1. Introduction

The primary purpose of this Interaction Profile for benzene, toluene, ethylbenzene, and xylenes (BTEX) 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 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 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 (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.

Benzene, toluene, ethylbenzene, and xylenes frequently co-occur at hazardous waste sites. Various combinations of these chemicals are among the most frequently found binary mixtures in completed exposure pathways at hazardous waste sites. Media contaminated with these chemicals include air, water, and soil. Contamination of groundwater can result in volatilization into indoor air when the groundwater is used as household water. In addition, contamination of groundwater and subsurface soil can result in migration of these chemicals into basements as soil gas. The chemicals are used as solvents in products such as paints and coatings, and are constituents of petroleum products, particularly gasoline, jet fuels, and kerosene. The BTEX chemicals are discussed in the Toxicological Profile on Total Petroleum Hydrocarbons (ATSDR 1999a), but more recent information, including a physiologically-based pharmacokinetic (PBPK) model for the whole mixture, has triggered this reassessment of the joint toxic action of these chemicals.

Each of the chemicals in the mixture of concern is volatile, well absorbed, extensively metabolized, and does not persist in the body for long periods of time. All of the BTEX chemicals can produce neurological impairment, and exposure to benzene can additionally cause hematological effects including aplastic anemia and acute myelogenous leukemia. The critical nature of the neurotoxicity (i.e., the noncancer effect expected to occur at the lowest exposure levels) is reflected by the use of neurological impairment as the basis for 9 of 13 MRLs for BTEX chemicals, including 6 of 8 inhalation MRLs (ATSDR 1995, 1997, 1999b, 2000). The carcinogenic (leukemogenic) potential of benzene is well established as indicated by its consensus classification as a human carcinogen by the National Toxicology Program (NTP 2001), U.S. Environmental Protection Agency (EPA) (IRIS 2001), and International Agency for Research on Cancer (IARC 1987). Ethylbenzene is possibly carcinogenic to humans based on a recent assessment by IARC (2000). Toluene and xylenes have been categorized as not classifiable as to human carcinogenicity by both EPA (IRIS 2001) and IARC (1999a, 1999b), reflecting the lack of evidence for the carcinogenicity of these two chemicals.