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APPENDIX D

HUMAN HEALTH NONRADIONUCLIDE TOXICOLOGICAL PROFILES

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CONTENTS

D1.0 INTRODUCTION D-1

D1.1 NONRADIATION INDUCED HEALTH EFFECTS D-1
D1.2 CANCER SLOPE FACTORS D-1
D1.3 REFERENCE DOSES D-1
D1.4 TOXICOLOGICAL PROFILES FOR NONRADIOACTIVE COCS D-2

D2.0 REFERENCES: D-5

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D1.0 INTRODUCTION

This appendix provides toxicity information for those nonradionuclide chemicals that were identified as contaminants of concern (COC) at the 200-CS-1 OU waste sites.

D1.1 Nonradiation Induced Health Effects

For nonradioactive contaminants, two general types of health effects were evaluated in the baseline risk assessment (BRA): cancer effects and adverse noncancer health effects. This distinction is made because the U.S. Environmental Protection Agency (EPA) generally assumes that a dose threshold exists for non-carcinogens, and that compensatory processes prevent the expression of adverse effects if humans are exposed to chemical doses below the threshold. No such threshold is generally assumed for carcinogens. Instead, it is generally assumed that there is a finite probability of developing cancer associated with any exposure to a carcinogen. As a result, carcinogens and non-carcinogens have separate toxicity criteria that are explained in greater detail below. In general, the toxicological effects of a compound are the dominant health effects of the chemical as determined by the EPA.

D1.2 Cancer Slope Factors

Cancer slope factors (SF) are chemical-specific potency values used to calculate the risk of cancer resulting from exposure to carcinogenic chemicals. A higher value implies a more potent carcinogen. EPA develops SFs from chronic animal studies or, where possible, from epidemiological data. Because animal studies use much higher doses over shorter periods of time than the exposures generally expected for humans, the dose-response relationship from the dose range used in animal studies is extrapolated to the low dose range generally experienced by humans typically using a "linearized multistage" (LMS) mathematical model. To ensure protectiveness, SFs are typically derived from the 95 percent upper confidence limit of the slope; thus, the actual risks are unlikely to be higher than those predicted using the SF, and may be considerably lower.

D1.3 Reference Doses

The Reference Dose (RfD) is the toxicity value used to evaluate noncarcinogenic effects resulting from exposures to chemicals. A RfD is an estimated dose threshold for noncarcinogenic effects. A chronic RfD is an estimate of a lifetime (70 years) daily chemical dose that is likely to result in no appreciable deleterious noncarcinogenic effects. A subchronic RfD is an estimate of the dose likely to result in no significant adverse effects over an exposure duration of approximately one tenth a human lifetime (i.e., 7 years). Because well-defined subchronic RfDs are not available for most chemicals, chronic RfDs may be used to estimate noncancer risks for all exposure scenarios. However, the use of chronic RfDs to evaluate subchronic exposures can overestimate potential risks.

To derive a RfD, a series of professional judgments are made to assess the quality and relevance of the human or animal data and to identify the critical study and the most critical toxic effect. These criteria are generally developed by EPA risk assessment work groups and listed in EPA risk assessment guidance documents and databases. Data typically used in developing the RfD are the highest no-observable-adverse-effect levels for the critical studies and effects of the non-carcinogen. For each factor representing a specific area of uncertainty

inherent in the extrapolation from the available data, an uncertainty factor is applied. Uncertainty factors generally consist of multiples of 10, although values less than 10 are sometimes used.

The inhalation Reference Concentration (RfC) is analogous to the oral RfD and is likewise based on the assumption that thresholds exist for certain toxic effects. The inhalation RfC considers toxic effects for both the respiratory system (portal-of-entry) and for effects peripheral to the respiratory system (extrarespiratory effects). In general, the RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The EPA Integrated Risk Information System (IRIS) presents a reference concentration (RfC) in milligrams per cubic meter (mg/m^3) to characterize the toxicity of non-carcinogens that are inhaled. These RfCs are converted to inhalation RfDs (milligrams per kilogram per day $[mg/kg/day]^{-1}$) by EPA ("Region 9 Preliminary Remediation Goals" [EPA 2004]). Chemical-specific inhalation RfDs are estimated by multiplying the RfC by an inhalation rate of 20 m^3 per day and dividing this product by an adult body weight value of 70 kg (EPA 2004).

