Kelly Randolph, DVM, MPH
Dennis M. Keefe, PhD
Center for Food Safety and Applied Nutrition
United States Food and Drug Administration
5100 Paint Branch Pkwy.,
College Park, MD 20740

July 14, 2016

Dear Dr. Randolph and Dr. Keefe,

The Endocrine Society appreciates the opportunity to provide comments on the food additive petition to amend and/or revoke specific regulations regarding specified ortho-phthalates in food contact materials. Founded in 1916, the Endocrine Society is the world’s oldest, largest, and most active organization dedicated to the understanding of hormone systems and the clinical care of patients with endocrine diseases and disorders. Our membership of over 18,000 includes researchers who are making significant contributions to the advancement of knowledge in toxicology, especially in the field of endocrine-disrupting chemicals (EDCs), a class of chemicals that includes phthalates.

Although we do not take a position on specific regulatory actions that should be taken by the FDA in response to the petitioners’ claims, new evidence accumulated over the past 5 years strongly implicates phthalates in a range of human health impacts, and these impacts incur significant costs on society. Furthermore, current policy governing EDCs might not take into consideration the full body of research into EDCs. In our comments we highlight recent research from Endocrine Society members that we ask the FDA to consider as you develop your response to the petition on ortho-phthalates.

**Information on Phthalates from the Endocrine Society’s Second Scientific Statement on EDCs**

On September 28, 2015, the Endocrine Society released an update to the breakthrough 2009 Scientific Statement on EDCs. The updated statement examined the state of scientific evidence on EDCs and risks posed to human health due to exposures to EDCs in topic areas for which the evidence was strongest. This comprehensive assessment of the scientific literature concluded that recent research has led “to a much fuller understanding of the endocrine principles by which EDCs act, including nonmonotonic dose-responses, low-dose effects, and developmental vulnerability.” In the studies reviewed within the Scientific Statement, phthalates were linked to obesity and diabetes, female and male reproductive health concerns, hormone-sensitive breast cancer, thyroid disruption, and neurodevelopmental effects. A copy of the Scientific Statement has been appended to this letter, and uploaded to the docket via regulations.gov. We encourage the FDA to review and consider the information contained in this scientific statement when evaluating the claims of the petitioners.

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Significant Costs Associated with Phthalate Exposure

Due to the links between EDCs and harms to human health, attention has focused on the economic costs associated with improper regulation of EDCs. A series of studies published last year in The Journal of Clinical Endocrinology & Metabolism found that health problems associated with EDC exposures cost the European Union more than €157 billion each year in healthcare expenses and lost productivity\(^2\). Of these costs, approximately €26 billion can be attributed to phthalates and chemicals in plastics and cans. These costs represent real harms to human health; for example, up to 145,000 attributable cases of endometriosis are associated with exposure to phthalates, representing costs of up to €1.25 billion\(^3,4\).

**In summary, we assert that new evidence accumulated over the past 5 years strongly implicates phthalates in a range of human health impacts, and that these impacts incur significant costs on society.** It is also worth noting that all phthalates that have been examined for reproductive and endocrine effects have been found to pose endocrine-related risks. A large number of the ortho-phthalates included in the petition have no published safety data, leading to concern within the scientific community about possible endocrine effects of these compounds. All of the ortho-phthalates share a common functional group and similar metabolic pathways, so they are likely to have similar endocrine effects. Because the phthalates are commonly used in food packaging and handling equipment, one of the greatest sources of exposure to humans is through food. A number of papers have demonstrated that processed foods and fast foods significantly increase phthalate exposures in humans, particularly in children, females, lower socio-economic groups, and non-hispanic blacks\(^5,6,7\). As discussed in this petition, infant formula and baby foods

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have been shown to contain high concentrations of various ortho-phthalates,\textsuperscript{8,9} which puts children at a high risk of exposure during critical developmental stages.

We ask that the FDA consider these and other relevant research findings in your evaluation of regulations for the use of ortho-phthalates in food contact materials. Thank you for considering our comments. If we can be of any further assistance in your efforts, please reach out to Joseph Laakso, PhD, Associate Director of Science Policy at jlaakso@endocrine.org.

Sincerely,

Henry Kronenberg, MD
President
Endocrine Society


\textsuperscript{9} Arnold Schecter et al. “Phthalate Concentrations and Dietary Exposure from Food Purchased in New York State.” \textit{Environ Health Perspectives} 2013 121:473-479.