

April 4, 2018

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Re: Draft NTP Research Report on the CLARITY-BPA Core Study

Dear Dr. Wolfe:

I write today as a scientist and as a doctoral student in toxicology at the University of Georgia (UGA). In February of this year, the National Toxicology Program (NTP) released its Draft Research Report on the Perinatal and Chronic Extended-Dose-Range Study of Bisphenol A in Rats, NTP RR 9. Contained in this letter are comments reflecting my thoughts regarding this study.

Whereas the preliminary findings of this NTP study bring excitement to many figures in the plastics industry who exclaim that bisphenol A (BPA) is indeed considered safe, these same findings garner much concern to many scientists such as myself and give us pause. Given the ubiquitous nature of BPA, and the finding that shows that BPA and its metabolites are detected in 90% of urine samples from the U.S. population in the National Health and Nutrition Examination Survey (NHANES) since at least 2003 (Calafat et al., 2008), the importance of the investigation into the safety (or lack thereof) in its continued use cannot be understated. In fact, it has been heavily researched thus far, and has uncovered findings that are not similar to those found in this NTP study. I will elaborate on such studies that seemingly contradict the findings of the CLARITY-BPA study.

BPA is a known endocrine disruptor.

Studies have shown that BPA is known to exhibit detrimental effects on reproductive health, including some studies using human models (Lassen et al., 2014). The advantage of using human models is, of course, the fact that clearer associations can be made, and inter-species extrapolations are not a factor. This study by Lassen et al. is one of many in the literature that show both an overwhelmingly high number of subjects with detectable urinary levels of BPA, as well as potential disruptions of the hypothalamic-pituitary-gonadal feedback system. The overwhelming number of publications showing strong evidence that BPA is an endocrine disruptor (Szybiak et al., 2017; Malaisé et al., 2018; Hu et al., 2018; and more) indicate discrepancies found in the current study utilizing animal models.

The endpoints of this study paint an incomplete picture.

According to the study at hand, the authors describe that CLARITY-BPA is a study conducted in accordance with Good Laboratory Practice (GLP), in which the endpoints include growth, evidence of tumorigenesis, and weight. An important thing to note, and one which the authors of this study make clear at the beginning of the report, is that this report that was released in February of this year was only part one of the experiment; therefore, the second part of this report, which promises to study “various health endpoints,” has not yet been released. The point in mentioning this aspect of the study is to emphasize the fact that as a scientist, I am missing evidence of some critical health endpoints (which I hope are to come in part two of this report.) The difficulty in using animal models to extrapolate health impacts to humans is that their reproductive cycles are vastly different from our own (Siman et al., 2017). Endpoints that scientists should expect to see for males include direct effects on spermatogenesis, morphological changes to the cell, decreased cell counts; decreased libido and fertility, which correspond to central nervous system effects or endocrine normality; abnormal sperm motility, and more (Yu 2018).

Similarly, we should expect to see additional endpoints to the female subjects in this study, including hormone levels such as luteinizing hormone, follicle stimulating hormone; histopathology of the ovary, uterus, vagina, pituitary gland, oviduct, and the mammary gland, and additional endpoints which might cause significant disruptions in the hypothalamic-pituitary-ovary axis (Yu 2018).

The complexity of the ideal study for BPA is matched only by the complexity of the chemical itself. It can be stated with complete confidence and certainty that BPA and its analogs, which constitute even larger knowledge gaps to the completely unstudied status while BPA undergoes much scrutiny, are entirely ubiquitous in the environment and thus, the bodies of over 90% of all people in the United States (Lassen et al. 2008).

While the esteemed researches in the NTP have undoubtedly put forth much effort into elucidating gross organ weights and other effects in the study subjects, the plastic industry celebrates while scientists remain concerned with the incomplete results. As a fellow scientist, I look forward to more conclusive results in the BPA studies to come so that we may see results that more closely corroborate the many studies that are found in literature, both in human and in animal subjects.

Sincerely yours,

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## Works Cited:

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7. “Yu 2018” Refers to lecture presentations provided by Dr. Xiaozhong Yu, MD, PhD, Department of Environmental Health Science, College of Public Health, University of Georgia.