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Re: **Toxic Substances Control Act (TSCA) Collaborative Research Program to Support New Chemical Reviews; Notice of Public Meeting and Request for Comments.** 87 Fed. Reg. 10784 (Feb. 25, 2022).

Dear Ms. Swenson:

The American Chemistry Council (ACC)[1] appreciates the opportunity to submit comments on the TSCA Collaborative Research Program to Support New Chemical Reviews and the draft EPA document entitled: *Modernizing the Process and Bringing Innovative Science to Evaluate New Chemicals Under TSCA.* Our comments on the following pages provide suggestions for collaborative research and modernization of the New Chemicals Program.

Please contact Jessica Ryman-Rasmussen at 202-249-6406 or jessica_ryman-rasmussen@americanchemistry.com if you have any questions.

Sincerely,

Jessica Ryman-Rasmussen, PhD, DABT
Senior Director, Chemical Management

[1] The American Chemistry Council (ACC) represents the leading companies engaged in the multibillion-dollar business of chemistry. ACC members apply the science of chemistry to make innovative products, technologies and services that make people's lives better, healthier and safer. ACC is committed to improved environmental, health, safety and security performance through Responsible Care®; common sense advocacy addressing major public policy issues; and health and environmental research and product testing. ACC members and chemistry companies are among the largest investors in research and development, and are advancing products, processes and technologies to address climate change, enhance air and water quality, and progress toward a more sustainable, circular economy.

## 1. Update and Refine Chemical Categories

- Greater clarity is needed regarding the approach EPA is taking to future categories, as well as the status of work that may have been already undertaken to inform the present categories.

For the 2010 chemical categories document update,[2] EPA refined existing categories and added new ones. Since that time, TSCA has been revised. In the new EPA document subject to comment, EPA states:

> *Rather than refining the existing categories – or adding new ones – to the 2010 document, OPPT is proposing to develop a systematic, transparent, and reproducible approach for modernizing both chemical categories and read-across methods. OPPT will work with ORD researchers and other collaborators to identify scientific information to support chemical categories and read-across methods, such as: structural (and other) boundaries; physical-chemical properties; structural alerts for hazard, fate, exposure, and/or functional uses; mechanistic and toxicokinetic data from NAMs; and/or, existing hazard data. The new approach will document the data used to inform chemical categories as well as the basis of any similarity or read-across applications in a systematic manner.*[3]

- This language indicates sweeping changes to categories that go far beyond the last update in 2010. If this is the case, it would be beneficial to stakeholders for EPA to state this more clearly. A discussion of the scope and specific methods used in this approach are needed. One or more examples would be helpful in illustrating the scope and methods of the proposed approach.

- Although EPA provides examples of what kinds of information may be identified to support chemical categories, EPA provides no information on exactly how this information will be used or if/how current categories will change. It is unclear if the Agency has started this work already. It would be beneficial to stakeholders for EPA to clarify the progress so far to facilitate more effective participation in the Agency Outreach going forward. Again, examples would be helpful.

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[2] TSCA New Chemicals Program (NCP) Chemical Categories. Last Revised August 2010.
[3] EPA, *Modernizing the Process and Bringing Innovative Science to Evaluate New Chemicals Under TSCA.* (Page 5).

- The External Peer Review & Outreach section indicates that there will be meaningful opportunities for public engagement and peer review for the implementation of any changes to the current categories. Further clarification of this would also be beneficial.

- For stakeholders who have undertaken work to inform categorization of a particular chemical under the guidance of the 2010 Document (or who are considering doing so), it is crucial to know if EPA will make chemical categorization decisions under the 2010 Document or if these decisions will be delayed (possibly for several years) until the modernized categories and read-across are in place.

- Linking of categories to Hazard Concerns facilitates the development and testing of new chemicals.

The 2010 Document[2] provides information on Hazard Concerns for each category. This information is useful, both for developing new chemistries and for planning toxicology studies to be conducted prior to PMN submission. Furthermore, tools that would assist in predicting if a new chemical was likely to fall into a category of concern (or likely to be analogous to a chemical in a category of concern) would provide clarity for both EPA reviewers and industry.

## 2. Develop and Expand Databases Containing TSCA Chemical Information

- Not all New Chemicals are data poor.

Although many chemicals subject to PMNs may be data-poor, this is not always the case. While it is true that typically in the US there is not an extensive set of prescribed experimental studies required for PMN submissions, this does not mean that information and knowledge of new chemicals is always sparse. New chemicals may have information in the form of chemical-specific testing data and/or data from other sources, such as read-across or modeling. Indeed, EPA's own default modeling approaches are arguably a type of information. Our knowledge about the chemical can be defined as what we understand about it based on the totality of the evidence.

- Chemical-specific testing data should be considered as superior to models and analogue data for grouping and risk assessment purposes.

