OMB Staff Comments on EGBE Final draft Tox Review and Final Draft IRIS Summary (documents dated Nov 2009)

General Comments:
OMB staff focused this review on EPA's responsiveness to the external peer review. Where EPA agrees with the comments, we suggest that appropriate conforming changes be made in the main text of the toxicological review and the IRIS summary.

EPA made revisions in response to the peer review comments and then went back to the peer reviewers to ensure that comments were appropriately addressed, as per the older IRIS process which existed during the review. We found it very helpful to look at the 2nd round peer reviewer comments. As those that commented had minimal further suggestions regarding the revisions, we accordingly defer to them as the experts and have only a few additional comments.

Scientific comments on Appendix A:

- In some cases, EPA uses non-exact language (eg." a few reviewers", "most reviewers"). As there were seven reviewers, it would be helpful if EPA were more specific in describing the number of reviewers that had the specific comment or recommendation.

- Page A-7, in describing comments on question A1, EPA notes that all reviewers found the study to be scientifically justified. When we look at the comments of Dr. Salmon (peer review report at page 36), it seems that he only states that the study was the best choice and then mentions concerns about using a study in rodents since humans are far less sensitive than rodents to the EGBE induced hemolysis. It may be helpful to present and respond to this comment.

- Page A-12, in responding to comments on B1, since all the reviewers asked why EPA did not use the 91 day drinking water study, it would be helpful for EPA's response to provide a rationale for not relying on the study in appendix A (as well as in the tox review). In addition, EPA states that the study has been included in chapter 5 for comparison purposes, however when we look in the tox review, chapter 5.2.4 only presents a graphic and it seems that all the derivations are in Appendix C. Perhaps EPA should consider adding the derivation, using the 91 day drinking water study to the section. In addition we could not find EPA's rationale for not using the study. In 5.2.2.3 EPA states that the POD's are similar but that seems to be the extent of the discussion. As the oral study would not require route-to-route extrapolation (as suggested by peer reviewers), it may be useful to expand the discussion regarding why EPA rejected the study. Similarly, in response to the public comment on page A-20, EPAs response should also include discussion of why the oral study was not preferred.

- Page A-12, in response to B2, EPA states that all comments found the extrapolation correct and objectively and transparently presented. We note that 1 reviewer commented that this was not his area of expertise and 2 reviewers commented that the extrapolation was not required if EPA used the drinking water study. The EPA discussion should mention these comments. It is also not clear that all the reviewers commented on the objective and transparent presentation.

- Page A-13, in response to B3, EPA states that there was general agreement that the selection was scientifically justified and transparently and objectively described. We note that Dr. Jollow commented that the factors need more explication and other commenters merely said the application of specific factors were appropriate. Please clarify how many of the commenters spoke to the transparency and objectivity of the selections.

- Page A-13, in response to C1 EPA states that all reviewers agreed with the EPA conclusion and that all reviewers commented that the justification of the descriptor had been sufficiently, transparently and objectively described. We note that one reviewer did not provide comments and other reviewers said the weight of evidence was adequately described. It would be helpful if EPA provided more clarity on the number of reviewers that commented that the justification of the descriptor had been sufficiently, transparently and objectively described. EPA may want to revise the response to reflect any changes made in characterizing the comments.

- Page A-15, as per comment above, in response to C3, please provide more clarity on the number of reviewers that found the analysis to be sound and transparently and objectively described. We note that 1 reviewer did not comment on this, at least one review called it only adequate, and it does not appear that all reviewers addressed all these issues. Please also check the characterization of the comments regarding questions C4 and C5.

Scientific Comments on the Tox Review:

- Page 1, EPA has edited the text to say that the oral slope factor and inhalation unit risk values represent "a plausible upper bound." The addition of "a plausible" does not appear to be consistent with the definitions in the IRIS glossary. Is there a citation that EPA can cite that represents official Agency position which determined that these are indeed "plausible" upper bounds?

- Page 2, states that the literature was reviewed through December 2008. Considering that over a year has passed, EPA may want to consider conducting a quick review to see if there are any new studies which can be considered.

- Page 51, line 33, we note that EPA has replaced the word "adverse" with "biologically significant." While "adverse" is defined in the IRIS glossary (in that adverse effect is defined, http://www.epa.gov/iris/help_gloss.htm#a), it is unclear what EPA means by the term "biologically significant" and how this is different than biological effects showing statistical significance, if in fact EPA does mean something different. Is this a new term of art? If so, it would be helpful to be clear about what this means. A footnote would be helpful. We note that this term is also used in other places as well throughout the document.

Scientific Comments on the IRIS Summary:

- The IRIS summary (and the tox review) should have a section which provides a link to, and information on, where readers can go to see the public docket (including interagency and public comments) related to the assessment.

- Page 2, in I.A.4, it may be useful for EPA to mention and describe the 91 day oral drinking water study. We also wonder if it makes sense for the confidence in the RfD to be the same as the confidence in the RfC considering that the RfD required route to route extrapolation.

Comment on the Peer Review Report:

- While we note that the peer review report is already final, we find it very helpful that the report provides short summaries of the background of the expert reviewers. The report also mentions the review panels the experts have participated in. It may also be helpful if the peer review reports were to include information discussing any monetary funding (perhaps through a grant, cooperative agreement, sole-source agreement, or competitive contract) that the expert reviewer may have received from EPA's ORD. This would be consistent with generally-accepted disclosure practices for peer reviewers, particularly for reviews with significant public policy implications.