For most chemicals, our scientific understanding of the hazards associated with dermal exposure is poor. There are very few toxicity data for a limited number of chemicals based on dermal routes of chemical exposure. As a result, toxicity data based on oral routes of exposure are often used to make estimates of the risks associated with dermal exposure to a chemical. Because many oral toxicity criteria are based on an administered dose, adjustments may be required in some cases to derive an absorbed dose (EPA/540/R 99/005, *Risk Assessment Guidance for Superfund. Vol. 1: Human Health Evaluation Manual, Part E; Supplemental Guidance for Dermal Risk Assessment*). To estimate dermal toxicity criteria, a gastrointestinal absorption factor can be applied to oral toxicity criteria that are based on administered doses.

D1.4 Toxicological Profiles for Nonradioactive COCs

Toxicological Profiles are provided for the following COCs:

- 2-Ethylhexanol
- Ammonia
- Bismuth
- Chloride
- Mesityl oxide
- N-Butylbenzenesulfonamide
- Phosphate
- Sulfate
- Sulfide

2-Ethylhexanol

2-Ethylhexanol or isooctanol is an organic compound used in the manufacture of a variety of products, including the manufacture of the diester bis(3-methylheptyl) phthalate (DEHP), a plasticizer.

People can be exposed to isooctanol by inhalation and through the skin and by accidental ingestion. However, harmful concentrations in air will not likely be reached due to evaporation of isooctanol at 20°C. Isooctanol irritates skin, eyes and the respiratory tract. It can also cause nausea and headache after inhalation, and diarrhea and vomiting after ingestion. Long-term or repeated exposure can result in defatting of the skin. The substance may also cause effects on the central nervous system ("Pocket Guide to Chemical Hazards: Isooctyl alcohol" [NIOSH 2005a]).

The National Institute for Occupational Safety and Health (NIOSH) has established recommended guidelines for occupational exposure to isooctanol. NIOSH recommends an exposure limit for skin of 50 ppm (270 mg/m^3) for an 8-hour workday and a 40-hour work week (NIOSH 2005a).

Ammonia

Ammonia has a very strong odor that is irritating and that can be smelled when it is in the air at a level higher than 50 parts per million (ppm). Therefore, it is likely ammonia will be smelled before a person is exposed to a concentration that will harm them. Ammonia has an inhalation RfC of 1.00×10^{-1} mg/m^3 ("Ammonia: inhalation RfC assessment" [IRIS 1991]). However, low levels of ammonia may harm some people with asthma and other sensitive individuals ("Toxicological profile for ammonia" [ATSDR 2004]).

Ammonia is a corrosive substance and the main toxic effects are restricted to the areas that have direct contact with ammonia (i.e., skin, eyes, respiratory tract, mouth, and digestive tract). There is no evidence that ammonia causes cancer. Ammonia has not been classified for carcinogenic effects by EPA, Department of Health and Human Services (DHHS) (NTP), or the International Agency for Research on Cancer (IARC). Ammonia can also have beneficial effects, such as when it is used as a smelling salt. Certain ammonium salts have long been used in veterinary and human medicine (ATSDR 2004).

Ammonia does not last very long in the environment, because it is recycled naturally. Nature has many ways of incorporating and transforming ammonia. In soil or water, plants and microorganisms rapidly take up ammonia. After fertilizer containing ammonia is applied to soil, the amount of ammonia in that soil decreases to low levels in a few days. In the air, ammonia will last about 1 week (ATSDR 2004).

