bone cancer risk also is increased because thorium may be stored in bone.

Oral, inhalation, and external exposure cancer slope factors used in the BHHRA for Th-228 are 1.32E-07 risk/pCi, 6.40E-11 risk/pCi and 7.76E-06 risk/yr per pCi/g soil, respectively. A dermal cancer slope factor was not calculated because this route of exposure is not evaluated in the BHHRA. Oral and inhalation RfDs are available in EPA's IRIS. Oral, inhalation, and external exposure cancer slope factors used in the BHHRA for Th-230 are 9.10E-11 risk/pCi, 2.85E-08 risk/pCi, and 8.19E-10 (risk × g)/(pCi × yr), respectively. A dermal cancer slope factor was not calculated because this route of exposure is not considered significant for radionuclides and is not evaluated in the BHHRA. Oral, dermal, and inhalation RfDs are not available for this element; therefore, systemic toxicity due to exposure to americium is not quantified in the BHHRA. Oral and inhalation exposure cancer slope factors used in the BHHRA for Th-232 are 8.47E-11 risk/pCi and 4.33E-08 risk/pCi, respectively. A dermal cancer slope factor was not calculated because this route of exposure is not evaluated in the BHHRA.

D5.3.9 Uranium (CAS 007440-62-2 for metal, CAS 013966-29-5 for Uranium-234, CAS 015117-96-1 for Uranium-235, and CAS 007440-61-1 for Uranium-238) (ATSDR)

Uranium is a mildly radioactive element that occurs widely in the earth's crust. It is found in all soils, most rocks, and, in lesser concentrations, in water, vegetation, and animals, including humans. Uranium emits a low level of alpha particles and a much lower level of gamma rays. Alpha particles are unable to penetrate skin, but can travel short distances in the body if ingested or inhaled. Consequently, uranium represents a significant carcinogenic hazard only when taken into the body, where alpha particle energy is absorbed by small volumes of tissue. Although the penetrating (gamma) radiation of uranium is not considered to be significant (ATSDR 1989), one of its daughter radionuclides is a strong gamma emitter; therefore, gamma radiation may be a concern in areas containing uranium.

Natural uranium contains the uranium isotopes U-238 (which averages 99.27% of total uranium mass), U-235 (0.725), and U-234 (0.0056%), each of which undergoes radioactive decay. Natural uranium, therefore, contains the radionuclide daughter products from the decay of U-238 and U-235 (Bowen 1979; ATSDR 1989). The half-lives of the isotopes are 200,000, 700 million, and 5 billion years for U-234, U-235, and U-238, respectively.

Uranium is a radioactive element, but it also is a metallic element. Toxicological effects from the ingestion of uranium are the result of the action of uranium as a metal and its radioactive properties. The primary toxic chemical effect of uranium is seen in kidney damage. Studies in rabbits, mice, and dogs showed effects on the kidney to be dose-related. Fetal skeletal abnormalities and fetal death were found in pregnant mice exposed to 6 mg/kg or uranyl acetate dihydrate.

The primary human exposure studies to uranium have been studies of uranium miners or uranium factory workers. These studies have shown an increase in lung cancer deaths among these workers, which may be attributable to the decay of uranium into radon and its daughters. These workers are exposed to high levels of uranium dust and fumes and other radioactive elements in confined conditions (ATSDR 1989).

Oral, inhalation, and external exposure cancer slope factors used in the BHHRA for U-234 are 7.00E-11 risk/pCi, 1.14E-08 risk/pCi, and 2.52E-10 ([risk × g]/[pCi × yr]), respectively. Oral, inhalation, and external exposure cancer slope factors used in the BHHRA for U-238 are 8.71E-11 risk/pCi, 9.25E-09 risk/pCi, and 1.14E-07 [(risk × g)/(pCi × yr)], respectively. The slope factors for U-238 include ingrowth of short-lived degradation products. A dermal cancer slope factor was not calculated for the uranium isotopes because this route of exposure is not considered significant for radionuclides and is not evaluated in the BHHRA. Oral, dermal, and inhalation RfDs are available for uranium and are listed earlier in this section.

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