June 9, 2011

Dr. Michael Babich
Directorate for Health Sciences
U.S. Consumer Product Safety Commission
4330 East West Highway
Bethesda, MD 20814

Re: Chronic Hazard Advisory Panel review of phthalates and phthalate alternatives

Dear Mike:

The Phthalate Esters Panel (PE Panel) of the American Chemistry Council has followed closely the deliberations of the Chronic Hazard Advisory Panel (CHAP) regarding children's exposure to phthalates and other plasticizers. The PE Panel represents the North American manufacturers of phthalates who would like to comment on the following issues that were discussed during the CHAP's most recent meeting on March 30 and 31 –

- the Panel's mandate, as outlined in Section 108 of the Consumer Product Safety Improvement Act (CPSIA),
- the importance of considering exposure as part of the Panel's assessment,
- the need to ensure consistency in the CHAP's approach to assessing cumulative risk,
- the level of protection to be achieved by CPSC, and
- the importance of considering previous reviews as part of the Panel's "*de novo*" assessment

I would respectfully request that these comments be shared with the CHAP members in advance of the next scheduled meeting.

<u>The Panel's Mandate</u>

The discussion among the CHAP members at the March meeting suggested continuing uncertainty regarding the scope of the review requested by Congress. In the enclosed September 24, 2010 letter to CPSC's General Counsel, Cheryl Falvey, the PE Panel highlighted the specific language of Section 108 of the CPSIA pertaining to the scope of the review. In that letter we noted that paragraph (A) of Section 108(b)(2) directs the CHAP "to study the effects on children's health of all phthalates and phthalate alternatives *as used in children's toys and child care articles*" (emphasis added). Paragraph (B) further directs the Panel to examine

phthalates "that are used in products for children." Moreover, Section 108(b)(3)(B) directs the Commission to evaluate the CHAP's recommendations regarding "any children's product containing any phthalates."

The clear language of the statute confirms that the CHAP's charge is uniquely focused on children's products – in particular children's toys and child care articles. The reference to "other sources, such as personal care products" in item (iv) in Section 108(b)(2)(B) is in the context of a cumulative assessment. Similarly, the reference to "pregnant women" in item (vii) of the same Section is solely as part of an assessment of the potential for *in utero* exposure.

The focus on children's exposure serves to simplify the CHAP's mandate. The Panel's effort is further simplified by the availability of an extensive amount of representative biomonitoring data from the Centers for Disease Control and Prevention (CDC). Despite the availability of the CDC data, CHAP members expressed at the March 2011 meeting a desire to develop a matrix of exposure scenarios to compare against the available CDC data. We note that an analysis of the published literature on exposure to phthalates has been conducted by Dr. Kathy Clark and was presented at the July 2010 CHAP meeting.[1] The analysis shows reasonable agreement between the published estimates of exposure from biomonitoring data and those estimates derived from exposure scenario analysis, and we would suggest that it can provide an excellent "reality check" for the CHAP's efforts. The only age group for which biomonitoring data is limited is for children less than 6 years of age, although the CHAP apparently has received unpublished infant exposure data from research done by Dr. Shanna Swan and additional data appear to be available for younger German children.[2]

At the March 2011 CHAP meeting, the CHAP members also discussed the need to evaluate the reliability of published exposure studies. We note that Dr. Clark has done precisely that for the studies she exhaustively compiled.[3] Similarly, Dr. Jane Teta provided an analysis of the reliability of the epidemiology studies in her written testimony for the July 2010 CHAP meeting.[4]

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1 Dr. Clark's report, "Human Exposure to Phthalates Esters," is available on the CPSC website at http://www.cpsc.gov/about/cpsia/chap0710.html. The analysis will be published in an upcoming issue of the peer reviewed journal *Human and Ecological Risk Assessment*.

2 Koch HM *et al.* Exposure to phthalates in 5–6 years old primary school starters in Germany—A human biomonitoring study and a cumulative risk assessment. *Int J Hyg Environ Health* doi:10.1016/j.ijheh.2011.01.009 (2011).

3 The concentration data for DINP and DIDP are available on the CPSC website at http://www.cpsc.gov/about/cpsia/chap/exxonDINPDIDPdb.pdf; the data for the other phthalates are available at http://www.cpsc.gov/about/cpsia/chapmain.html.

