EASTMAN

July 12, 2010

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

Re: CHAP Feedback on CPSC Staff Reports:
Toxicity Review for Di-n-butyl Phthalate (Dibutyl Phthalate or DBP), and
Toxicity Review for Di(2-ethylhexyl) Phthalate (DEHP)
(as posted on http://www.cpsc.gov/about/cpsia/chap0410.html)

Dear Dr. Babich,

Eastman Chemical Company is, and always has been committed to the safety of its products. As a manufacturer of two of the ortho-phthalates under review by the CHAP, Eastman welcomes this opportunity to, as comprehensively as possible, review the available scientific information regarding the known toxicology of this family of substances.

As I am sure many people are aware, ortho-phthalates have a long history of use, in a wide variety of applications. In general, ortho-phthalates have a low order of acute toxicity, and to the best of our knowledge, there have been no adverse outcomes in humans related to long-term exposure to ortho-phthalates.

While there have been adverse findings in animal studies regarding reproductive and carcinogenicity outcomes, the relevance of these studies to humans remain questionable. The scientific validity of the more recent reports of reproductive and developmental issues related to ortho-phthalate exposure in humans also remains questionable.

Because of their long history of use, there is an abundance of toxicological data for this family of substances. The ortho-phthalates have been reviewed by a number of regulatory bodies, and have been evaluated under several programs to evaluate the potential exposure-based risks associated with High Production Volume chemicals. These programs include the Orgranisation for Economic Cooperation and Development (OECD) and Environmental Protection Agency's HPV programs. In spite of this abundance of information, there is no definitive scientific evidence that disproves the safety of this family of substances.

We appreciate the efforts of the CPSC in commissioning a third-party review of the toxicology of the ortho-phthalates in question. In order to ensure that all of the evidence is evaluated fairly, we would like to point out statements that are made in these reviews which may be misleading, as well as pointing out some factual errors in these reviews. These comments have been captured in the attachment enclosed.

We note that the CPSIA does not allow for further review by the CHAP of the restrictions introduced by this law.

Once again, Eastman appreciates the opportunity to provide comments to ensure that the information reviewed by the CHAP is as complete and accurate as possible.

Sincerely,

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Attachment

CHAP Feedback on CPSC Staff Reports

Regarding the toxicological review of Dibutyl phthalate (DBP):

1. The review incorrectly states the conclusion of the 2004 publication by Hauser et al. which describes medications as a source of human exposure to phthalates (discussed in the "Exposure" section on Page 6 of the review). The review states that Hauser concluded that "concentrations of levels approaching a NOAEL of 50 mg/kg/day can possibly contribute to the testicular dysfunction reported to be associated with DBP exposure in other studies." The paper by Hauser et al. does not draw this conclusion. The conclusion of this paper was that they had:

   > "identified an individual with a urinary MBP level two orders of magnitude higher than the U.S. population 95th percentile and linked this unusually high urinary MBP concentration with the use of a specific medication that contained DBP. However, because this is a case report on a single patient, replication of this finding in other populations is needed to definitively conclude that the medication was the main contributor to the very high urinary concentration of MBP."

   The CPSC DBP review seems to downplay the fact that Hauser's paper was a description of a case study involving a single patient. In addition, the mis-statement of Hauser's conclusions gives the reader the incorrect impression that typical daily use of medications may lead to exposures close to the NOAEL.

2. On page 9 of the review, in the section on "Systemic Effects", the author's incorrectly use the term "hypospadic." The correct name of the disorder is hypospadias.

3. On page 12 of the review, in the summary of the section on "Sensitization," the last statement is very misleading. The statement that "There is not sufficient data to conclude that DBP is a strong sensitizer under the FSHA" implies that there may be a lesser issue of DBP as a sensitizer. It should be noted that DBP is not classified as sensitizer in the US or EU, and is in fact still listed as an acceptable ingredient in personal care products by the Cosmetic Ingredient Review (CIR) Expert Panel (pages 34-32 of: Annual Review of Cosmetic Ingredient Safety Assessments--2002/2003. Int.J.Toxicol. 24 Suppl 1:1-102, 2005.)

