

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 the implementation of the New Chemicals Review Program 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). We support actions by the United States Environmental Protection Agency (EPA) to make affirmative safety findings for new chemicals. In our comments, we identify specific process improvements to ensure that the New Chemicals Review Program can more effectively and transparently review new chemicals for safety, and we also make specific recommendations aimed at ensuring EPA is able to evaluate new chemicals for the ability to interfere with hormonal systems.

Process Improvements to New Chemicals Review Program

The Points to Consider Document relies on the use of both qualitative and quantitative assessments of submitted data to arrive at decisions and potential risk management strategies. As EPA seeks to make affirmative safety findings for chemicals, the agency should track and publicly disclose the percentage of evaluations that are based in whole or in part on qualitative assessments. This information would help all stakeholders identify data gaps where additional testing or new methodologies are needed. Both hazard identification, including information about the endpoint(s) used, and exposure estimates, should be evaluated and reported separately along with the final risk assessment determinations.

A standard definition for the term 'reasonably foreseen conditions of use', including intended and unintended sources of exposure throughout the life of the product, and how that chemical will be used, would ensure transparency for all stakeholders. All potential uses for a new chemical must be determined, assessed, and publicly documented by EPA to avoid situations where the use(s) of a chemical expands following evaluation by EPA. Otherwise, additional increases in exposures above those estimated by EPA may routinely occur and prove harmful to human health and the environment. As an example, a variety of per- or polyfluoroalkylated substance (PFAS) as alternatives to PFOA or PFOS, could have reasonably foreseen as production intermediates or replacements for uses that include application for stain resistance on carpets and clothing, constituents of food contact materials, and components of aqueous film-forming firefighting foams. All of these foreseeable uses should be included in the assessment to ensure all routes of exposure



are accounted for, and to avoid underestimating cradle-to-grave exposures in product life-cycle exposure analysis.

EPA should consider additional evaluation of all possible chemical fates in the environment and the human body, including degradants and metabolites, to identify those uses that should be restricted and to prevent regrettable uses of chemicals outside of EPA's sphere of knowledge. Because chemical uses can change, hazard information should be weighed more heavily than exposure information. For chemicals where there is the potential for high hazard, decisions should not rely heavily on exposure estimates, and we urge EPA to keep the public informed of the chemical hazard and outcome of the evaluation. Knowing the hazard of a chemical up front will improve the ability of manufacturers and consumers to understand how certain chemicals should be utilized or avoided.

Finally, we encourage EPA to ensure that the process for chemical reviews proceeds swiftly and efficiently, and with sufficient data from chemical manufacturers. In the absence of sufficient information about chemical hazard or exposure, EPA should not assume that a chemical is safe, and EPA should be able to request additional information from applicants. We also suggest that EPA estimate the amount of time required for each step in the standard review process, so that timeframes and expectations are clarified.

Evaluation of Chemicals for Endocrine Activity

We are especially concerned that endocrine-disrupting chemicals or endocrine-specific endpoints are not included as potential sources of information on new chemicals from manufacturers in either the Points to Consider document or the outline for the New Chemicals Decision Guidelines Manual. As we note in our earlier comments on the New Chemicals Review Program¹, EDCs are a class of chemicals for which significant deficiencies in regulatory testing persist. To begin to correct these deficiencies, EPA should ensure that data on sensitive endpoints, such as mammary gland development, are collected so that chemicals can be evaluated for their potential to interfere with hormone activity. Potential approaches are included in the Tiered Protocol for Endocrine Disruption (TiPED – www.tipedinfo.com), a battery of tests designed to interrogate a chemical's effects on the endocrine system and identify problematic chemicals. Recent reports from the National Academies have specified opportunities to improve the evaluation of chemicals at low doses and the identification of non-monotonic dose responses (NMDR)^{2,3}. These reports highlight ways that

¹ <https://www.endocrine.org/-/media/endsociety/files/advocacy-and-outreach/society-letters/endocrine-society-comments-on-new-chemicals-review-program-under-amended-tsca.pdf?la=en> Accessed January 18, 2018.

² National Academies of Sciences, Engineering, and Medicine. 2017. Application of Systematic Review Methods in an Overall Strategy for Evaluating Low-Dose Toxicity from Endocrine Active Chemicals. Washington, DC: The National Academies Press. <https://doi.org/10.17226/24758>.

³ National Research Council. 2014. Review of the Environmental Protection Agency's State-of-the-Science Evaluation of Nonmonotonic Dose-Response Relationships as they Apply to Endocrine Disruptors. Washington, DC: The National Academies Press. <https://doi.org/10.17226/18608>.



EPA could incorporate more modern science and mechanisms for doing so, in particular for chemicals and classes of chemicals that have the potential to interact with hormonal pathways.

Incorporating these recommendations will enable the EPA to more transparently, efficiently, and effectively evaluate new chemicals, including EDCs, for potential human health hazards. 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,

A handwritten signature in blue ink that reads "Angel Nadal".

Angel Nadal,
Chair, EDC Advisory Group
Endocrine Society