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Dr. Margaret Hamburg
Commissioner
Office of the Commissioner
Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993-0002

cc: Dr. Jesse Goodman, Chief Medical Officer
Dr. Josh Sharfstein, Assistant Commissioner
Dr. Linda Birnbaum, Director, National Institute of Environmental Health Sciences
Dr. John Bucher, Director, National Toxicology Program

Dear Commissioner Hamburg:

We are a group of independent (mostly university) researchers with extensive experience working with endocrine disrupting compounds and in particular bisphenol A (BPA). We represent no single interest, entity, organization or corporation. The purpose of this letter is to bring to you our serious concerns regarding the Food and Drug Administration's toxicity studies for BPA just underway at the National Center for Toxicological Research (NCTR).

The FDA, in conjunction with the National Toxicology Program, plans to spend over 5 years and 10 million dollars studying BPA. We have several concerns: First, the proposed research is flawed scientifically in ways that bias toward false negatives in the results. Second, we find it troubling that the FDA is proposing to spend such a large amount of money on such a well-researched chemical. Third, we know of no review process of the project to assure quality research. Fourth, we are deeply troubled that the agency would announce these research plans in light of its public decision to release a reassessment of BPA by November 30th. We elaborate on these concerns below.

While Dr. Dan Doerge of NCTR presented only an outline of the study designs for BPA to the public on August 17, 2009, there were several issues in the presentation that raised important red flags. For example, the Charles River Sprague-Dawley rat strain will be employed in these studies, but it is not an appropriate animal model because it has been shown to be relatively insensitive to estrogenic compounds; prior studies show that this applies to the rats that were purchased from Charles River to start the NCTR colony in the 1970s. This is therefore a

very serious problem. Also serious is the use of gavage, which could significantly impair the ability of experiments to reveal effects on developing animals.

We were also alarmed with the lack of attention by the Science Board or the NCTR to address the details of what endpoints would be measured, how, and why these endpoints were selected, the timing of endpoint measurements (and how it relates to the development of the animal), and the means of extracting tissues. The NTP Expert Panel on BPA recommended several areas needing further research, and the information available suggests that these have not been considered. A primary omission is appropriate neurobehavioral research. The NCTR has the capability of conducting much needed pharmacokinetic studies but has questionable capability in other areas.

We understand that these concerns were conveyed to the NCTR by scientists at the National Institute of Environmental Health Sciences, but were rejected by NCTR officials. Given the substantial role of NIEHS in funding this research, we find the rejection of NIEHS analysis very problematic.

FDA's plans to spend significant time and money on a very well researched chemical are disturbing. There are already over 900 peer-reviewed studies in the published literature and the NIEHS has initiated a $7 million program (GO grants) to address several key data gaps identified by the Center for the Evaluation of Risks to Human Reproduction's report on BPA released last year. The potential for fiscal waste, we believe, is magnified by our serious concerns that there are significant study design flaws in the NCTR's research plans, as noted above.

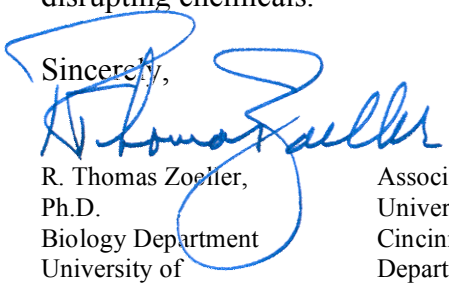
We are deeply troubled that the agency would announce these research plans in light of its decision to release a reassessment of BPA by November 30th. This disconnect between research and reassessment raises concerns about whether the FDA is striving to resolve the critical public health issues raised by widespread exposure to BPA, or is avoiding making a decision because of the pending research, the results of which will not be available for review for many years.

We strongly recommend that the agency immediately halt the studies with rats. At the very least, if they are to be carried out, they should be designed in ways that incorporate the scientific expertise of the National Institute of Environmental Health Sciences. Currently, not only are they scientifically flawed, they also represent a serious waste of time and public money. We strongly believe that given the extensive peer-reviewed literature, the Chapel Hill Consensus Statement on BPA and the CERHR-NTP's Monograph on BPA, there is sufficient research and independent review available for the agency to make a decision as to whether, as the law dictates, there is "reasonable certainty" that this chemical is "not harmful."

The problem before the agency will not be resolved with more research that is poorly designed. What is needed is a thorough reform of regulatory science. Currently regulatory toxicology studies do not reflect up-to-date and scientifically accepted knowledge about endocrine disrupting compounds, like BPA, and the ability of these compounds to exert adverse health effects at low doses. We direct the Commissioner to the recent report of The Endocrine Society on Endocrine Disrupting Chemicals, enclosed with this letter, which outlines scientific concerns about the impact of these chemicals on public health.

We hope that you welcome these comments as a sincere effort to build a constructive bridge between the FDA and the scientific community. We welcome the opportunity to meet with you and your staff to elaborate on the details of our concerns regarding the agency's research plans for BPA as well as to hold a broader dialog on the need to reform regulatory science to incorporate NIH-funded research and the current understanding of endocrine disrupting chemicals.

Sincerely,



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