

APPENDIX D
HUMAN HEALTH NONRADIONUCLIDE TOXICOLOGICAL PROFILES

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1 **D1.0 INTRODUCTION**

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

4 **D1.1 Nonradiation Induced Health Effects**

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

15 **D1.2 Cancer Slope Factors**

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

26 **D1.3 Reference Doses**

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

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

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

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

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

26 **D1.4 Toxicological Profiles for Nonradioactive COCs**

27 Toxicological Profiles are provided for the following COCs:

- 29 • 2-Ethylhexanol
- 30 • Ammonia
- 31 • Bismuth
- 32 • Chloride
- 33 • Mesityl oxide
- 34 • N-Butylbenzenesulfonamide
- 35 • Phosphate
- 36 • Sulfate
- 37 • Sulfide

39 **2-Ethylhexanol**

40 2-Ethylhexanol or isooctanol is an organic compound used in the manufacture of a variety of
 41 products, including the manufacture of the diester bis(3-methylheptyl) phthalate (DEHP), a
 42 plasticizer.

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

8 The National Institute for Occupational Safety and Health (NIOSH) has established
9 recommended guidelines for occupational exposure to isooctanol. NIOSH recommends an
10 exposure limit for skin of 50 ppm (270 mg/m³) for an 8-hour workday and a 40-hour work
11 week (NIOSH 2005a).

12 **Ammonia**

13 Ammonia has a very strong odor that is irritating and that can be smelled when it is in the air
14 at a level higher than 50 parts per million (ppm). Therefore, it is likely ammonia will be
15 smelled before a person is exposed to a concentration that will harm them. Ammonia has an
16 inhalation RfC of 1.00×10^{-1} mg/m³ (“Ammonia: inhalation RfC assessment” [IRIS 1991]).
17 However, low levels of ammonia may harm some people with asthma and other sensitive
18 individuals (“Toxicological profile for ammonia” [ATSDR 2004]).

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

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

31 Many physical and chemical properties of ammonia are a function of pH levels. For instance,
32 at pH 9.25 half of the ammonia will be in the un-ionized form (NH₃) and half will be in the
33 ionized form (NH₄⁺). At pH 7.25, 99% of the ammonia will be ionized. The volatility of
34 ammonia increases with increasing pH. The rate of volatilization of ammonia from water will
35 increase with increasing pH (generally only important above pH values of ~7.0) and
36 temperature, and can be influenced by other environmental factors. Agitation will also
37 increase the rate of volatilization (ATSDR 2004). Adsorption to sediment should increase
38 with increasing organic content, increased metal ion content, and decreasing pH. Ammonia,
39 however, can be produced in, and subsequently released from, sediment. In surface water,
40 groundwater, or sediment, ammonia can undergo sequential transformation by two processes
41 in the nitrogen cycle, nitrification and denitrification, which would produce ionic nitrogen
42 compounds, and from these, elemental nitrogen. The ionic nitrogen compounds formed from
43 the aerobic - process of nitrification, NO₂ and NO₃, can leach through the sediment or be
44 taken up by aquatic plants or other organisms. High concentrations of nitrate in groundwater

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

4 **Bismuth**

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

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

21 **Chloride**

22 No toxicological information is available for chloride.

23 **Mesityl oxide**

24 No toxicological information is available for mesityl oxide.

25 **N-Butylbenzenesulfonamide**

26 No toxicological information is available for n-Butylbenzenesulfonamide.

27 **Phosphate**

28 No toxicological information is available for phosphate.

29 **Sulfate**

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

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

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

4 **Sulfide**

5 No toxicological information is available for sulfide.

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