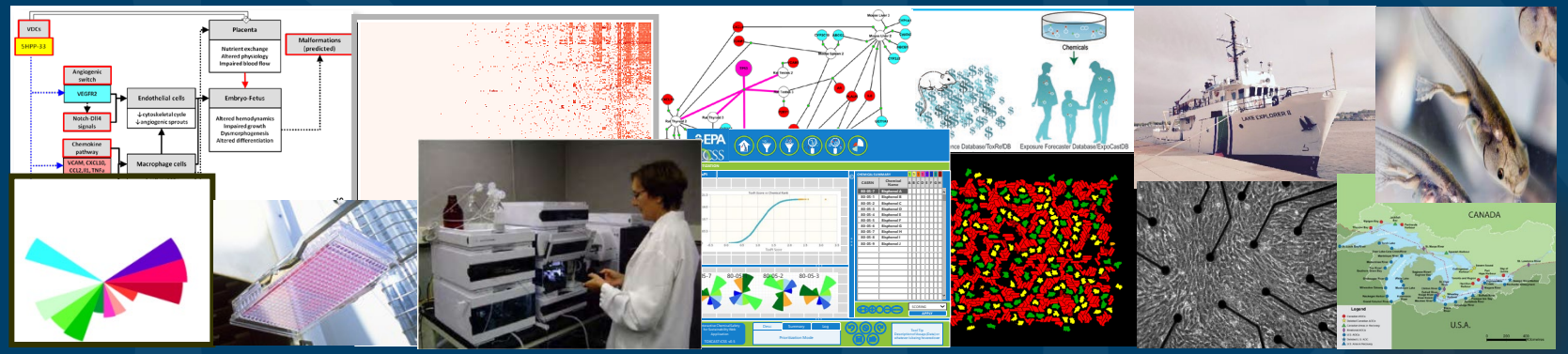
Development and Application of NAMs at EPA



Making Progress on NAMs Workshop

May 13, 2021

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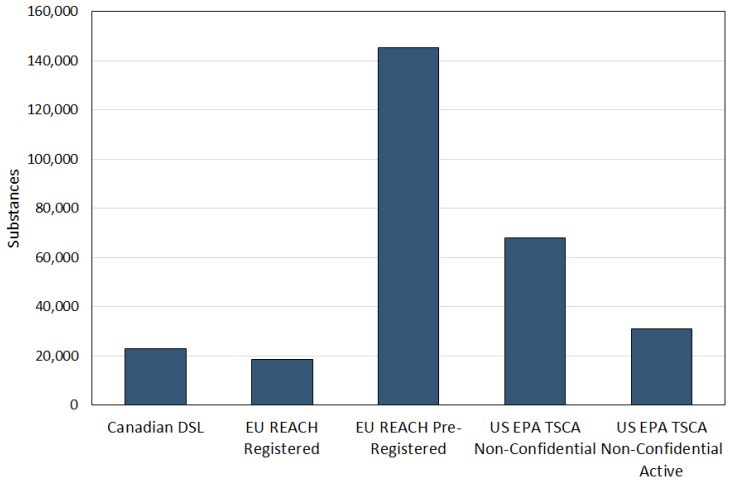
Center for Computational Toxicology and Exposure

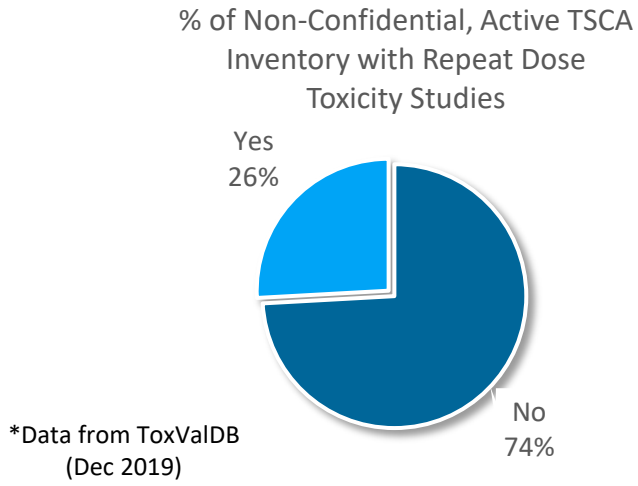
The views expressed in this presentation are those of the presenter and do not necessarily reflect the views or policies of the U.S. EPA

Let's Not Lose Sight of the Multiple Underlying Challenges in Evaluating the Risks of Chemicals

