Peer Review Workshop on the Benchmark Dose Technical Guidance Document

CHARGE TO REVIEWERS

Background

U.S. EPA's Risk Assessment Forum (Forum) has been active in promoting research and discussion on benchmark dose (BMD) issues since 1990. In 1993 the Forum sponsored a colloquium on the applications of BMD methods to noncancer risk assessment. The focus of this colloquium was to review a Forum draft report that outlined the techniques and presented the major questions and decisions involved in applying the benchmark dose method. Following this a Forum technical panel published a background document on the use of BMD in health risk assessment. In the ensuing years the Forum sponsored several workshops and symposia on the BMD approach, including a 1996 external peer review on a previous draft of the *Benchmark Dose Technical Guidance Document*. An Agency review was held on the revised document during the winter of 2000. Comments from this Agency review have resulted in the draft document presently undergoing review. Following the external peer review this December the technical panel will consider comments received and revise the document for final Forum review.

In your review, please address the following issues and questions on the *Draft Benchmark Dose Technical Guidance Document*.

Charge Questions

I. Preparation for Computing a Benchmark Dose: Selecting Data and an appropriate Benchmark Response level.

1. What concepts and terms related to the benchmark dose (BMD), if any, do we need to define more clearly?
2. The literature review cites works that have helped to develop the BMD approach. Do you have suggestions for inclusion of other work?
3. What additional discussion, if any, is needed to clarify the description of the selection of studies and endpoints for the BMD?

II. Modeling to compute a Benchmark Dose: Model selection, fitting, and confidence limits.

4. Model selection and fitting
   a. What additional discussion is needed to ensure adequate presentation of the proposed defaults for the parameters for various models?
   b. Discuss the adequacy of the criteria to evaluate the fit of the model.

Would you recommend additional criteria?

c. What are the advantages/strengths of using the methods described to select among "equally" fitting models? What other methods should be considered in making a selection?

5. Use of confidence limits
   a. Discuss the approaches described to compute confidence limits.
   b. Discuss the soundness of the criteria used to deviate from using a 95% one-sided confidence interval for the BMDL.
6. Examples: What additional concepts, if any, should be illustrated by an example?

III. Interpretation and Using the Benchmark Dose

7. The guidance document summarizes the elements of the reporting requirements needed to document BMD computations. Is the inclusion of each of these elements reasonable in light of the document's guidance, or would further discussion be useful?
8. What other comments do you have about the approach to benchmark dose described in the document? What changes to the approach would you like to see, and, very importantly, why?