OMB Staff Comments on 2-Hexanone Final draft Tox Review and Final Draft IRIS Summary

General Comments:
OMB staff focused this review on EPA's responsiveness to the peer review comments and found EPA to be generally very responsive to peer reviewer concerns. Scientific concerns are noted below.

Scientific comments on Appendix A:

- Page A-10/A-11: in response to questions C2 or C3 it would be helpful text to point out that EPA has changed the BMR from 10% to 5%. This is mentioned in passing in response to general question 4 (page A-4). A more rigorous discussion of the peer review comments, and scientific deliberations, which led to this change (which leads to a 50% reduction in the point of departure), would be helpful in the section which discusses the quantification of the RfC.

- On page A-14, EPA notes that a peer reviewer suggested that EPA provide a summary of TOXNET values. EPA responds that "EPA does not generally report toxicity values of other agencies in its IRIS assessments. Such values are frequently revised, and maintaining their accuracy is not possible."
    - We note that previously EPA had provided, in section 6 of the tox review, a citation to the NIH supported TOXNET database. This webpage provides useful information on what other organizations and international governments have concluded on toxicity of the compound. It is unclear why EPA is now deleting this reference in light of the peer reviewer comment. We would trust the NIH would do the best job possible to keep the database accurate and while EPA does not need to take responsibility, NIH likely has appropriate disclaimers-in fact NIH provides information on when the databases have been updated (see http://toxnet.nlm.nih.gov/html/toxnet_update.html).
    - Perhaps EPA could add this useful link back to the tox review and provide a footnote disclaiming that EPA is not responsible for its accuracy.

Scientific Comments on the Tox Review:

- Page 101, EPA states that the overall confidence in the RfC is low to medium. EPA also notes that the the uncertainty factors applied total 3000, which is the maximum EPA will apply when creating an IRIS value and accounts for uncertainty in four different areas. We question whether the overall confidence should be low, instead of low to medium. While, we agree with the EPA statement that the benchmark dose modeling increases confidence, it does not decrease the application of uncertainty factors in four different areas and thus the uncertainties are still at the maximal level.