4. CONCLUSIONS

This interaction profile recommends the use of component-based approaches that assume additive joint toxic action in exposure-based assessments of possible noncancer or cancer health hazards from inhalation or oral exposure to mixtures of chloroform, 1,1-dichloroethylene, trichloroethylene, and vinyl chloride resulting from water contamination near hazardous waste sites. This recommendation is based on the following factors. There are no direct data available to characterize health hazards (and dose-response relationships) from mixtures containing all four components. Similarly, PBPK/PD models have not yet been developed that would predict pertinent target doses of the components under scenarios involving exposure to mixtures of all four components. Finally, available information on toxic actions of the individual components indicates that joint actions of chloroform, 1,1-dichloroethylene, trichloro-ethylene, and vinyl chloride on several toxicity targets are plausible, including hepatic, renal, immunological, neurological, developmental effects, and cancer. With data on the individual components suggesting possible sites of joint toxic action, but no data available on the toxicity or behavior of the complete mixture, a default component-based approach was therefore recommended.

Weight-of-evidence analyses of available data on the joint toxic action of mixtures of these components indicate that the available scientific evidence suggests less-than-additive interactions among these components for most endpoints, but only at concentrations sufficiently high as to saturate metabolism. For the neurological effects of chloroform, these same mechanisms of metabolic saturation would result in more available parent compound, and therefore an increased toxicity, and for the neurological effects of trichloroethylene, the impact of this mechanism is indeterminate. However, as these concentrations are unlikely to be achieved in exposures resulting from water near hazardous waste sites, it is recommended that additivity be generally assumed in exposure-based assessments of health hazards from exposure to mixtures of these components. The additivity approach to screening for potential noncancer health hazard involves the estimation of endpoint-specific hazard indexes using MRLs from the toxicological profiles and TTDs derived in this interaction profile. This approach is appropriate when the hazard quotients of at least two of the components equal or exceed 0.1 (ATSDR 2004a). Potential cancer risk is estimated by adding the chemical-specific risks for chloroform and vinyl chloride.

Endpoint-specific hazard indexes (e.g., hazard indexes for hepatic effects) or cancer risks for the same duration (e.g., chronic) can be summed across routes to estimate the aggregate hazard or risk, if it is likely that the same individual or group of individuals would be exposed by both routes. If an endpoint-specific hazard index exceeds one, or the total cancer risk for these chemicals equals or exceeds $1x10^{-4}$, then further evaluation is needed (ATSDR 2004a), using biomedical judgment and community-specific health

outcome data, and taking into account community health concerns (ATSDR 1992). For very high exposures, 100-fold or more above the MRLs or TTDs, interactions may occur, and their impact can be estimated using the weight-of-evidence results, as summarized above.