

## 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 exposure to mixtures of carbon monoxide, formaldehyde, methylene chloride, nitrogen dioxide, and tetrachloroethylene. 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 five 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 five components. Finally, available information on toxic actions of the individual components indicates that joint actions of carbon monoxide, formaldehyde, methylene chloride, nitrogen dioxide, and tetrachloroethylene on several toxicity targets are plausible, including hematological effects, cardiovascular effects, respiratory effects, neurological alterations, hepatic injury, 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 or the relevant submixtures, a default component-based approach assuming additivity was therefore 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, with the majority of limited available interaction data suggesting additive interactions. Data are inadequate to characterize the possible modes of joint action on most of the pertinent toxicity targets. Therefore, it is recommended that additivity be generally assumed as a public health protective measure in exposure-based assessments of health hazards from exposure to mixtures of these components.