Any available chemical-specific testing data should be considered superior to EPA's default models or data/information from analogues for use in risk assessment, as testing data is empirically derived. However, if such empirical data is not available or is incomplete, NAMs can potentially be applied to understand potential biological effects, likely fate and transport in the environment, and predicted exposures to humans and ecosystems. A framework (such as an Integrated Approach to Testing and Assessment (IATA)) to assist in determining the need for new information may be helpful in this regard.

- EPA should explore if analogue data can be made available to stakeholders without compromising CBI and if similar data from FDA could be added.

Currently, stakeholders outside of EPA do not have access to analogue databases, which are a significant source of scientific information to EPA. Stakeholder access to this data would be helpful, both for the development of new chemistries and for planning regulatory submissions. Also EPA should explore if FDA has relevant data on drugs/food additives, etc. that could be added to this database to expand the chemistries represented.

## 3. Develop and Refine QSAR and Predictive Models for Physical-Chemical Properties, Environmental Fate/Transport, Hazard, Exposure, and Toxicokinetics.

- All QSAR models used by EPA, model defaults, and model peer review should be made available for data generation, interpretation, and transparency.

Any current and future QSAR models used by EPA should be made available to all stakeholders. For current models used by EPA, ACC is not aware of any available information regarding how defaults are derived. This information should be provided for all current and future models to facilitate data interpretation. Peer review of models should involve engagement of subject matter experts for the identification and/or development/update of models. Additionally, the peer review process followed by EPA for all current and future models should be described and all peer review reports made available, especially any strengths or limitations of a given model noted by the model reviewers. ACC suggests that this information be made available for all current and future models. This information is critical, both to facilitate independent data generation by stakeholders, to interpret model results, and for the sake of transparency.

- EPA should explore if FDA has data that may expand the applicability domain of current and future QSAR models.

It is reasonable to presume that FDA may have a wealth of data on drugs, food additives, etc. that could be added to the database(s) upon which QSAR models are built. Such additional information from FDA may assist in both the development of new QSAR models and the use of existing QSAR models by expanding the applicability domain.

## 4. Explore Ways to Integrate and Apply NAMs in New Chemical Assessments

- There are three immediate ways EPA could integrate and apply NAMs in New Chemical Assessments.

- EPA should evaluate the Threshold of Toxicological Concern (TTC) approach. It has been shown that risk-based priority screening can be carried out efficiently for approximately six thousand chemicals at once by integrating a computational NAM method for toxicity with EPA ORD's advanced method for human exposure modeling.[4] As warranted, EPA could accept this approach for immediate use in TSCA by adding it to the agency's list of alternative test methods or strategies that do not require new vertebrate animal testing.

- EPA should develop and implement a process to receive and evaluate external nominations for NAMs for specific uses in TSCA. This will enable industry, academia, research institutes, etc., to submit nominations and ensure that the nomination and review processes are sufficiently robust so that NAMs are fit-for-purpose and provide information of equivalent or better scientific reliability and quality to that which would be obtained from vertebrate animal testing.

- EPA (and OECD) should adopt and use a uniform, yet flexible, framework to develop, document, and communicate the level of scientific confidence in specific NAMs intended for distinct uses. Such a scientific confidence framework is needed to meet the legal requirements of TSCA that NAMs must "... provide information of equivalent or better

[4] Utilizing Threshold of Toxicological Concern (TTC) with high throughput exposure predictions (HTE) as a risk-based prioritization approach for thousands of chemicals. Computational Toxicology Volume 7, August 2018, Pages 58-67.

scientific quality and relevance for assessing risks of injury to health or the environment."[5]

## 5. Develop a TSCA New Chemicals Decision Support Tool to Modernize the Process

- The Decision Support Tool must help EPA meet its statutory deadlines.

Currently, EPA is not meeting its statutory deadlines for PMNs. The Decision Support Tool must facilitate a marked improvement in EPA's PMN evaluation timelines.

- The Decision Support Tool must both integrate NAMs and be interoperable with IUCLID.

The NAMs and other scientific information used for new chemicals will have to be integrated by the Decision Support Tool and be interoperable with IUCLID. Given the growing list of NAMs, integration and interoperability will likely be challenging. Dialogue with ECHA related to current NAMs incorporation into IUCLID and future plans may be helpful in this regard.

## External Peer Review & Outreach

### The regulatory scientific community must continue to work together to meet its shared responsibility to produce the data and analyses that fulfill the mandates of TSCA.

Together, the regulatory scientific community (which includes government researchers, private sector scientists and institutions, animal welfare organizations, and academics) has made large strides on NAMs in the first 5 years of TSCA implementation. We are further encouraged by EPA's recent decision to create a collaborative research program to improve and modernize the methods used to review and evaluate new chemicals. We recommend EPA create opportunities for broad collaborations with scientific experts across the breadth of the regulatory science community. Contributions from academia, industry and other scientific experts should not be excluded, but rather welcomed as part of the collective responsibility of the regulatory science community to harness the power of NAMs to improve the scientific basis and efficiency of new chemical reviews.

[5] 15 U.S.C. § 2603(h)(2)(A).