

**Charge to External Reviewers for the
IRIS Toxicological Review of Urea
September 2010**

The U.S. Environmental Protection Agency (EPA) is seeking an external peer review of the scientific basis supporting the human health assessment of urea that will appear on the Agency's online database, the Integrated Risk Information System (IRIS). IRIS is prepared and maintained by the EPA's National Center for Environmental Assessment (NCEA) within the Office of Research and Development (ORD). Currently an IRIS assessment of urea does not exist on the database.

The current draft health assessment includes an evaluation of the available data and a determination that the data are insufficient for the derivation of toxicity values. A cancer descriptor for urea is included. Below is a set of charge questions that address scientific issues in the assessment of urea. Please provide detailed explanations for responses to the charge questions. Please consider the accuracy, objectivity, and transparency of EPA's analysis and conclusions in your review.

General Charge Questions:

1. Is the Toxicological Review logical, clear and concise? Has EPA clearly synthesized the scientific evidence for noncancer and cancer hazard?
2. Please identify any additional studies that would make a significant impact on the conclusions of the Toxicological Review.
3. Please discuss research that you think would be likely to increase confidence in the database for future assessments of urea.

Chemical-Specific Charge Questions:

(A) Oral reference dose (RfD) for urea

1. An RfD for urea was not derived. Is the rationale for not deriving an RfD scientifically justified and clearly described? Please identify and provide the rationale for any studies that should be selected as the principal study and any endpoint that should be considered as a critical effect.

(B) Inhalation reference concentration (RfC) for urea

1. An RfC for urea was not derived. Is the rationale for not deriving an RfC scientifically justified and clearly described? Please identify and provide the rationale for any studies that should be selected as the principal study and any endpoint that should be considered as a critical effect?

(C) Carcinogenicity of urea

1. Using EPA's 2005 *Guidelines for Carcinogen Risk Assessment* (www.epa.gov/iris/backgr-d.htm), the Agency concluded that there is "inadequate information to assess the carcinogenic potential" of urea. Please comment on the selection of the cancer descriptor. Is the cancer descriptor scientifically justified and clearly described?

2. EPA did not derive a quantitative estimate of the carcinogenic potential of urea. Do the data support an estimation of a cancer slope factor for urea? If a quantitative estimate is proposed, please identify the data set and a description of the method that should be used.