



EPA Activities on New Approach Methods:

Update from the Office of Pollution Prevention and Toxics

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MAY 26, 2022, ICCVAM PUBLIC FORUM



Frank R. Lautenberg Chemical Safety for the 21st Century Act

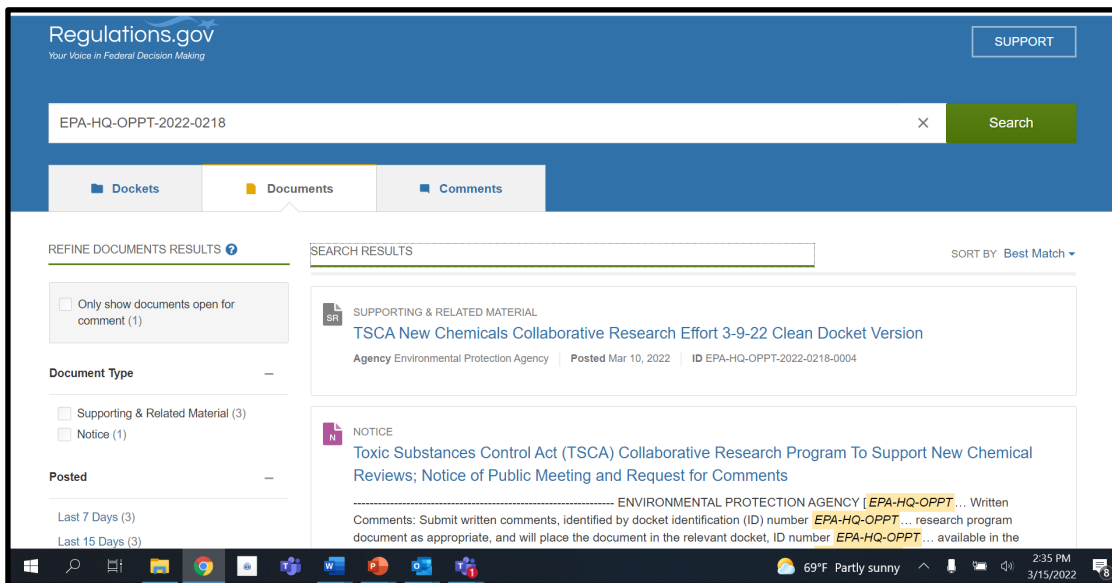
- The Toxics Substances Control Act (TSCA) was originally enacted in 1976. In 2016, TSCA was amended by the Frank R. Lautenberg Chemical Safety for the 21st Century Act.
 - Section 4 (h) entitled Reduction of Testing on Vertebrates
- Prior to requesting testing using vertebrates:
 - Consider reasonably available existing information, and
 - Encourage and facilitate (Section 4(h)(1)(B)(i, ii and iii):
 - “Scientifically valid test methods and strategies that reduce or replace use of vertebrate animals while providing information of equivalent or better scientific quality and relevance that will support regulatory decisions;
 - The grouping of 2 or more chemical substances into scientifically appropriate categories...; and
 - The formation of industry consortia to jointly conduct testing to avoid unnecessary duplication of tests...”

Statutory Mandate: Section 4(h)2

- 4(h)(2) - Implementation of Alternative Testing Methods—To promote the development and timely incorporation of new scientifically valid test methods and strategies that are not based on vertebrate animals, the Administrator shall –
- 4(h)(2)(A) - “...not later than 2 years after the date of enactment....develop a strategic plan to promote the development and implementation of alternative test methods and strategies to reduce, refine, or replace vertebrate animal testing ...”
 - Published June 22, 2018
 - <https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/strategic-plan-reduce-use-vertebrate-animals-chemical>
- List of Alternative Test Methods and Strategies (or New Approach Methodologies [NAMs]): https://www.epa.gov/sites/default/files/2021-02/documents/nams_list_second_update_2-4-21_final.pdf

New Chemicals Collaborative Research Program

- OCSPP is proposing to develop and implement a multi-year collaborative research program in partnership with the ORD and other federal entities focused on approaches for performing risk assessments on new chemical substances under TSCA.
- EPA held a virtual public meeting on April 20 and 21, 2022
- Board of Scientific Counselors will review in fall 2022.
- <https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/new-chemicals-collaborative>

A screenshot of the Regulations.gov website showing a docket for EPA-HQ-OPPT-2022-0218. The page includes a search bar with the docket ID, navigation tabs for Dockets, Documents, and Comments, and a list of search results. The first result is titled "TSCA New Chemicals Collaborative Research Effort 3-9-22 Clean Docket Version" and is categorized as "SUPPORTING & RELATED MATERIAL". The second result is a "NOTICE" titled "Toxic Substances Control Act (TSCA) Collaborative Research Program To Support New Chemical Reviews; Notice of Public Meeting and Request for Comments". The page also features a sidebar for refining search results and a Windows taskbar at the bottom.

