1. Introduction

The primary purpose of this Interaction Profile for 1,1,1-trichloroethane, 1,1-dichloroethane, trichloroethylene, and tetrachloroethylene 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 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.

An unpublished analysis of ATSDR Public Health Assessments of 1,608 National Priority List (NPL) hazardous waste sites indicates that the mixture of 1,1,1-trichloroethane, 1,1-dichloroethane, trichloroethylene, and tetrachloroethylene was found at 210 sites and was the most frequently occurring mixture of four volatile organic chemicals. This occurrence frequency was the basis for choosing the mixture as the subject of this profile. Contaminated media at sites with this mixture included groundwater (186/210 sites), soil (45/210 sites), and air (25/210 sites). Categories of activities associated with detection of this mixture in water samples included waste storage/treatment/disposal (35% of sites), manufacturing and industry (29%), waste recycling (9%), and "other" miscellaneous activities (18%). Other activity categories associated to a lesser degree with detection of the mixture in groundwater included "affected area/natural resource" (5% of sites), residential (2%), mining/extracting/processing (1%), and government (2%). The most frequent completed exposure pathway for volatile organic chemicals at these sites involved private well water. Completed exposure pathways involving municipal water or air contaminated with volatile organic chemicals were less frequent. Volatile organic chemicals were unimportant in most completed exposure pathways involving soil.

Each of the chemicals in the mixture of concern is volatile, has good hydrocarbon solvent properties, and does not persist in the body for long periods of time. They have been widely used in dry cleaning and textile-processing (tetrachloroethylene), vapor degreasing of fabricated metal parts (tetrachloroethylene, trichloroethylene, and 1,1,1-trichloroethane), or manufacturing of other chemical products such as vinyl chloride and high vacuum rubber (1,1-dichloroethane). Only one of the four chemicals, trichloroethylene, is extensively metabolized; the remaining three are predominately excreted unmetabolized in exhaled breath. The critical noncancer health effect in humans (i.e., the effect expected to occur at the lowest exposure levels) for each of these chemicals, regardless of exposure route or duration, is neurological impairment. Reflecting this expectation, neurological effects form the basis of ATSDR's inhalation and oral MRLs for these chemicals (ATSDR 1990, 1995, 1997a, 1997b).

Although some evidence of cancer, of varying weight, has been found in rodent studies for high doses of each of these chemicals, low level exposure of humans may not present high risks for cancer. The Environmental Protection Agency (EPA) (IRIS 2001) assigned 1,1,1-trichloroethane to Cancer Group D (Not Classifiable as to Human Carcinogenicity), 1,1-dichloroethane to Cancer Group C (Possible Human Carcinogen), and trichloroethylene and tetrachloroethylene to the boundary between Group C (Possible Human Carcinogen) and Group B2 (Probable Human Carcinogen). EPA lists no oral slope factors or inhalation unit risks for these chemicals on its Integrated Risk Information System (IRIS) (2001) database, but is currently evaluating several approaches to extrapolating from rodent tumor data to derive estimates of human cancer risks at environmentally relevant exposure levels of trichloroethylene and tetrachloroethylene. The National Toxicology Program (NTP 2001) list of chemicals reasonably anticipated to be human carcinogens includes trichloroethylene and tetrachloroethylene, but not 1,1-dichloroethane or 1,1,1-trichloroethane. IARC (2001) has not assigned a cancer classification for 1,1-dichloroethane, but assigned 1,1,1-trichloroethane to Cancer Group 3, not classifiable as to human carcinogenicity, and trichloroethylene and tetrachloroethylene to Cancer Group 2A, probably carcinogenic to humans.