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CONSUMER PRODUCT SAFETY COMMISSION
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Memorandum

Date: December 16, 2014

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THROUGH: Stephanie Tsacoumis, General Counsel
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SUBJECT : Staff Responses to Questions for the Record from Commissioner Buerkle about
the Notice of Proposed Rulemaking (NPR): Prohibition of Children's Toys
and Child Care Articles Containing Specified Phthalates

This memorandum provides staff responses to the questions for the record from Commissioner Buerkle about the NPR for the Prohibition of Children's Toys and Child Care Articles Containing Specified Phthalates.

Questions from Commissioner Buerkle

1. *CHAP table 2.1 (p. 24) summarizes the NOAELs for developmental endpoints affecting male reproductive development. These values were used as the points of departure in case 3 of the cumulative risk assessment. See CHAP table 2.15 (p. 66). For DINP, the value in table 2.1 is 50 mg/kg-d, based on Boberg et al. 2011. However, CHAP Appendix A (page Appendix A 25) shows a higher NOAEL (300 mg/kg-d) for the Boberg study. Does the CHAP Report explain this apparent discrepancy? If not, how did the staff evaluate this point in its assessment?*

The toxicological information associated with DINP is summarized in the CHAP report on pages 95 to 98 and A-22 to A-25 (CHAP 2014). On page A-23, the CHAP set a consensus no observed adverse effect level (NOAEL) for DINP-induced increases in multinucleated gonocytes and nipple retention at 300 mg/kg-d. In the discussion on page 97 to 98, the CHAP included an additional reference in their review (Clewell *et al.*, 2013).

The CHAP wrote:

“... data from Clewell *et al.* (2013b) show that the NOEL for DINP-induced MNGs is approximately 50 mg/kg-day. Taken together, the data from Boberg *et al.* (2011), Hannas *et al.* (2011b), and Clewell *et al.* (2013a; 2013b) indicate that the developmental NOAEL based on antiandrogenic endpoints (nipple retention, fetal testosterone production, and MNGs), is between 50 and 300 mg/kg-day. Taking a conservative approach, the CHAP assigns the NOAEL for DINP at 50 mg/kg-day. However, the CHAP also wants to point out that a simple extrapolation based upon relative potencies (as described by Hannas *et al.*, 2011b) with 2.3-fold lesser potency of DINP than DEHP (in terms of fetal testicular T reduction) would lead to a NOAEL of 11.5 mg/kg-day for DINP. This scenario is reflected in case 2 of the HI approach.”

2. *Did the CHAP identify any systematic difference(s) in phthalate exposure between pregnant women and women of reproductive age generally? If so, what was the source of exposure uniquely affecting pregnant women?*

The CHAP reported, “In NHANES 2005–2006, comparing pregnant women to nonpregnant women in this age range, the exposures were not found to be significantly different. In the upper percentiles, as well as with weighted analyses, there are indications that exposures might be higher in pregnant women than in women in general or in the rest of the NHANES population (CPSC 2014, p. 36).”

3. *The CHAP obtained exposure data from the SFF study. See CHAP Report, p. 35. When were these SFF exposure measurements taken? Has all the data made available to the CHAP been made available to the public?*

Measurements in the SFF study were made from 1999 to 2005 (CHAP 2014, p. 39). The data are on the CPSC website: <http://www.cpsc.gov/PageFiles/169897/SFF-Biomonitoring-Data.pdf>.

4. *The staff Briefing Package (p. 27) states that “the CHAP used the latest available data at the time they performed their analysis.” It is difficult to understand how this statement can be true. When did the CHAP conduct their analysis?*

As explained below, the CHAP based their calculations on the 2005-2006 dataset (this data was revised in 2012). The CHAP also reviewed the 2007-2008 NHANES summary data. In addition to the NHANES data, the CHAP also relied upon data from the Study for Future Families (SFF) for data on infants.

