CPSC Commissioner Meetings – 12/10/2014

- CPSC staff indicated during the briefing meeting that the CHAP "reviewed" the more recent NHANES data sets. The data sets are too big and complex to "review" without fully re-analyzing the values, especially when the "ups and downs" are for phthalates of differing potencies . The CHAP had adequate time to do so. The results would have been significantly different using the CHAP methodology, as shown in the figures below. Note in the lower figure that the 2009/2010 NHANES data, which were available to the CHAP within its cutoff date, give an HI well below 1.

Figure 1 Significant Downward Exposure Trend in DEHP Metabolite Levels Using Mono(2-ethyl-5-carboxypentyl Phthalate (2E/5C) As An Example (95th percentile)[5]

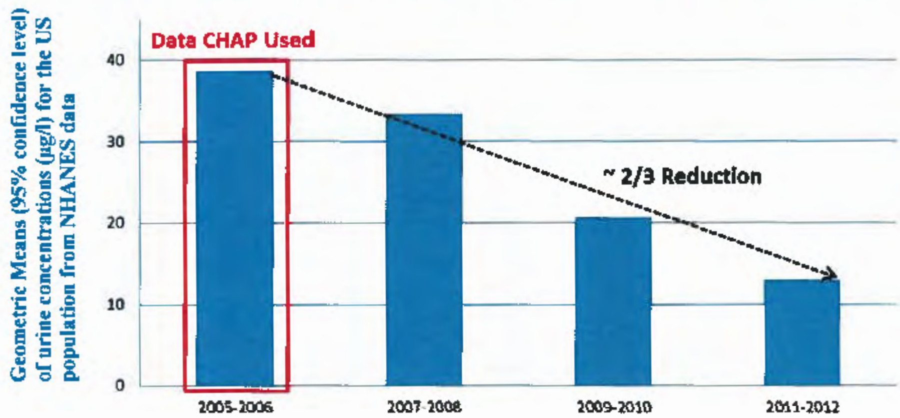
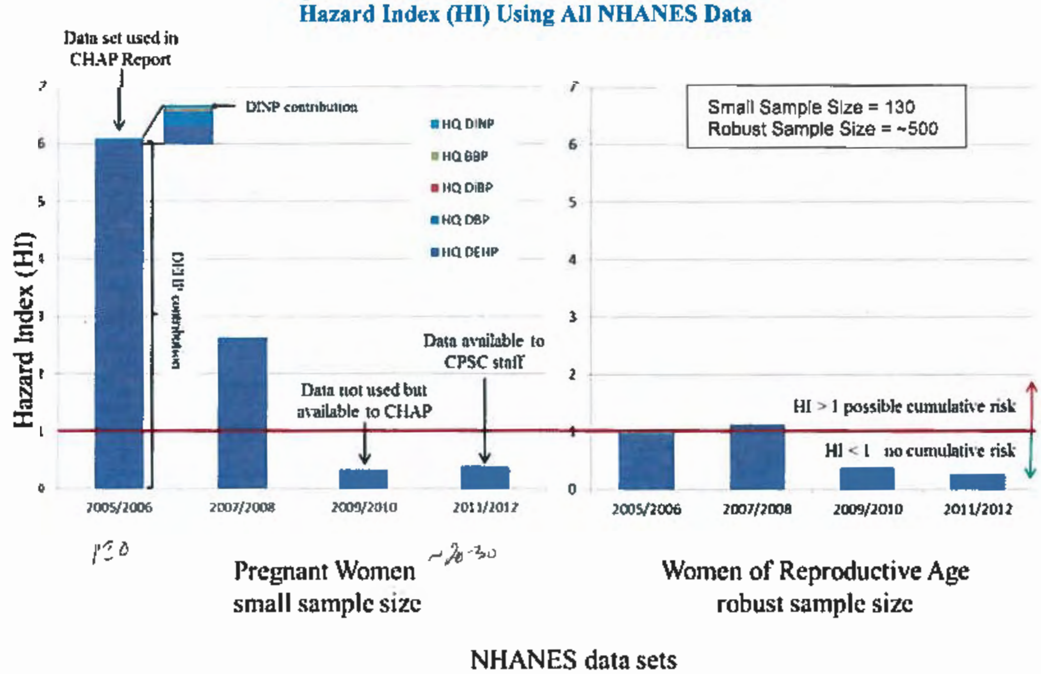


Figure 2 Significant Downward Trend in CRA Hazard Index (HI) Using All NHANES Data


Data set used in CHAP Report
DINP contribution
DEHP contribution
HQ DINP
HQ BBP
HQ DIBP
HQ DBP
HQ DEHP
Small Sample Size = 130
Robust Sample Size = ~500
Hazard Index (HI)
Data available to CPSC staff
Data not used but available to CHAP
HI > 1 possible cumulative risk
HI < 1 no cumulative risk
2005/2006
2007/2008
2009/2010
2011/2012
Pregnant Women
small sample size
Women of Reproductive Age
robust sample size
NHANES data sets

