



NTP
National Toxicology Program

CERHR Second Expert Panel Meeting on Bisphenol A

August 6-8, 2007

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Introductory comments

- Dr. John Bucher
 - Audit of literature and earlier drafts of the BPA Expert Panel Report
 - Conflict of interest review of NTP contracts
- Dr. Robert Chapin
 - Review of criteria developed for evaluation of literature
 - Panel activities since March meeting
 - Consideration of public comments
- Dr. Mike Shelby
 - Meeting logistics
 - Charge to panel
 - Agenda



NTP CERHR Bisphenol A Review Update

- August 2006 initial draft sent to expert panel by contractor
- December 2006 draft with expert panel input released for public comment
- March 2007 draft updated literature and included panel additions in response to public comments
- Allegations of potential conflict of interest with support contract
- 1st expert panel meeting on Bisphenol A- March 5-7, 2007
 - April 20, 2007 Interim draft expert panel report released for public comment
- 2nd expert panel meeting- Aug 6-8, 2007



Steps to Address Issues Related to Conflict of Interest

- Review all NTP contracts for potential for conflict of interest
- Develop COI language to incorporate in all NTP contracts
- Conduct an audit of draft BPA expert panel reports
 - Audit the literature search/selection for the initial draft of the BPA expert panel report
 - Audit the fidelity of changes to the December and March versions of the expert panel report



Audit

- Period covered
 - February 2006 to March 2007
- Materials covered
 - Literature summarized by contractor in preliminary draft- August 2006
 - Literature provided to expert panel for review- August 2006 to March 2007
 - E-mail records of changes requested by expert panel to August 2006 and December 2006 drafts
- Contributors
 - Literature review- NIEHS staff
 - Changes to draft expert panel reports- Dynamac Inc.



Literature Audit

- Strategy
 - Search PubMed using bisphenol and the CAS# for BPA (80-05-7)
 - Review titles of resulting 4900 references according to set criteria
 - Review titles on web site for BPA maintained by Dr. Fred vom Saal,
<http://endocrinedisruptors.missouri.edu/vomsaal/vomsaal.html>
 - Compare identified references with bibliography in August 2006 draft
 - Compare identified references with all references made available to the expert panel



Literature Audit

- Selection criteria
 - Reproduction and development (*in vivo* and *in vitro*), animal and human studies
 - *In vivo* measures of estrogenicity in relevant species
 - Absorption, disposition in the body, and metabolism during pregnancy
 - Body burden when related to pregnancy/children
 - General toxicity
 - Studies of BADGE, BISGMA, BIS-DMA (chemicals with a BPA core structure) included if related to reproduction/developmental toxicity
 - Immunological or neurological measures not resulting from exposure during development
 - Studies in non-traditional species that included (1) developmental exposure and/or (2) endpoint(s) related to reproductive organs or function
 - *In vitro* assays of estrogenicity (excluding estrogen receptor binding/transcriptional activation/cell proliferation/yeast variants)
 - *In vitro* estrogen response genes in cells from reproductive organs
 - Comparisons of batteries of *in vitro* screens for estrogenicity
 - Vitellogenin (protein produced in oviparous vertebrates in response to estrogens)



Literature Audit

- Findings
 - Approximately 50 papers identified that were presumably available in February 2006 that were not in the bibliography of the August 2006 draft
 - Nine of these papers were added to the December 2006 or March 2007 drafts
 - Approximately 50 papers were identified that were not included in the 742 references under consideration by the expert panel for the December 2006 and March 2007 drafts.
 - Review of these citations resulted in 5 additional papers sent to panel for consideration

- Conclusion
 - Appropriate reference materials were made available to the expert panel for their consideration during development of the December 2006 and March 2007 draft expert panel reports.



Audit of Requested Changes

- Strategy
 - Dynamac staff audited e-mail records of requests to the contractor from the expert panel members for changes to the December 2006 and March 2007 draft expert panel reports.
- Findings
 - Six changes requested in over 300 e-mails containing from 1 to more than 50 separate requests were not included in the December 2006 or March 2007 drafts.
 - These changes have been made to subsequent drafts.
 - Additional changes to the drafts were identified that were not identified in records of e-mail requests from the expert panel.
 - These changes were reviewed and attributed to the addition of new literature from updated literature searches, and changes as a result of the contractor's editing and fact checking processes.
- Conclusions
 - The contractor reliably made changes to the draft reports requested by expert panel members.



Overall Audit Conclusions

- The audit provided assurance that the draft BPA expert panel reports include consideration of all relevant references and reliably include changes requested by the expert panel members.
- NTP concludes that the draft expert panel reports are useful for the CERHR evaluation of BPA



NTP Contracts Review for Potential Conflict of Interest

- Strategy

- A working group of the NTP Board of Scientific Counselors conducted a review of NTP contracts to:
 - Assess potential conflicts of interest (COI)
 - Develop recommendations appropriate for reducing the potential for conflicts to occur
 - Address mechanisms for mitigating any current or future COI

- Conclusion

- The working group found no evidence of actual or apparent COI in its review of NTP contracts; however, it did recommend a number of best practices and areas where improvements could be made.



Conflict of Interest clause for NTP contracts

- Language developed to specifically address contractor responsibilities with regard to COI
- Being added to all existing and future NTP contracts