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To: [Hatlelid, Kristina](#); [Babich, Michael](#)
Cc: [Mike Dourson](#)
Subject: Peer Review Report for CHAP Phthalate Document
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Attachments: [CPSC_Task_5_Peer_Review_Report_8_12_13_FINAL.pdf](#)

Dear Dr. Babich and Dr. Hatlelid:

TERA is pleased to deliver this report summarizing the peer review of the Draft Report to the U.S. Consumer Product Safety Commission by the CHRONIC HAZARD ADVISORY PANEL ON PHTHALATES AND PHTHALATE ALTERNATIVES (May 15, 2013). The report contains the comments of four expert reviewers. We found their comments insightful and extensive. As we read through and organized these comments into this report, several important themes emerged.

- *Discussion of uncertainties with the available data and results.* As with any risk assessment, there are uncertainties with the data and the approaches used to analyze and utilize the available data. The reviewers identified a number of areas where the CHAP might enhance its discussion of uncertainties in the data, for example in the use of spot urine samples for biomonitoring data, differential exposure of the fetus and mother, and development of the RfDs (see below). The experts found the approach to assess cumulative risk (i.e., use of Hazard Indices [His]) as a useful way to evaluate risk and communicate the results. They did, however, comment on the need for further clarity in discussing and communicating the interpretation of the results (see below).
- *Use of Reference Doses (RfDs).* A very important part of the CHAP's work is the derivation of RfDs to compare with potential exposure and reach conclusions regarding risk. The experts suggest that the bases for the derived RfDs need further description and explanation. In particular they noted further explanation is needed regarding the selection of the end point and explanation why other endpoints were not used, the selection of uncertainty factors, and the different levels of confidence in each of the RfDs. They also suggested consideration of using benchmark doses rather than NOAELs. The CHAP chose to focus on target organ toxicity, specifically anti-androgen effects and calculated RfDs for this particular endpoint. Readers may be confused with the CHAP using the term RfD for the risk values developed for this document. RfDs by definition are based upon the most sensitive effect (i.e., the critical effect) for any particular chemical (U.S. EPA 2002). To avoid confusion, the CHAP should consider distinguishing their anti-androgen RfDs (perhaps label them RfDaa) to make it clear that these are target organ/endpoint specific and to sidestep any potential criticism or confusion for deriving RfDs based upon an effect that may not be the most sensitive. Others have explored and used the concept of target organ specific RfDs (e.g., EPA, California EPA and ATSDR) and the CHAP might consider considering these as support for their approach. For example, EPA (U.S. EPA 2007) discusses "hazard quotient values developed for organs that are not the critical organ in the IRIS Assessment, or for which a reference value has not been formally established." To further address the unevenness in confidence of the RfDaas, the CHAP might also consider choosing only one RfDaa for each chemical rather than have some chemicals for which the difference in RfDaas is up to 25-fold. Extending this thought, the

CHAP might also consider contrasting its RfDaas and the resulting HIs or MOEs with corresponding HIs and MOEs based on the traditional critical effect RfDs for these same chemicals.

- *Transparency and clarity and communicating results.* The CHAP was charged with conducting a *de novo* examination of the risks associated with phthalates and phthalate alternatives in children's toys and child care articles. In their May 15, 2013 draft report they provide recommendations to the Commission on specific phthalates and phthalate alternatives. Their draft report describes the CHAP process, scientific data, and support for their recommendations. The experts provide helpful comments on areas where they think the presentation and scientific discussions should be enhanced and clarified. They include some thoughtful comments and suggestions about communicating the risk conclusions. The CHAP may also want to consider including the work of LaKind et al. (2008) on biomonitoring equivalents (BEs) and in particular consider showing the CHAP's information on chemical toxicity and human biomonitoring in a graphic format. For example, the attached figure from LaKind et al. (2008) shows interpretation of population biomonitoring data in exceedance of BEs that are associated with toxicological points of departure and Reference Doses (RfD) or other toxicity risk values. BEs have been developed for several of the phthalate esters based upon the available data and this work might be useful to discuss and cite (e.g., Aylward et al. 2009a, 2009b; Hayes et al., 2011). In addition, Benson (2009) explored many of these same issues the CHAP grappled with and his work might be further utilized in this report.

Overall the reviewers thought that the CHAP addressed its charge and were impressed with the magnitude of this effort and the results. If the CHAP has clarifying questions regarding this report, we would be happy to assist in obtaining answers from the individual expert reviewers.

Sincerely,

Jacqueline Patterson

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