Docket: EPA-HQ-OPPT-2022-0218



Background: New Chemicals Collaborative Research Program

- The TSCA New Chemicals program serves a "gatekeeper" role to manage potential risk to human health and environment from chemicals new to the marketplace; EPA receives ~ 500 new chemical submissions annually.
- TSCA section 5 requires that any person planning to manufacture or import a non-exempt new chemical substance (i.e., a chemical not on the TSCA Inventory) notify EPA before beginning that activity. This notice is known as a premanufacture notice (PMN).
- EPA is generally required to review these PMNs within 90 days, which consists of assessing the potential risks to human health and the environment of the chemical under the conditions of use, and to make an affirmative determination.
- Where the chemical substance presents or may present an unreasonable risk, EPA must take action to prevent those risks before the chemical can enter commerce.

Challenges and Opportunities

1. Update, refine and transparently document category, read-across and analogue science and process
2. Collate and integrate internal databases; identify and incorporate appropriate external databases
3. Modernize and refine the best available non-proprietary QSAR approaches and predictive models for use in evaluating new chemicals under TSCA
4. Implementing both the 2018 Strategic Plan to Promote the Development and Implementation of Alternative Test Methods Within the TSCA Program and the 2021 EPA New Approach Methods Workplan
5. Develop a modernized decision support tool to increase transparency and efficiency

	Research Area	Challenge	Approach	Expected Outcome(s)
1	Update and Refine Chemical Categories	Currently 56 TSCA categories, last updated 2010	Systematically define chemical categories and analogues for read-across using structural (and other) boundaries; physical-chemical properties; structural alerts for hazard, fate, exposure, and/or functional uses; existing hazard data; and/or, <i>in vitro</i> mechanistic and toxicokinetic data from NAMs	This will increase the efficiency of new chemical reviews and promote the use of the best available data to protect human health and the environment.

Research Area	Challenge	Approach	Expected Outcome(s)
2 Develop and Expand Databases Containing TSCA Chemical Information	Existing TSCA information is not computationally accessible or easily searchable	<p>Extract and curate available TSCA CBI study information</p> <p>Continue extraction and curation of physical-chemical property, environmental fate, hazard, and exposure information (non-CBI) in ORD databases</p> <p>Map information in ORD databases to standardized reporting templates and store in an International Uniform Chemical Information Database (IUCLID)</p>	<p>The TSCA CBI information will be combined with publicly available sources to expand the amount of information available, enhancing chemical reviews and enabling efficient sharing of chemical information across EPA. Safeguards for CBI will be maintained as appropriate in this process.</p>

	Research Area	Challenge	Approach	Expected Outcome(s)
3	Develop and Refine QSAR and Predictive Models for Physical-Chemical Properties, Environmental Fate/Transport, Hazard, Exposure, and Toxicokinetics	Currently used models are not always publicly accessible, easy to update with additional chemicals, or the best performing for all chemistries	<p>Develop and update QSAR and predictive models using existing data and curated data from Research Area #2</p> <p>Evaluate models to determine the best suite for use by OPPT for regulatory purposes</p>	Updated models that reflect the best available science, increase transparency, and a process for updating these models as science allows.

	Research Area	Challenge	Approach	Expected Outcome(s)
4	Explore Ways to Integrate and Apply NAMs in New Chemical Assessments	<p>Reduction in the use of vertebrate animals in accordance with TSCA Section 4(h)</p> <p>Many PMN submissions are data poor</p> <p>Amended TSCA requires affirmative determination regarding unreasonable risk</p>	<p>Develop and evaluate a suite of <i>in vitro</i> NAMs for informing new chemical evaluations</p> <p>Use mechanistic and toxicokinetic <i>in vitro</i> NAMs to inform and refine chemical categories in Research Area #1</p>	<p>A suite of NAMs that could be used by external stakeholders for testing and data submissions under TSCA as well as informing and expanding new chemical categories</p>

	Research Area	Challenge	Approach	Expected Outcome(s)
5	Develop a TSCA New Chemicals Decision Support Tool to Modernize the Process	Searching, collating, and integrating data for new chemical assessments is inefficient and costly	Build proof of concept software workflow that integrates all data streams in a new chemical risk decision context	A decision support tool that will efficiently integrate all the data streams (<i>e.g.</i> , chemistry, fate, exposures, hazards) into a final risk assessment and transparently document the decisions and assumptions made. This will facilitate the new chemicals program tracking decisions over time and evaluating consistency within and across chemistries.

Beginning the work

- Research will be initiated in FY23.
- Research during the 2023-2026 timeline will provide a foundation for continued improvement to meet the needs of new chemicals evaluation.
- The research is expected to complement the EPA NAMs Work Plan, in which we seek to establish scientific confidence and demonstrate application of NAMs as well as develop NAMs that fill critical information gaps.
- Partnerships:
 - OPPT, ORD, and NIH (DNTP/NIEHS, NICEATM, and NCATS)
 - Other regulatory partners, such as ECHA



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Thank You!
