

1. Introduction

The primary purpose of this Interaction Profile for uranium, fluoride, and cyanide 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.

Table 1. Data from 2001 CERCLA Priority List of Hazardous Substances

Compound	NPL Ranking
Uranium	94
Hydrogen Fluoride	248
Fluoride	261
Cyanide	28
Hydrogen Cyanide	139
Nitrate	216

Source: 2001 CERCLA Priority List of Hazardous Substances. Online at: <http://www.atsdr.cdc.gov/clist.html>

Uranium and fluoride are used in conjunction with nitrate when separating isotopes of uranium via the gaseous diffusion process. This process has been used at several U.S. Department of Energy (DOE) facilities, and continues to be used today. In addition, cyanide has been reported with great frequency as a contaminant at National Priorities List (NPL) sites. Review of ATSDR’s documents with site-specific information showed that uranium, fluoride, cyanide, and nitrate were reported at one site (Pantax Plant site), while three-component submixtures were reported at eight additional sites: Eastern Michaud Flats, Monticello Mill, Alcoa/Lavaca Bay, Depue/New Jersey Zinc/Mobil Chemical, Hipps Road Landfill, Riverbank Army Ammunition Plant, Savanna Army Depot, and Santa Susana Field Laboratory.

Data on the rankings of the individual compounds in the mixture, based on the 2001 CERCLA Priority List of Hazardous Substances, are presented in Table 1. 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.

ATSDR toxicological profiles are available for cyanide, uranium, and fluoride (ATSDR 1997, 1999b, 2001d); these documents are the primary sources of information presented in the Appendices concerning the toxicokinetics, health effects, mechanisms of action, and health guidelines for these chemicals. No toxicological profile or MRLs are available for nitrate; however, U.S. EPA (IRIS 2002) has derived an oral reference dose (RfD) for nitrate. The bases for available MRLs as well as other pertinent health effects are presented in Table 2 and in Appendices A, B, C, and D.

Table 2. Potential Health Effects of Concern for Intermediate and Chronic Oral Exposure to the Mixture Uranium, Fluoride, Cyanide, and Nitrate (see Appendices A, B, C, and D)^a

Uranium	Uranium Radiation	Fluoride	Cyanide	Nitrate
<i>Renal</i> Hepatic Endocrine (Thyroid)	Cancer	<i>Musculoskeletal</i> Reproductive (Testicular) Neurological Renal	<i>Reproductive</i> <i>(Testicular)</i> Developmental Neurological Renal	Hematological

^aThe 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.