Number of Substances

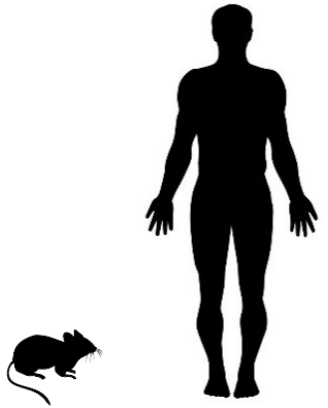


Amount of Data

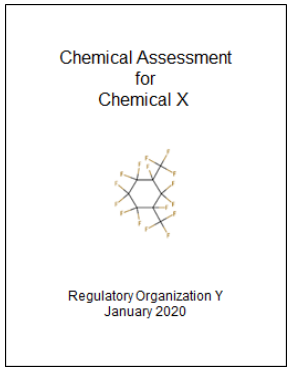


*Data from ToxValDB (Dec 2019)

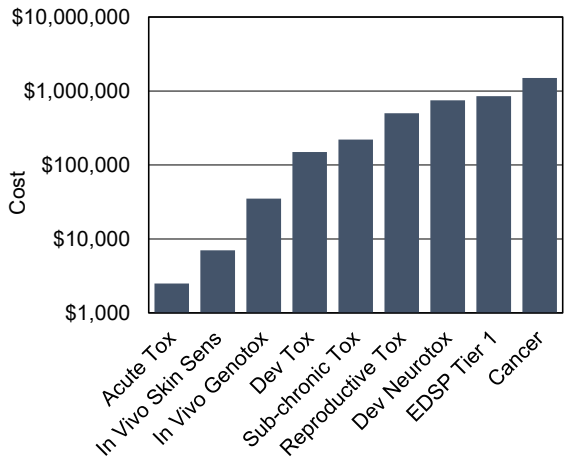
Reliability/Relevance



Time



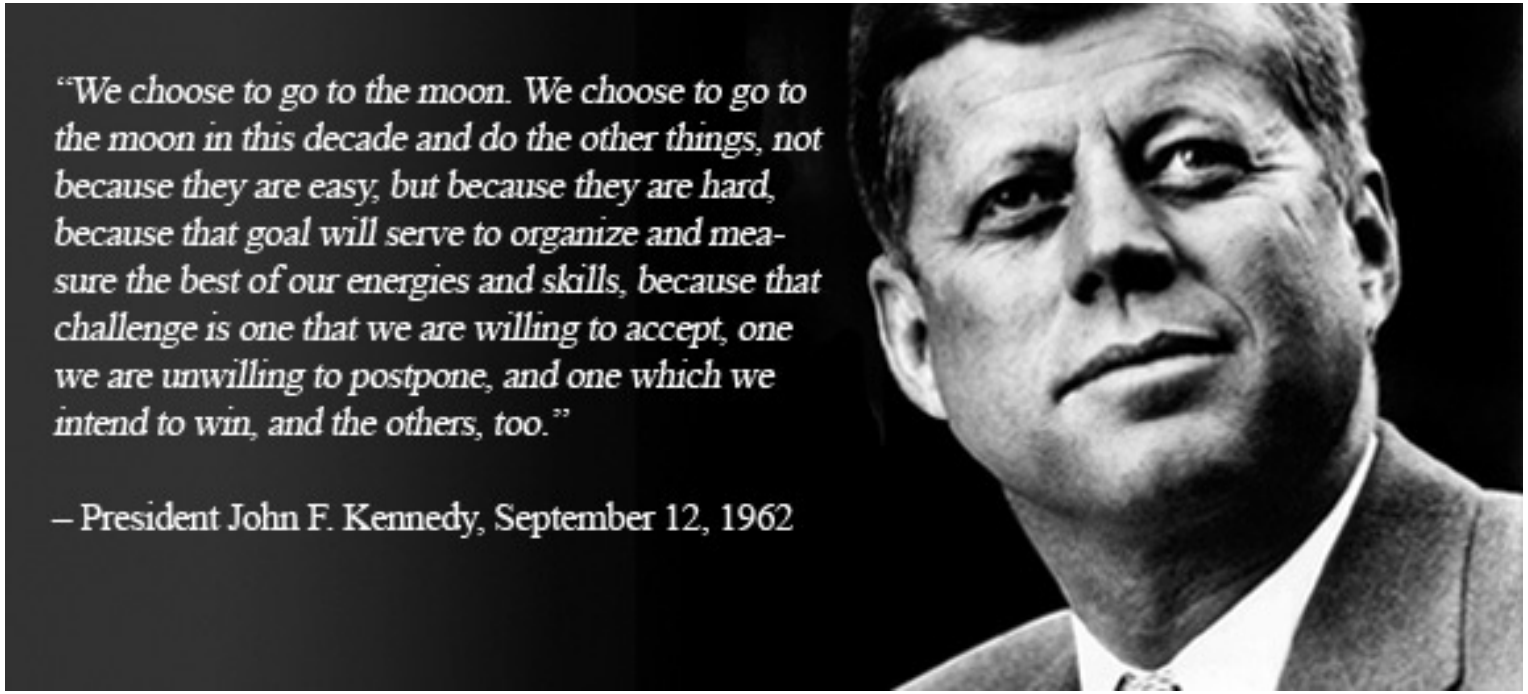
Economics



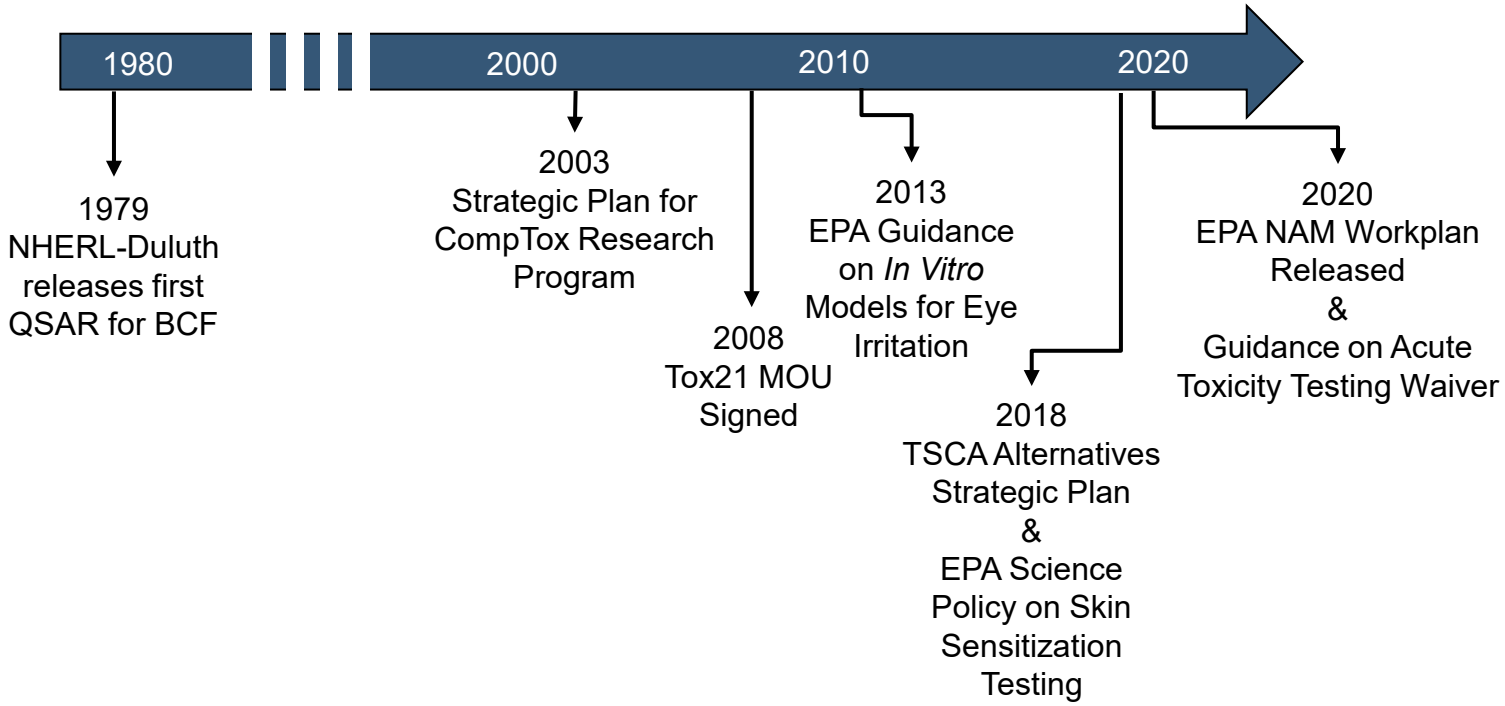
Broad Range of Decision Contexts

EPA United States Environmental Protection Agency

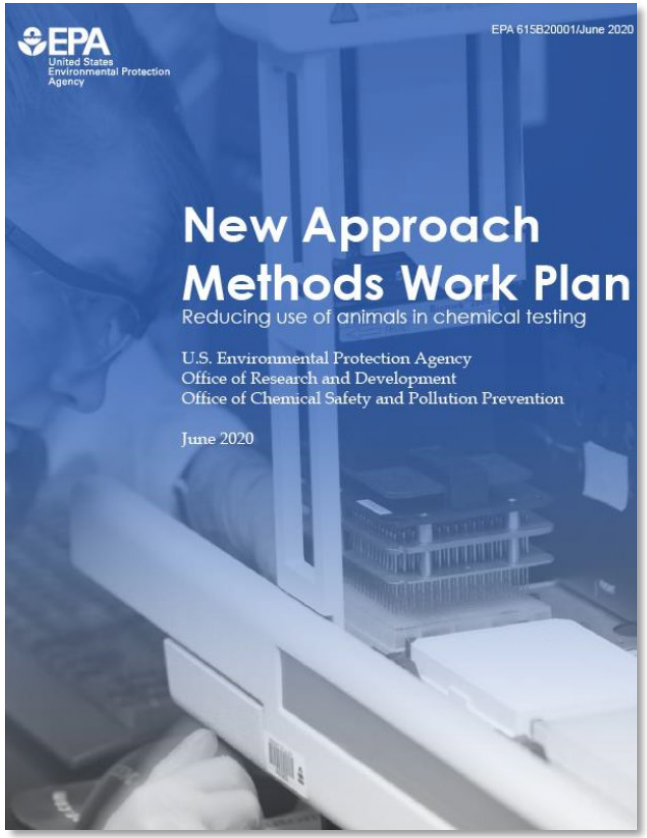
Goals Spur Action and Help Focus Efforts



