Charge to Reviewers for the Toluene Toxicological Review and IRIS Summary

The U.S. EPA is conducting a peer review of the scientific basis supporting the health hazard and dose response assessment for toluene that will appear on the Agency's online data base, the Integrated Risk Information System (IRIS). Peer review is meant to ensure that science is used credibly and appropriately in derivation of these dose-response assessments. External peer reviewers have been provided with the following charge questions:

1) **RfD Derivation**

a) *Principal Study, Section 5.1.1*: Two subchronic animal studies are available (NTP, 1990; Hsieh et al., 1989). The previous IRIS entry (1990) utilized the 13 week oral gavage study (NTP, 1990) for the derivation of an RfD. The 28 day drinking water study (Hsieh et al., 1989) was not considered. This latter study has now been chosen as the principal study. Is this the correct choice for the principal study?

b) *Critical Effect, Section 5.1.1*: The critical effect is identified as *immunological effects*: *decreased thymus weight*. Is this the correct critical effect and is it adequately described?

c) *Methods of Analysis, Section 5.1.2*: Is the point of departure determined appropriately, i.e., benchmark dose approach?

d) *Uncertainty Factors, Section 5.1.3*: Are the appropriate uncertainty factors applied? Is the explanation for each transparent?

2) **RfC Derivation**

a) *Principal Study, Section 5.2.1*: Several human epidemiological studies are available. The study used in the previous IRIS file (Foo et al., 1990) is not used in the reassessment; the study by Zavalic et al. (1998) is chosen as the principal study. Is this the correct choice for the principal study? Are adequate explanations given to explain why this study was chosen over the other available studies? An attempt is made to explain the choice of principal study, critical effect and NOAEL by examining the entire data base. Was this attempt successful?

b) *Critical Effect, Section 5.2.1*: The critical effect is identified as impaired color vision. Is this the correct critical effect and is it adequately described?

c) *Methods of Analysis, Section 5.2.2*: Is the point of departure determined appropriately, i.e., NOAEL/LOAEL approach versus benchmark dose approach?

d) *Uncertainty Factors, Section 5.2.3*: Are the appropriate uncertainty factors applied? Is the explanation for each transparent?

3) **Cancer Weight-of-Evidence Classification**

The weight of evidence and cancer characterization are discussed in Section 4.6. Have appropriate criteria been applied from both the 1986 EPA Guidelines for Carcinogen

Risk Assessment (Federal Register 51 (185):33992-34003) and the 1999 EPA draft revised Guidelines for Carcinogen Risk Assessment (Review Draft, NCEA-F-0644, July 1999. Risk Assessment Forum)?