Brain Tumor End Points Workshop
January 20, 2006
Bethesda North Marriott Hotel and Conference Center
5701 Marinelli Road, Bethesda, MD

Presented by the U.S. Food and Drug Administration and the American Association for Cancer Research
Co-sponsored by the American Society of Clinical Oncology

QUESTIONS TO THE PANEL

The following questions will be considered <u>separately for each group of endpoints</u> (imaging based versus patient reported outcomes)

1. <u>Analytic validity of the instrument</u>
   How good is the instrument in measuring differences, *e.g.* tumor size or change in symptoms?

   1.1. What are the limits of accuracy of the instrument?
   1.2. What are the limits on reproducibility of results?
      1.2.1. To what extent should variations be expected between assessors?
      1.2.2. To what extent should variations be expected among different facilities?
      1.2.3. Can instrument reproducibility be maintained in a community setting?
   1.3. What confounders limit accuracy and reproducibility?
   1.4. What are the considerations for determining frequency of serial assessments?
   1.5. How is instrument quality defined and monitored?

2. <u>Clinical relevance of the endpoint</u>
   How well does the endpoint reflect clinical benefit?

   2.1. Are existing criteria for assessing the endpoint adequate?
      2.1.1. If not, should new criteria be developed?
      2.1.2. If so, what factors should be accounted for by the new criteria?
   2.2. For what populations is the endpoint relevant?
   2.3. What interpretation or clinical correlation is needed as a corollary?
   2.4. What confounders of clinical relevance can be identified?
   2.5. Should a period of time to allow for a therapy to have its biological effect be permitted to pass prior to removing a patient from study due to progression? If such a time period is allowed, how much, if any, progression can occur during that time period?

The following questions will be considered in the final <u>General Discussion</u> session only.

1. <u>Individual Endpoints</u>
   1.1. What if any non-survival endpoints reflect or predict clinical benefit?
   1.2. What if any endpoints available now may be *reasonably likely* to predict clinical benefit?

2. <u>Composite Endpoints</u>
   2.1. What evaluation techniques discussed are complementary?
   2.2. What composite endpoints would be reasonable?

3. <u>Endpoint Development</u>
   3.1. What if any potential endpoints should be explored apart from those discussed?
   3.2. What questions should be brought from this workshop to ODAC for further consideration?