1. Introduction

The primary purpose of this Interaction Profile for strontium, cobalt, cesium, trichloroethylene, and polychlorinated biphenyls (PCBs) is to evaluate data on the toxicology of the "whole" mixture and the joint toxic action of the chemicals in the mixture in order to recommend approaches for assessing the potential hazard of this mixture to public health. To this end, the profile evaluates the whole mixture data (if available), focusing on the identification of health effects of concern, adequacy of the data as the basis for a mixture Minimal Risk Level (MRL), and adequacy and relevance of physiologically-based pharmacokinetic/pharmacodynamic (PBPK/PD) models for the mixture. The profile also evaluates the evidence for joint toxic action—additivity and interactions—among the mixture components. A weight-of-evidence (WOE) approach is commonly used in these profiles to evaluate the influence of interactions in the overall toxicity of the mixture. The weight-of-evidence evaluations are qualitative in nature, although the Agency for Toxic Substances and Disease Registry (ATSDR) recognizes that observations of toxicological interactions depend greatly on exposure doses and that some interactions appear to have thresholds. Thus, the interactions are evaluated in a qualitative manner to provide a sense of what influence the interactions may have when they do occur. The profile provides environmental health scientists with ATSDR Division of Toxicology's (DT) recommended approaches for the incorporation of the whole mixture data or the concerns for additivity and interactions into an assessment of the potential hazard of this mixture to public health. These approaches can then be used with specific exposure data from hazardous waste sites or other exposure scenarios.

Review of ATSDR's documents with site-specific information showed that stable or radioactive forms of cesium, cobalt, and strontium were found together at seven sites: Oak Ridge National Laboratory, Hanford Site, Brookhaven National Laboratory, Idaho National Environmental and Engineering Laboratory (INEEL), Nevada Test Site, Savannah River Site, and Lawrence Livermore National Laboratory. Other nonradioactive chemicals, such as volatile organic compounds (VOCs), semi-volatile compounds, and heavy metals were found at these sites. These included mercury, chromium, selenium, cyanide, fluoride, nitrate, sodium, sulfate, trichloroethylene, PCBs, 1,1-dichloroethene, toluene, diethylphthalate, hydrazine, 2-amino 4,6-dinitrotoluene, N-nitroso-methylenediamine, and fission and activation products. Trichloroethylene was reported together with radionuclides of cesium, cobalt, and strontium at Brookhaven National Laboratory and INEEL sites. PCBs were reported together with radionuclides of cesium, cobalt, and strontium at Oak Ridge and INEEL sites. These sites are not likely a public threat, due to limited access of the sites to the public and different aquifers for public water supplies, and some cannot be properly assessed because of lack of data; however, several sites were concluded to be hazardous to on-site workers and those involved with environmental restoration and management (e.g., Hanford site).

Evaluation of the available environmental fate data for the components of the mixture suggests that in the event of exposure, the primary route of exposure of nearby populations to mixtures of these chemicals in soil is likely to be oral, resulting from contamination of soil and/or groundwater. Available reports of chemical use and prior chemical release at the sites of concern indicate that strontium, cobalt, and cesium radionuclides, rather than the stable forms of these metals, are of greatest concern for possible adverse health effects, owing primarily to the expectation that the radiation-related effects of exposure to the radionuclides will occur at lower exposure levels of the component than the majority of chemical effects. While data on the effects of ingested strontium radionuclides are available, data on the toxic and/or carcinogenic effects of ingested radiocobalt and radiocesium are lacking. However, as the most sensitive effects of the radionuclides are expected to come from emitted radiation, a reasonable estimate as to potentially sensitive targets for oral exposure to radiocobalt and radiocesium can be made from examining the toxicokinetics of the stable compounds, as well as the tissues that are sensitive to external exposure to cobalt or cesium radiation. Recent ATSDR toxicological profiles are available for all of the components that comprise the mixture (ATSDR 1997, 2000, 2001c, 2001d, 2001e); these documents are the primary source of information presented in the Appendices concerning the toxicokinetics, health effects, mechanisms of action, and health guidelines for these chemicals. The ATSDR Toxicological Profile for Ionizing Radiation (ATSDR 1999) was also consulted for information pertinent to the health effects and mechanisms of the radionuclides. The bases for the MRLs as well as other pertinent effects are summarized in Table 1 and in Appendices A, B, C, D, and E.

Table 1. Potential Health Effects of Concern for Intermediate and Chronic Oral Exposure to the Mixture Radiostrontium, Radiocobalt, Radiocesium, Trichloroethylene, and Polychlorinated Biphenyls (see Appendices A, B, C, D, and E)

Radiostrontium	Radiocobalt	Radiocesium	Trichloro- ethylene	PCBs
Musculoskeletal **Cancer** **Hematological** Immunological	***Hematological*** **Cancer** **Neurodevelopmental** **Reproductive** Immunological	**Cancer** **Neurodevelopmental** **Reproductive** Immunological Hematological	***Neurological*** Hepatic Immunological Renal Hematological	***Immunological*** ***Neurological*** **Cancer** **Neurodevelopmental** Dermal Endocrine Hepatic Reproductive Hematological

The basis for the MRL is bolded and italicized; other sensitive effects are bolded; and less sensitive effects in common across two or more compounds are listed without bold or italics.