

December 2006

## **Charge to External Peer Reviewers for the Toxicological Review and IRIS Summary of 2,2,4-Trimethylpentane**

The U.S. Environmental Protection Agency (EPA) is seeking an external peer review for a health assessment of 2,2,4-trimethylpentane that will appear on the Agency's online database, the Integrated Risk Information System (IRIS).

Peer review of this assessment is being sought to ensure that all available data relevant to the toxicological assessment of 2,2,4-trimethylpentane have been appropriately and objectively evaluated. The draft documents for review consist of the Toxicological Review and accompanying IRIS Summary for 2,2,4-trimethylpentane. Please provide detailed responses to the charge questions below.

### **General**

Question 1 - Are there additional key published studies or publicly available scientific reports that are missing from the draft document that might be useful for the discussion of the hazards of 2,2,4-trimethylpentane?

### **Oral reference dose (RfD) for 2,2,4-trimethylpentane**

Question 2 - No oral RfD has been derived in the current draft assessment. Has the rationale and justification for not deriving an RfD been transparently described? Is the rationale scientifically justified and appropriate?

### **Inhalation reference concentration (RfC) for 2,2,4-trimethylpentane**

Question 3 - No inhalation RfC has been derived in the current draft assessment. Has the rationale and justification for not deriving an RfC been transparently described? Is the rationale scientifically justified and appropriate?

### **Mode of Action for Kidney Toxicity**

Question 4 - Does the Toxicological Review provide sufficient information to support a conclusion that there is a causal relationship between accumulation of  $\alpha_{2u}$ -globulin and the pathology observed exclusively in the male rat kidney in response to 2,2,4-trimethylpentane exposure?

Question 5 - The majority of the studies available for 2,2,4-trimethylpentane were designed only to investigate various aspects of  $\alpha_{2u}$ -globulin-induced nephropathy. Thus, data and information on effects in target organ systems other than the kidney are limited in quantity and quality (e.g. liver). Has the available information on effects unrelated to  $\alpha_{2u}$ -globulin-associated nephropathy been adequately and appropriately described?

## **Carcinogenicity of 2,2,4-trimethylpentane**

Question 6 - Has the appropriate cancer descriptor been chosen? Has the rationale and justification for not deriving a quantitative cancer assessment been transparently described? Do you agree with EPA's rationale, justification and conclusion?