4 Dr. Teta's presentation for the July 2010 CHAP meeting, "Statement on behalf of the Phthalate Esters Panel of the American Chemistry Council" and her written report, "Review of Phthalates Esters Epidemiology," are available on the CPSC website at http://www.cpsc.gov/about/cpsia/chap0710.html.

The Importance of Exposure Information for the CHAP's Evaluation

The discussion at the March meeting included a suggestion that the CHAP only consider hazard as part of its assessment. While it is correct that exposure to individual substances may change over time (e.g., as a result of future CPSC action), it is critically important that the CHAP include consideration of exposure in its evaluation. Simply put – without exposure there can be no risk. To exclude consideration of the potential for exposure in the CHAP's assessment, and to focus solely on hazard, would be to ignore a fundamental tenet of the risk assessment process. The biomonitoring data clearly indicate that, despite widespread use, exposure to these substances is very low. Based on the preliminary results presented in late March and on the publication by Koch *et al.* 2011, in fact, it is only at the very highest end of the estimated range (based on the biomonitoring data) that cumulative exposures approached the suggested reference levels.

The Need for Consistency in the Cumulative Screening Assessment

The CHAP also continued discussion of the inclusion of other substances in its cumulative screening assessment, including a presentation by CHAP members incorporating pesticides and other substances in a preliminary analysis of hazard index (HI) data. The CHAP members appeared to agree that it would not be appropriate to include other substances in its cumulative screening assessment. During this discussion CHAP members expressed concern about the lack of exposure data for these other substances and the fact that the approach to assessing risk from multiple substances based on their potential to produce a "common adverse outcome" was still in its infancy. On a more practical level, moreover, inclusion of other substances is inconsistent with Congress' direction in Section 108(b)(2)(B) of the CPSIA to "consider the cumulative effect of total exposure *to phthalates*"(emphasis added). Focusing on cumulative exposure to phthalates will provide the most useful information for CPSC, and we encourage CHAP members not to extend its analysis to other, unrelated substances.

Even among the phthalates, however, it is important that the CHAP's approach remain consistent. CHAP members agreed some time ago to focus on laboratory animal data suggesting male reproductive developmental effects as the health endpoint(s) for its cumulative screening assessment. Yet, the HI information presented at the last two CHAP meetings appears to have included di-n-octyl phthalate (DnOP) and di-isodecyl phthalate (DIDP), for which available rodent studies have failed to produce evidence of male developmental effects. It appears that in the process of developing a preliminary HI model for discussion purposes, DnOP and DIDP were included simply because they are listed in the CPSIA and exposure data exist.

Moreover, CHAP members have suggested the need to consider diethyl phthalate (DEP) in the cumulative screening assessment despite the fact that animal studies have not shown

that DEP causes male developmental effects**,** which was noted by Drs. Paul Foster and Earl Gray in their testimony to the CHAP at the July 2010 meeting. The suggestion to consider DEP appears to be based on epidemiological data, much of which has been discounted by the National Toxicology Program's Center for the Evaluation of Risk to Human Reproduction (CERHR) and European authorities. In other studies, information on the level of DEP in biomonitoring samples is limited as it is combined with other phthalates to produce a composite score. These studies do not provide sufficient justification for inclusion of DEP in the CHAP's cumulative screening assessment.[5]

The CHAP also has included diisononyl phthalate (DINP) in its preliminary HI screening assessment, apparently based on two limited studies which suggest evidence of minor effects on androgen-sensitive tissues and a reduction in fetal testicular testosterone, a hypothesized sentinel event for some of the male reproductive effects for which no threshold has been established. We note that Section 108 (b)(2)(B)(v) of CPSIA requires that the CHAP "review all relevant data, including the most recent, best available, peer-reviewed, scientific studies of these phthalates and phthalate alternatives that employ objective data collection practices or employ other objective methods."

For these reasons, prior to finalizing its preliminary HI screening assessment, we believe that it is important that the CHAP clearly define the criteria to be used for a substance's inclusion in the HI evaluation and that the Panel carefully evaluate each phthalate and phthalate substitute against those criteria.

