4. Conclusions

There are no direct data available to characterize health hazards (and dose-response relationships) from mixtures containing all four of the components. Similarly, PBPK/PD models have not yet been developed that would predict pertinent target tissue 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 uranium, fluoride, cyanide, and nitrate on three toxicity targets are plausible, specifically: reproductive effects, neurologic alterations, and renal effects. For two of the components, fluoride and nitrate, the most sensitive health effect does not appear to be a shared target with other components, but should be considered when evaluating sites containing the potential health hazards resulting from exposure to the mixture. 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 or the relevant submixtures, a default component-based approach that assumes additive joint toxic action in exposure-based assessments of possible noncancer health hazards from oral exposure to mixtures of uranium, fluoride, cyanide, and nitrate was recommended.

Weight-of-evidence analyses of available data on the joint toxic action of mixtures of these components indicate that scientific evidence for greater-than-additive or less-than-additive interactions among these components is limited and generally inadequate to characterize the possible modes of joint action on most of the pertinent toxicity targets. For two component pairs, cyanide's effect on the toxicity of uranium radiation and nitrate's effect on cyanide toxicity, less-than-additive effects of the two compounds are predicted. For one component pair, fluoride and cyanide, the available data suggest greater-than-additive joint action in both directions. No other greater-than-additive or less-than-additive interactions were indicated from the available data. Therefore, it is recommended that additivity be assumed as a public health protective measure in exposure-based assessments of health hazards from exposure to mixtures of these components.