Charge for the Peer Consultation Workshop on Research Needs Related to the IRIS Draft Toxicological Review of Naphthalene
April 7, 2005

EPA's Integrated Risk Information System (IRIS) Program is reassessing the inhalation carcinogenicity of naphthalene following the release of a National Toxicology Program (NTP, 2000) study indicating evidence of nasal tumors in rats. As a result of this new information, EPA put forth for external review in July 2004 a draft document indicating that naphthalene is a likely human carcinogen. The reassessment contains the derivation of an inhalation unit risk. One of the topics discussed at the peer review meeting was the need for further research to characterize naphthalene's carcinogenic mode of action. The Agency has decided to hold a peer consultation workshop on this topic before determining a course of action on the IRIS assessment of naphthalene.

Several documents are being provided for informational purposes to assist the panel in understanding the current state of the science. These documents include:

- Draft Toxicological Review of Naphthalene: In Support of Summary Information on the Integrated Risk Information System (IRIS) (NCEA-S-1707) (June 2004)
- Final Report on the External Peer Review for the IRIS Reassessment of the Inhalation Carcinogenicity of Naphthalene (August 2004)
- List of Recent Naphthalene Literature

In addition, the NTP studies (NTP, 1992, 2000) on naphthalene carcinogenesis are available at <http://ehp.niehs.nih.gov/ntp/docs/ntp.html> Information regarding the consideration of naphthalene for the 11th Report on Carcinogens is available on the NTP website <http://ntp.niehs.nih.gov/index.cfm?objectid=03C9AC68-0C5D-98D4-B8A03F6335C73E3D>

Please provide detailed responses to the following charge questions:
(1) What specific studies would clarify whether naphthalene induces olfactory epithelial and respiratory epithelial tumors in rats through a genotoxic mechanism? Discuss specific issues related to these studies, e.g., if metabolite formation is needed, how would this be accomplished; if Ames tests are proposed, then what strains and tissue fractions would be best, etc.?

(2) Which studies would be the most critical for elucidating whether a genotoxic mode of action is operating?

(3) What resources (level of effort, funds, time) would be required to perform the suggested studies?

(4) If the critical studies identified above show that genotoxicity is not likely under conditions that lead to tumors in vivo, what critical studies or evaluations could be used to see if effects on cell cycling/proliferation (including apoptosis) or cytotoxicity might play a role in tumor formation?

(5) What resources (level of effort, funds, time) would be required to perform the suggested studies?