Charge to the Expert Panel

The NAS panel shall, based upon available literature, theory and experience use its best judgment, and rationale, to provide guidance to the Agency on the following areas of the human health risk assessment for inhalation exposures to formaldehyde: 1) identification of potential adverse non-cancer health effects; 2) assessment of carcinogenic potential; 3) exposure-response analysis for identified endpoints; 4) quantitative risk assessment methods; and 5) evaluation of sources of uncertainty in the health assessment. Specifically, the panel will address the following questions:

(A) Inhalation Reference Concentration (RfC) for Formaldehyde

1. Please review and comment on the draft's analysis of the potential non-cancer health effects attributable to inhalation exposure to formaldehyde. Has EPA fairly and soundly evaluated the weight of the evidence that formaldehyde causes the effects identified in the assessment? Has it appropriately identified and noted the limitations of the available studies and the conclusions that can be supported by these studies?
2. Please review and comment on the draft's evaluation regarding which studies are informative as to the points of departure for the quantitative derivation of an Inhalation Reference Concentration (an estimate, with uncertainty spanning perhaps an order of magnitude, of a continuous inhalation exposure to the human population, including sensitive subgroups, that is likely to be without an appreciable risk of deleterious effects during a lifetime). Has it selected studies of suitable quality for the quantitative analysis done? Has it appropriately determined which levels to consider points of departure for those effects? Please review and comment on its determinations as to when and how to make appropriate adjustments for exposure duration and whether alternatives were adequately considered and presented.
3. Please review and comment on the draft's evaluation of the studies with respect to the development of uncertainty factors to derive an Inhalation Reference Concentration from points of departure from the sensitive non-cancer effects of formaldehyde. In doing so, please review and discuss the evaluation of the extent to which the available studies likely capture the range of human variability in response and the completeness of the database for purposes of identifying the hazards of formaldehyde inhalation and deriving a reference concentration.

(B) Carcinogenicity of Formaldehyde

1. Please comment on the cancer weight of evidence narrative in the draft, developed pursuant to the EPA's 2005 *Guidelines for Carcinogen Risk Assessment* (www.epa.gov/iris/backgr-d.htm). Is the weight of evidence narrative scientifically supported?
2. Please review and comment on the draft's quantitative estimations of reasonable upper estimates of the potential human cancer risk attributable to inhalation of formaldehyde at low concentrations.
    a. The draft uses as its preferred quantitative estimates dose-response relationships between several cancers and cumulative inhalation exposure to formaldehyde.

Please review and comment on the scientific support for the choices made in developing those estimates. Please include consideration of issues such as the appropriate dose metric given the study design, the alternative metrics, and the suitability of alternative metrics for use in evaluating environmental and residential inhalation exposures to formaldehyde.

b. The draft provides, as partial supporting quantitative analysis, estimates of dose-response quantification from animal studies of nasal tumors. Please review and comment on the scientific rationale for the choices made to develop those supportive estimates. In doing so, please consider the analysis of the sensitivity of low-dose estimates of potential biologically-based dose-response models of formaldehyde upper respiratory tract cancer to small changes in model design or model inputs.