May 21, 2018

Thomas Sinks, PhD
Director, Office of the Science Advisor
Environmental Protection Agency
1200 Pennsylvania Avenue NW
Washington, DC 20460

Re: EPA-HQ-OA-2018-0259

Dear Dr. Sinks,

On behalf of the Endocrine Society, I appreciate the opportunity to express our concerns to the United States Environmental Protection Agency (EPA) regarding the proposed regulation *Strengthening Transparency in Regulatory Science*. 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 advancing our understanding of the effects of exposures to chemicals that interfere with hormone systems, also known as endocrine-disrupting chemicals (EDCs). We have been involved in global efforts to minimize public harms from exposure to EDCs through science-based policies and effective testing and regulatory strategies.

While the Endocrine Society supports appropriate public access to data and methodology for independent validation, the proposed rule is unclear and difficult to describe operationally. We are therefore concerned that the proposed regulation will restrict the ability of the EPA to develop and implement effective restrictions on hazardous chemicals. As such, this rule would increase the potential for human health harms due to chemical exposures.

**More details are needed regarding the effects of the proposed rule on evaluation of scientific research**

The Endocrine Society is concerned that efforts by the EPA to "ensure that the data and models underlying scientific studies that are pivotal to the regulatory action are available to the public in a manner sufficient for independent validation and analysis" will inappropriately restrict the types of studies that can be used in regulatory decision-making. Clinical research involving sites of environmental disasters, or epidemiological studies documenting population-level effects of environmental exposures, are not only complicated, but are impossible to independently replicate in a controlled setting. Moreover, the raw data for these studies may involve confidential patient information or identifying features such as genetic information that cannot easily be anonymized or protected.

We agree that "robust peer review plays a critical role in independently validating key findings and ensuring that the quality of published information meets the standards of the scientific and technical community." We also note that the focus on standardized test methods, consistent data evaluation procedures, and good laboratory practices (GLP), while appropriate for evaluating industry-funded studies in contract labs where the risk of conflicts of interest is high, may inappropriately marginalize academic studies funded by the National Institutes of Health (NIH) or other research funding agencies that have undergone rigorous peer review at the time of grant submission and then again before

publication in high-quality academic journals. Having been independently validated via peer-review, rigorous epidemiological research and disaster studies helped establish appropriate justifications for previous regulatory actions. Taxpayers expect that publicly-funded research will be used to improve public health and maximize the return on their investment in scientific research. EPA should ensure that publicly-funded, peer-reviewed studies are not disadvantaged during agency scientific reviews, and we strongly recommend that EPA provide more information about how historical and new studies will be treated under the proposed regulation, and clarify the types of data, accessibility, and validation that would be considered sufficient.

**Policies should be consistent with other research agencies**

The NIH has established effective policies governing the sharing of data among researchers and with appropriate access by the public at large. Also, many journals, including the Endocrine Society, are establishing guidelines and standards for the submission of datasets to repositories that are consistent with NIH policies and the FAIR (findable, accessible, interoperable, re-usable) principles for scientific data management and stewardship. Therefore, research that abides by these policies and has been published in high-quality peer-reviewed journals should be considered independently validated and sufficiently available to the public.

We appreciate that certain business information may need to be kept confidential; however, Confidential Business Information (CBI) may be necessary in some cases for scientific experts to evaluate the potential for hazards due to chemical exposures e.g., in consumer products. Responsible authorities, including state agencies, the EPA, and independent scientific reviewers should be able to request and have access to CBI when necessary to evaluate these hazards.

**Evidence of adversity should take precedence over model fit**

The Endocrine Society agrees that there is growing empirical evidence of unconventional dose-response curves, in particular non-monotonic dose response (NMDR) and effects at low doses that may not be seen at high doses. Such features are frequently observed for EDCs, and should be recognized by regulatory agencies in efforts to reduce harms due to exposure. However, we are concerned that the introduction of model uncertainty based on competing models at low-dose ranges will result in a lack of appropriate regulatory activity, even where there is strong evidence for low-dose adversity in peer-reviewed publications. Where there is evidence for adversity, particularly at low-dose ranges, it cannot be assumed that there exists a threshold below which no risk exists; EPA should therefore adopt a precautionary approach to management of hazardous chemicals with low-dose effects.

**A 30-day comment period is insufficient for detailed review**

The Endocrine Society has numerous concerns and questions regarding the scope of the proposed regulation and effects on regulatory actions by the agency. In light of these questions and the potential for widespread public health impacts, a 30-day comment period is insufficient for adequate public consultation and evaluation of the proposed regulation. We respectfully request a 60-day extension of the comment deadline as well as a public hearing on the proposed rule. A 90-day comment period and additional explanation in the context of a hearing will help all stakeholders, including scientific and medical organizations such as the Endocrine Society, better assess the proposed rule and comment on potential public health impacts.

**Summary of Recommendations**

In conclusion, the Endocrine Society is very concerned that the proposed rule *Strengthening Transparency in Regulatory Science* lacks transparency, is unclear about data utilization and modeling of low-dose effects, and will result in harmful effects on public health. Transparency in the development and implementation of regulatory actions is a complicated request that requires a carefully constructed rule. As an overarching recommendation, we urge the EPA to construct rules governing transparency and data access that are consistent with the National Academies report on Science and Decisions: Advancing Risk Assessment[1]. This document has numerous recommendations related to transparency in regulatory actions, including recommendations regarding how scientific information should be collected, evaluated, and assimilated in risk assessments. We also encourage EPA to:

- Clarify how historical and new studies will be treated under the proposed rule, including how model uncertainty will treat studies demonstrating low-dose effects.
- Ensure that publicly-funded, peer-reviewed studies that comply with NIH data deposition and access policies are considered available to the public in a manner sufficient for independent validation and analysis.
- Ensure that CBI is made available to independent scientific reviewers upon request when necessary.
- Adopt a precautionary approach for chemicals where there exists evidence of low-dose adverse effects.
- Extend the public comment period and allow for a public hearing on the proposed rule.

Incorporating these recommendations will allow for a more thoughtful and thorough evaluation of the proposed rule and its effects. Thank you for considering the Endocrine Society's comments. If we can be of any further assistance, please contact Joseph Laakso, PhD, via e-mail to jlaakso@endocrine.org.

Sincerely,

Susan Mandel, MD, MPH
President
Endocrine Society

[1] National Research Council. 2009. *Science and Decisions: Advancing Risk Assessment*. Washington, DC: The National Academies Press. https://doi.org/10.17226/12209.