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Dr. George Borlase (via email: GBorlase@cpsc.gov)
Associate Executive Director
Office of Hazard Identification and Reduction
U.S. Consumer Product Safety Commission
4330 East West Highway
Bethesda, MD 20814

Dear Dr. Borlase,

We would like to commend the CPSC science staff for their work done on the re-analysis of the CHAP report using the more up-to-date NHANES data. We were pleased that when completing an independent assessment the science staff came to similar conclusions as those made by our own scientists. The staff document provided a clear outline of the process they followed to replicate the CHAP findings and the scope of the task, which was limited to replication/validation of the CHAP methodology, assessment of the appropriate subpopulations, and application of the methodology to specific target populations in the recent data sets.

Herein, we wish to bring to your attention a couple of points from the re-analysis report results, that were outside of the scope of what the staff independently assessed, but were carried forward from the CHAP analyses. These points have troubling implications for how they could be interpreted by non-science audiences, and have basic science concepts that have been misapplied. We would appreciate if we could discuss these concerns with the CPSC science staff as well as outline the basic principles that the CHAP has misapplied.

First, we would like to point out that Table 7 of the report can give the impression that individuals with hazard indices (HIs) above 1 (found only above the 95th percentile) are at risk, and that this translates to a meaningful portion of the population being placed at risk. This is simply not a correct conclusion. The NHANES dataset utilizes spot samples which can "spike" in a single instance but cannot be assumed to be representative of chronic exposures. It has been demonstrated that spot samples from individuals may be used to approximate a population's exposure over time, but cannot be used to represent a specific individual's exposure over time. With a large enough sample size, the 50th percentile of the spot samples approximates a typical individual's average exposure over time, and the 95th percentile is a very conservative estimate that is protective of any individuals in the measured population that may experience higher than average exposures.

It is unclear why the CHAP included the "percent of individuals" with HI's above 1. Evaluation of spot urine samples indicates they are inappropriate for evaluating "individual risk", but can only be used as a surrogate to determine population risk. The depiction by the CHAP of percent of individuals with HI > 1, gives an impression of individuals at risk, and this is an inappropriate usage of the data. This issue is discussed in Section III.B and in greater detail in Appendix A of the comments we submitted to the docket on August 6.

Second, we note that the CHAP's "Case 2" is based on modeled no observable adverse effect level (NOAEL) values that are inconsistent with actual NOAELs developed with substance-specific data. The CHAP assumed the relative potency of DINP and DEHP is constant across all endpoints. This is problematic since potency across phthalates is not the same for various endpoints. This fact would have been clear to the CHAP if they had compared their modeled values to actual values which are available in multiple published studies. This inconsistency in potency inappropriately inflates the contribution of risk to the cumulative risk assessment for phthalates other than DEHP.

The Hannas *et al.* (2011) study upon which Case 2 is based compared the effects of phthalates (including DEHP and DINP) on testosterone production. The CHAP noted that DEHP was 2.3-fold more active than DINP. The CHAP then hypothesized that the same relative potency relationship would hold for the downstream adverse endpoints (genital malformations) measured for DEHP in other experiments. For such effects, the CHAP used three studies (Grande *et al.*, 2006; Andrade *et al.*, 2006a; Christiansen *et al.*, 2010) to set a NOAEL for DEHP. Using that NOAEL (5 mg/kg/day), and the potency estimates derived from the Hannas results, the CHAP calculated a hypothetical NOAEL for DINP of 11.5 mg/kg/day (2.3 x 5 mg/kg/day) and used that value as the point of departure for Case 2. It is important to note, however, that the ultimate adverse effects seen after DEHP exposure are not seen after DINP exposure; therefore, there is an intrinsic difference in hazard potential for the two chemicals.

In short, the Case 2 analysis is illogical for the following argument. Clewell *et al.* (2012a), based on actual DINP studies, concluded that a testosterone reduction is observed at a NOAEL of 100 mg/kg/day. The CHAP implies that testosterone is a precursor to genital malformations. At the same time, the CHAP also concludes that malformations occur at a much lower level NOAEL of 11.5 mg/kg/day. This NOAEL is not based on actual data but derived from DEHP because in actual fact, genital malformations are not observed with DINP. Also, if testosterone is only impacted at NOAEL's higher than 100 mg/kg/day, it is illogical to assume that at a level 10x lower those malformations would occur. This issue is discussed in detail in Part 2, Section V.C and Appendix A of the comments we submitted to the docket on April 14.

Results of the cumulative risk assessment for Case 2 are not relevant based on actual data, and this case should therefore not be brought forward for regulatory decision making. In the base case it is inappropriate to indicate there is a range of individuals with HI's > 1, and even more inappropriate that the high end of the range is based on risk estimates from modeled NOAELs that are experimentally demonstrated to be artificially low.

We appreciate your willingness to consider these important issues, and we are happy to provide any additional information that would assist the CPSC science staff as you progress through the rulemaking process.

If you have any questions, please do not hesitate to contact Dr. Jennifer Foreman at 908-730-3298.

Sincerely,

A handwritten signature in blue ink, appearing to read "Chris W. Hale".

Cc: Dr. Alice Thaler, CPSC
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