ENDOCRINE SOCIETY
Hormone Science to Health

January 22, 2018

Nancy Beck
Deputy Assistant Administrator, Office of Chemical Safety and Pollution Prevention.
Environmental Protection Agency
1200 Pennsylvania Ave NW #4000
Washington, DC 20004

Dear Dr. Beck,

The Endocrine Society appreciates the opportunity to provide comments on approaches for identifying potential candidates for prioritization under the amended Toxic Substances Control Act (TSCA). 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. The Society's membership of over 18,000 includes researchers who are making significant contributions to our understanding of the effects of exposures to manufactured chemicals that interfere with hormone systems – an area of science investigating endocrine-disrupting chemicals (EDCs).

In the proposed methods under consideration by EPA, elements of both hazard and exposure are evaluated when assessing chemicals. However, we view hazard as the more important of the two elements when evaluating chemicals for prioritization. Hazardous properties are fundamental to the chemical. Exposures, on the other hand, can change significantly over time and location in unpredictable ways, deviating significantly from estimates. As we also note in our comments on the New Chemicals Review Program, unanticipated or new uses of chemicals can arise, further complicating exposure estimates. Regardless of the final approaches used by EPA, we strongly recommend that:

- Chemical hazard be given priority consideration over exposure estimates when evaluating chemicals for potential prioritization.
- Detailed explanations of the process used to evaluate chemicals for prioritization be publicly available.

To evaluate chemicals for endocrine hazards, we note that EPA is proposing to use a suite of high-throughput assays to score chemicals for estrogen receptor (ER) or androgen receptor (AR) bioactivity. While we appreciate that EPA must develop approaches using new and alternative methods (NAM) to rapidly evaluate the expanding universe of TSCA chemicals for potential harms, we are concerned that these high-throughput approaches have not been sufficiently validated and demonstrated effectiveness in identifying chemicals of concern. Our understanding is that the models used to evaluate data on ER and AR bioactivity discounted potential low-dose effects or non-monotonic dose response (NMDR). Finally, we note with concern that an exclusive focus on the ER and AR pathways will result in a lack of coverage for other endocrine pathways that could be disrupted by chemicals. To improve the ability to appropriately evaluate and prioritize chemicals for potential endocrine effects EPA should:

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- Publish studies demonstrating the validity of the proposed ER and AR assays and their ability to predict endocrine effects.
- Incorporate models that allow for low-dose effects and NMDR.
- Survey the academic literature to identify chemicals with potential effects on the endocrine system, especially for chemicals that may affect pathways not covered by the ER and AR assays. For example, interactions with the progesterone and vitamin D receptors may have deleterious effects.

We understand that screening the universe of TSCA chemicals for prioritization is a challenging task. By incorporating the recommendations above, the EPA will be able to make the best use of available data and transparently communicate the results of pre-prioritization screening to all stakeholders. Thank you for considering our comments. If we can be of any assistance, please do not hesitate to contact Joseph Laakso, PhD., Director of Science Policy at jlaakso@endocrine.org.

Sincerely,

Angel Nadal,
Chair, EDC Advisory Group
Endocrine Society