ENDOCRINE SOCIETY
Hormone Science to Health

To: Members of the European Food Safety Agency (EFSA) Panel on Food Contact Materials, Enzymes and Processing Aids (CEP)

Re: Re-evaluation of the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs

Submitted in response to **Public Consultation Number PC-0109**

1. Summary

As 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, we have long recognized the effects of endocrine-disrupting chemicals (EDCs) such as BPA on sensitive endocrine systems and we commend the Panel for their revised analysis of BPA's health effects. The Endocrine Society supports the overall conclusion of the Panel to establish a new tolerable daily intake (TDI) of 0.04 ng of BPA per kilogram of body weight per day based on the most sensitive health outcome category (immune system) to BPA exposure. We also share the Panel's concerns regarding BPA-associated harms to other systems as a result of endocrine disruption, including metabolism, neurodevelopment, and male and female reproduction.

While we appreciate that the Panel's remit was limited to BPA, we note that the strong evidence for effects at very low levels raises further questions about the safety of replacements for BPA in various applications, including food contact materials. Increasing evidence suggests that replacement chemicals, which are often structurally similar to BPA, may have similar hazardous properties and effects. We therefore urge EFSA and other agencies to recognize the serious need for aggressive action to reduce our exposure to this hazardous group of chemicals to achieve health-protective objectives that consumers depend on.

1.3.3. NTP CLARITY-BPA program

We welcome the Panel's careful consideration of both the Core and Grantee studies comprising the CLARITY-BPA program and appreciate the Panel's approach to integrating both arms of the program. We do want to note several technical issues specific to the Core study that are important to consider in the interpretation of effects due to BPA exposure. These include the use of historical rather than concurrent controls as comparators, the methodology for monitoring estrous cyclicity, and the statistical approach and consideration for non-monotonicity both in the CLARITY study and in Appendix B of the EFSA draft opinion. Specifically, the statistical approach to non-monotonicity used by EFSA would benefit from more appropriate mathematical structures and statistical treatment involving independent scientists. Our detailed comments are included in the attached

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document, and we reiterate that some of the effects reported in the Core study are in fact indicative of non-monotonic dose responses and should be considered significant.

Attachment:
https://ntp.niehs.nih.gov/ntp/about_ntp/rrprp/2018/april/publiccomm/laakso20180409_508.pdf

2.2. Literature Search

We commend the panel for extending the literature search period to cover additional CLARITY-BPA grantee studies that were published after the initial date and expanding the evidence search for genotoxicity through July 2021. While the revised TDI for BPA is a reasonable response to the evidence of harms described in the literature published within the window described in the protocol, it is important to recognize that the opinion is unlikely to reflect the totality of effects for a variety of endpoints due to the omission of studies published prior to 2013. The new protocol used to derive the proposed TDI used a different systematic review protocol that would have treated these earlier studies differently. Consequently, evidence about key endpoints including mammary gland effects is incompletely assessed in the current study. To be clear, we contend that a more thorough assessment of earlier literature would only add to the justification for the Panel's conclusion by increasing the evidence base for the proposed TDI.