Many physical and chemical properties of ammonia are a function of pH levels. For instance, at pH 9.25 half of the ammonia will be in the un-ionized form (NH_3) and half will be in the ionized form (NH_4^+). At pH 7.25, 99% of the ammonia will be ionized. The volatility of ammonia increases with increasing pH. The rate of volatilization of ammonia from water will increase with increasing pH (generally only important above pH values of ~7.0) and temperature, and can be influenced by other environmental factors. Agitation will also increase the rate of volatilization (ATSDR 2004). Adsorption to sediment should increase with increasing organic content, increased metal ion content, and decreasing pH. Ammonia, however, can be produced in, and subsequently released from, sediment. In surface water, groundwater, or sediment, ammonia can undergo sequential transformation by two processes in the nitrogen cycle, nitrification and denitrification, which would produce ionic nitrogen compounds, and from these, elemental nitrogen. The ionic nitrogen compounds formed from the aerobic - process of nitrification, NO_2 and NO_3, can leach through the sediment or be taken up by aquatic plants or other organisms. High concentrations of nitrate in groundwater

can cause methemoglobinemia in infants when contaminated water is ingested. Elemental nitrogen formed from the anaerobic process of denitrification is lost by volatilization to the atmosphere (ATSDR 2004).

Bismuth

Bismuth has a long history of use in pharmaceuticals. Insoluble bismuth salts are used pharmaceutically as antacids and to control diarrhea and are considered to be nontoxic. They are also used externally for their astringent and slight antiseptic properties and in some cosmetics (*Casarett and Doull's Toxicology: The Basic Science of Poisons, 4th ed* [Amdur et al. 1991]; *Casarett and Doull's Toxicology: The Basic Science of Poisons 5th ed* [Klassen et al. 1996[).

Bismuth compounds are insoluble and are poorly absorbed from the gastrointestinal tract or when applied to the skin. The primary route of excretion of bismuth is in urine. Bismuth has been found to be a nephrotoxicant. Acute renal failure can occur following oral doses of some bismuth compounds, particularly in children. Bismuth can also cause neural injury leading to emotional disturbances, encephalopathy, and involuntary muscle twitches. Bismuth has also been shown to cause hyperpigmentation. The symptoms of chronic toxicity in humans consist of decreased appetite, weakness, rheumatic pain, diarrhea, fever, metal line on the gums, foul breath, gingivitis, and dermatitis. Jaundice and conjunctival hemorrhage are rare but have been reported (Amdur et al. 1991; Klassen et al. 1996). There is no information available regarding an oral RfD, carcinogenicity, or oral slope factor.

Chloride

No toxicological information is available for chloride.

Mesityl oxide

No toxicological information is available for mesityl oxide.

N-Butylbenzenesulfonamide

No toxicological information is available for n-Butylbenzenesulfonamide.

Phosphate

No toxicological information is available for phosphate.

Sulfate

The sulfate ion, SO_4, is one of the major anions occurring in natural waters. The majority of sulfates, with the exception of lead, barium, and strontium sulfates, are soluble in water. Sulfate may be reduced to sulfide, volatilized to the air as H_2S, precipitated as an insoluble salt, or incorporated into living organisms. Sulfate occurs naturally in soils, sediments, and rocks. Sulfates are discharged into surface waters in the atmospheric fallout from coal-fired power plants, and from the metallurgical roasting process. Additionally, sulfate is emitted by diesel engines ("Toxicity summary for Sulfate" [RAIS 2005]).

The sulfate ion is poorly absorbed from the human intestine; however, some absorption of the component ions of sulfate salts does occur. The symptom is a laxative effect after ingestion of drinking water containing sulfates, and children appear to be more sensitive than adults. Adults rapidly acclimate to the laxative effects of sulfates; however, it is unknown how

rapidly this adaptation is acquired or lost. Sulfates have been shown to increase the absorption of fluoride from the rat intestinal tract (RAIS 2005). There is no information available regarding an oral RfD, carcinogenicity, and oral slope factor.

Sulfide

No toxicological information is available for sulfide.

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