Level of Protection to be Achieved

In March, the CHAP members also discussed the level of protection to be achieved by the phthalate regulations. The CPSIA does not provide a "bright line" to use in assessing the need to continue the interim restrictions on DnOP, DIDP, and DINP and/or to restrict other plasticizers. Rather paragraphs (2)(B)(vii) and (3)(A) of Section 108(b) of the statute instruct the CHAP and the Commission, respectively, to ensure a "*reasonable* certainty of no harm . . . with an adequate margin of safety"(emphasis added).[6] Although it was suggested during the March

[5] This conclusion was supported by the comments of CHAP member Dr. Hauser at the March meeting when he noted that these epidemiology studies "…didn't assess specific chemicals…so it could be the DEP, it could be something else that they're exposed to, or it could be lifestyle differences." (See the media file of the March 2011 CHAP Meeting at http://www.cpsc.gov/vnr/asfroot/chap03312011.asx.)

[6] The standard "reasonable certainty of no harm" also is used in the Federal Food Drug and Cosmetic Act (FFDCA), as amended by the Food Quality Protection Act (FQPA) of 1996. *See* FFDCA Section 408(b)(2)(A)(ii). Congress intended the standard in the FQPA to mean that "that the aggregate exposure to the pesticide chemical residue will be lower by an ample margin of safety than the level at which the pesticide chemical residue will not cause or contribute to any known or anticipated harm to human health." H.R. Rep. No. 104–669 (1996), at 41. Congress did not, however, provide guidance on criteria to be used to assess the likelihood that such exposure might occur.

meeting that the CHAP should seek to provide protection regardless of the likelihood of harm, such an interpretation is not consistent with the term "reasonable." Congress' use of that term suggests a certainty that can be generally agreed upon and/or one that appeals to common sense. As such, the PE Panel believes it is appropriate to apply traditional statistical criteria to determine whether a "reasonable certainty of no harm" has been achieved.[7]

A statistical treatment is particularly appropriate in light of the CHAP's apparent decision to use an HI approach in its cumulative screening assessment for phthalates. While the HI represents the ratio of estimated exposures to the level(s) at which no harm is expected to result, an HI greater than 1.0 does not indicate a likelihood of adverse effects. The HI cannot be translated to a probability that adverse effects will occur, moreover, and is unlikely to be proportional to risk. The National Resource Council's Committee on the Health Risks of Phthalates expressed caution about the use of HIs when it noted that:

> HIs larger than unity cannot necessarily be taken to indicate a larger than zero effect of the mixture . . . although they are treated as indicators that there is potentially such a nonzero effect.[8]

The HI also may be overly health protective since the reference dose used in the calculation is based on the most sensitive health endpoint, not necessarily the endpoint(s) on which the HI is calculated. In its Guidelines for risk assessment of chemical mixtures, the Environmental Protection Agency (EPA) notes that "[w]hen the Hazard Index is calculated for some different, less sensitive effect, the [reference dose] will be too low . . . and the Hazard Index will be too large."[9]

<u>What Is To Be Considered for the CHAP's *De Novo* Review</u>

Regarding the instruction to the CHAP in Section 108(b)(2)(B) to conduct a *de novo* review of phthalates, we note that *de novo,* while requiring the panel to make its own conclusions, nevertheless also embraces and builds on past efforts**.** Indeed, CPSIA section 108(b)(2)(B) specifically directs, "The findings and conclusions of any previous Chronic Hazard Advisory Panel on this issue and other studies conducted by the Commission *shall be reviewed*

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[7] The PE Panel has submitted information to the CHAP indicating that caution should be used when interpreting the tails of the distribution of population-based biomonitoring data based on spot samples for biologically transient compounds like the phthalates (Aylward *et al.*, March 25, 2011). As a consequence, the PE Panel believes that measures of the central tendency of these data are the most appropriate statistical information to consider.

[8] National Research Council. Phthalates and Cumulative Risk Assessment – The Task Ahead. National Academies Press, Washington DC (2008), at 88.

[9] EPA. Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures. EPA/630/R-00/002 (August 2000), at 82.

by the panel but shall not be considered determinative"(emphasis added). As you are aware, there have been a considerable number of comprehensive reviews of the phthalates of interest to the CHAP, including the 2001 CHAP review of DINP and reviews of several phthalates by the CERHR and European Union. The CHAP would be remiss if it were to disregard these previous findings. Rather, the PE Panel believes that Congress intended that the CHAP build on the conclusions of these previous expert opinions, considering any new data that have emerged since their completion.

Please do not hesitate to contact me at (202) 249-6727 or steve_risotto@americanchemistry.com if you have any questions about the information provided above.

Sincerely,

Steve Risotto

Stephen P. Risotto
Senior Director

cc: CPSC General Counsel Cheryl Falvey

Enclosure