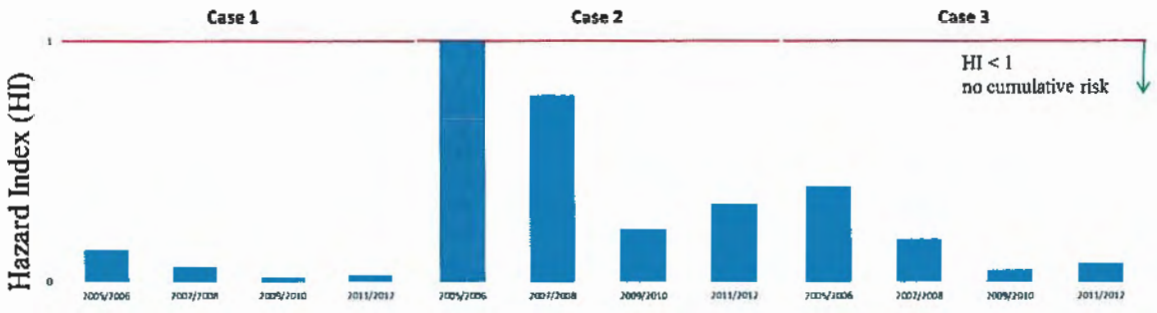
NHANES recommends at least 150 subject

- The CPSC staff needs to clearly define the "standard" for "reasonable certainty of no harm." Consistent with the staff briefing package it should be defined as a "hazard index [HI]" of less than 1 at the 95% exposure level using the most current CDC NHANES data."

  The HI analysis has multiple layers of conservatism built into it, so that an HI less than 1 at the 95% exposure level is indicative that no restriction for DINP should be recommended. To avoid being irrational, arbitrary, and capricious, the staff must reanalyze the CRA conclusions using the most recent NHANES data to determine the appropriate HI.

  The figure below depicts how the HI differs for each Case outlined in the CHAP report if DINP accounts for all of the exposure. The analysis highlights the decreased potency of DINP for the endpoint in question.

Figure 3 Hazard Index (HI) Trends Using All NHANES Data Available for Each Case in CHAP Report, for DINP Only



HI if DINP accounts for all Phthalate Exposure used in the CRA

- CPSC staff stated during the briefing meeting that there are multiple new studies allegedly documenting the anti-androgenicity characteristics of DINP. To the contrary, there are several new studies that show the anti-androgenic effects observed in rats are not applicable to humans. CPSC staff should be required to clearly identify the "new" published studies that demonstrate DINP is anti-androgenic. Also, in keeping with the intent of the CPSIA, CPSC staff should review and utilize any "new" data that demonstrates that the anti-androgenic effects of phthalates are not relevant to humans (Sharpe and Boekelheide publications).

- The CHAP failed to address uncertainties around phthalate alternatives. A lack of data does not equal safer products. Any alternative considered should be subjected to the same rigorous weight-of-evidence-based scrutiny and regulation. The CPSC should consider including in the "weight of evidence" a weighting for uncertainty if a substitute is less studied than what it is replacing. DINP is among the most exhaustively evaluated chemicals and has a proven safety record.

- The CHAP expanded the definition for the scope of the interim prohibited phthalates beyond that in the CPSIA. The CPSIA refers to "children's toy that can be placed in a child's mouth." However the CHAP expanded the scope to apply to "children's toys." This change was further endorsed by the CPSC staff. We have shown that the data do not support continuing the interim ban; they certainly do not support an expansion of its scope.

SHARPE AND BOEKELHEIDE PUBLICATIONS

Sharpe:

"Conclusions: Exposure of human fetal testes to DBP is unlikely to impair testosterone production as it does in rats. This has important safety and regulatory implications."

R. T. Mitchell, A. J. Childs, R. A. Anderson, S. van den Driesche, P. T. K. Saunders, C. McKinnell, W. H. B. Wallace, C. J. H. Kelnar, and R. M. Sharpe, Do Phthalates Affect Steroidogenesis by the Human Fetal Testis? Exposure of Human Fetal Testis Xenografts to Di-n-Butyl Phthalate (2012). J Clin Endocrinol Metab, 97(3):E341–E348.

Boekelheide

"The recent use of fetal testis xenotransplants to study phthalate toxicity suggests that the human fetal testis responds like the mouse fetal testis; it appears refractory to phthalate-induced inhibition of testosterone production. Although this result is unfulfilling from the perspective of identifying environmental contributions to human reproductive maldevelopment, it has important implications for phthalate risk assessment. "

Kamin J. Johnson, Nicholas E. Heger, and Kim Boekelheide (2012). Of Mice and Men (and Rats): Phthalate-Induced Fetal Testis Endocrine Disruption Is Species-Dependent. Toxicological Sciences 129(2), 235–248.