Regarding the toxicological review of Dibutyl phthalate (continued):

4. There are a few statements in the discussion section, which begins on page 23, which are either mischaracterizations or misstatements of the data on DBP.

    - On page 24 of the review, we disagree with the statement that "The human data by Swan et al. showed an association between MBP and anogenital distance (AGD) in male infants." The Swan study utilized a weight-corrected measure, which was referred to as Anogenital Index, or AGI. The clinical significance of AGI in humans is not known, as it is a measure that was defined by this study.

    - In this same paragraph, it is misleading to state at the end that "These studies provide sufficient evidence that DBP can be considered developmentally toxic under the FHSA." This statement implies that Swan's data can be used to support an FHSA designation of "developmentally toxic," while the relevance of this study in supporting an FHSA designation is not clear.

    - Once again, the discussion section states that there is not enough evidence "to consider DBP a strong sensitizer." This misleads the reader to believe that there are sensitization issues with DBP, when no such issues exist.

Regarding the toxicological review of diethylhexyl phthalate (DEHP):

1. In the executive summary, the statement that "Sufficient animal data existed to support the conclusion that DEHP was a carcinogen and a reproductive and developmental toxicant" should be clarified to reflect that while NTP still makes this conclusion, IARC considers DEHP to be Group 3 – not classifiable as to its carcinogenicity to humans.

2. In the "Introduction" section on page 1 of the review, it is stated that the review is "intended to be utilized as part of an individual and cumulative phthalate risk assessment." We believe that this statement is somewhat premature, as the panel has not made a decision as to the role of the cumulative risk approach in their review.

3. On page 5, in the "Manufacture, Supply, and Use" section, the statement in the first paragraph that "DEHP can also contain bisphenol A (CAS No. 80-05-7) at concentrations ranging from 0.025 to 0.5%." is very misleading. This statement is made immediately after a discussion of the impurities that are typically found in DEHP, implying that bisphenol A is an impurity of the DEHP manufacturing process. The cited source (ECB, 2008) actually states that "Some DEHP is, when requested by the user, supplied with 'Bisphenol A'; 4,4'-isopropylidenediphenol (CAS No. 80-05-7) as an additive in the range of 0.025 to 0.5%." In this case, bisphenol A is an additive. Because bisphenol A has its own toxicological issues, it is both unfair and scientifically unjustified to cloud the review of DEHP with this mention of bisphenol A.

4. On page 6, also in the Manufacture, Supply, and Use" section, the statement that "DEHP uses can be divided into two categories: 1) use as a polymer, and 2) use as a nonpolymer" is incorrect. DEHP is used *in* polymers and non-polymers. DEHP is not a polymer, nor does it polymerize under normal use conditions. It is slightly troubling to see such a blatant error in the basic description of the uses of DEHP.

5. On page 29, in the "Metabolism: oral exposure" section, it is stated that dimethyl phthalate (DMP) is a "major urinary metabolite" in both mice and hamsters (Albro, et al., *J. Chromatograpy*, 244: 65-79, 1982). To the best of our knowledge, this is not in agreement with the currently accepted understanding of the metabolism of DEHP. This reference to DMP as a metabolite of DEHP appears to be unique to this particular journal article, and is not supported by any other studies.

6. On page 38, in the "Hazard Information" section, the discussion of carcinogenicity data does not mention the fact that IARC currently considers DEHP to be in Group 3, "not classifiable as to its carcinogenicity to humans." While the National Toxicology Program's Report on Carcinogens supports the review's conclusion that DEHP is a "possible human carcinogen", not presenting the IARC designation for DEHP unfairly ignores an entire wealth of research and discussion regarding the potential mechanism of DEHP-induced carcinogenicity in rodents, and the relevance of these mechanisms to humans.