There have been 4 NHANES data sets between 2005 and 2012. As described on the CDC website¹, the NHANES data sets are revised, on occasion, due to errors in chemical analyses or errors in the statistical weighting of the NHANES population. Below, we discuss these NHANES datasets.

NHANES 2005-2006 Dataset. The CHAP based their calculations of the hazard index for pregnant women on exposure data in the latest NHANES data that were available at the time of the CHAP's analyses, which is the 2005–2006 data, as revised in February 2012. As explained in the CHAP report (CHAP 2014, p. 35):

“This cycle of NHANES was the most recent version in which phthalate data were available at the time of our analyses. Previous cycles were not combined with the 2005–2006 data due to study design changes associated with fasting requirements.”

The 2005–2006 data were revised by NHANES in February 2012 (CDC 2012a, b). The CHAP revised its analyses to include the revised data (i.e., from the 2012 revision) before completing the draft CHAP report. The 2005-2006 NHANES data set included data on larger numbers of pregnant women than the subsequent NHANES data sets.

NHANES 2007-2008 Dataset. As reflected in multiple locations in the CHAP report, the CHAP also reviewed the 2007–2008 NHANES summary data. The CHAP considered and discussed 2007–2008 NHANES summary data for the general population when comparing to the 2005–2006 data set and in relation to concentrations of individual phthalates (CHAP 2014, pp. 39, 42, 74, 75, 87, 98, 111). The 2007–2008 NHANES data first became available in October 2010, but were revised in September 2011 and January 2012.

NHANES 2009-2010 Dataset. NHANES data for 2009–2010 became available in September 2012. These data became available after the analysis was completed. Thus, the CHAP did not review the 2009-2010 dataset.

NHANES 2011-2012 Dataset. The 2011–2012 NHANES data were available in July 2014, then withdrawn August 2014. The revised 2011–2012 NHANES data were available in October 2014.

SFF Data. NHANES does not include data on children younger than age 6 years old. Therefore, the CHAP used additional data from the Study for Future Families (SFF) to obtain data on infants. This study covers the time period 1999–2005. The SFF is a study of infant-mother pairs. Mothers were tested both during and after pregnancy. To staff's knowledge, there is no plan to update this study. Even if the hazard index for pregnant women was recalculated based on new NHANES exposure data, the risk estimates for infants and their mothers would remain the same because the SFF data is separate from the NHANES data. Using the SFF data, the CHAP estimated that up to five percent of pregnant women and infants had a hazard index greater than one.

¹ <http://www.cdc.gov/exposurereport/>

5. *The staff Briefing Package (p. 27) states that “phthalate exposures in the U.S. population, as measured by biomonitoring, have remained essentially constant for about a 10-year period.” What is the 10-year period being referenced here? What analysis, if any, is this statement based on? Does the statement consider 95th percentile exposures, which are crucial to the CHAP’s cumulative risk assessment, as well as mean (or median) exposures?*

This statement refers to the approximately 10-year period beginning with NHANES data from 1999 to 2000 until 2009–2010. The 2009–2010 NHANES data are the first to suggest any clear temporal trends in phthalate exposure. The staff’s conclusion is based, in part, on a review of NHANES data summaries, which include median and 95th percentile exposures (CDC 2012). Staff’s conclusion is further supported by a recent review by EPA (EPA 2013) and other recent publications (Lioy *et al.*, 2014; Zota *et al.*, 2014; Zota and Woodruff 2014).

6. *Why does the CHAP use the term “infant” to describe children up to 3 years old? Is that usage consistent with normal CPSC terminology?*

The CHAP analyzed SFF biomonitoring data on subjects 2 months–36 months of age to assess phthalate exposures (page Appendix D-1). The average age of these subjects was 13 months old, with the majority being 16 months old or younger. These subjects were termed “infants” in the CHAP report and in publications on the SFF study (Sathyanarayana *et al.*, 2008a, b). The infant ages considered by the CHAP for the exposure activity scenarios were 0 to <1 year old (Appendix Table E1-7, page E1-13).

7. *Does the CHAP report provide any explicit discussion or explanation as to why the CHAP intended their recommended future prohibition on DINP to extend beyond toys that can be mouthed to all children’s toys? Is it possible that the CHAP was not advertent to this distinction?*

The CHAP recommended that DINP be permanently banned in all children’s toys and child care articles. The Co-chair of the CHAP, Dr. Lioy has confirmed that the CHAP intended the DINP prohibition to extend beyond toys that can be mouthed. The CHAP report does not explain why DINP should be prohibited in all children’s toys, rather than only children’s toys that can be placed in a child’s mouth.

8. *How, specifically, will the staff analyze more recent exposure data, including the 2009/2010 NHANES dataset as well as other research provided through the comment period?*

Absent Commission direction to the contrary, staff plans to analyze the hazard index calculations for pregnant women using the 2011/2012 and earlier NHANES data sets and

the same approach and methodology as the CHAP, to the extent possible. Additionally, staff will review and consider all public comments, including any additional recent exposure data and new scientific literature.

9. *Can staff analyze more recent exposure data using the same models the CHAP already developed for estimating exposures from NHANES data? If not, why not? Can the impact of the more recent data be further analyzed by substituting values in the same models or spread sheets that were used by the CHAP for their cumulative risk assessment?*

The CHAP analyzed NHANES and SFF data using SAS statistical software. Staff would use the same methods used by the CHAP to analyze more recent exposure data. There are no spreadsheets into which the staff can easily enter new data, and there are very likely differences in the sample size and study design from cycle to cycle. The staff notes that the 2009–2010 data include a smaller number of pregnant women and no information on infants. The staff also notes that statistical comparisons across data sets from different time periods may be difficult due to the differences in the study design and number of subjects from year to year.

10. *Will the CHAP exposure model(s) and spread sheet formats be made public? If so, when? If not, why not?*

Staff and the Office of General Counsel are assessing the applicable considerations and legal constraints.

11. *Does the staff intend to establish a cutoff date for new scientific studies and data to be considered in the rulemaking? If so, will it be the same as the CHAP's deadline of December 31, 2012? If not, what date will be used?*

The staff will consider new scientific literature published at least through the end of the public comment period for the Notice of Proposed Rulemaking.

12. *In the NHANES data, are the exposures of pregnant women to the five phthalates statistically different from those for women of reproductive age generally?*

The CHAP reported, “In NHANES 2005–2006, comparing pregnant women to nonpregnant women in this age range, the exposures were not found to be significantly different. In the upper percentiles, as well as with weighted analyses, there are indications that exposures might be higher in pregnant women than in women in general or in the rest of the NHANES population (CHAP report, p. 36).”

13. *Draft NPR p. 17. Why were the 95th percentile exposures for pregnant women in the SFF data so much less than for the NHANES data?*

Staff does not know the reasons why the two different data sets resulted in different results for the 95th percentile exposures for pregnant women.

14. *Can we quantify the difference in exposure from handling toys versus directly mouthing them?*

Yes, but the factors used for estimating transfer of the phthalate from the consumer product to the skin, dermal metabolism of the phthalate, absorption of the phthalate from the skin (location dependent), and systemic uptake from the skin are much less developed and potentially more uncertain than estimating transfer from oral mouthing. This makes it difficult to compare exposures from the two scenarios.

15. *The staff Briefing Package (p. 18) quotes the CHAP as follows: “DINP does induce antiandrogenic effects in animals, although at levels below that for other active phthalates” This statement is ambiguous and potentially highly misleading. Should the term “levels” in this statement be interpreted as referring to levels of exposure or to the levels of antiandrogenic effects? In other words, does the statement mean that DINP causes less significant health effects than active phthalates at comparable exposures or does it mean that DINP causes antiandrogenic effects at lower exposures than active phthalates?*

The CHAP’s statement means that DINP causes the same effects on male reproductive development as other “active” phthalates. The only difference is that DINP is less potent.

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