EPA Has Been Working To Develop and Apply New Approach Methods for Decades

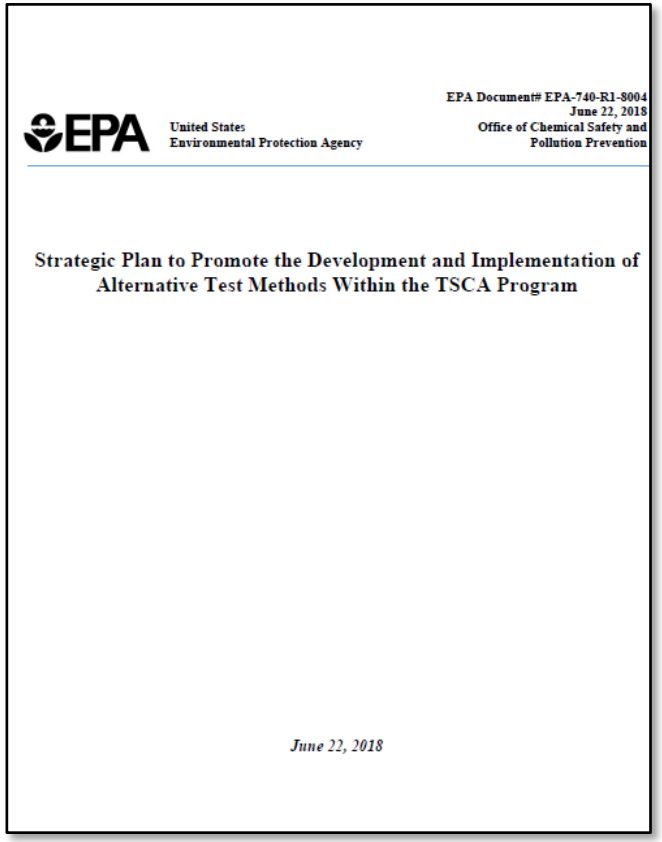


Making Progress Requires a Plan…



Focused on Agency-wide action

Focused on research



Focused on TSCA

Evaluate Regulatory Flexibility for NAMs

Strategy:

- Perform a thorough review of existing statutes and programmatic regulations, policies and guidance to identify mammalian testing requirements that may not allow flexibility for the Agency to apply NAMs.
- Consider options for introducing flexibility on implementing and/or using appropriate NAMs for regulatory purposes.

Deliverable: EPA report on findings of the review and options in 2021.

Initial Findings:

- The major environmental statutes do not prevent EPA from considering information from NAMs.
- Most of the statutes and regulations include general statements such as the necessity of upholding scientific standards and using “the best available science”.
- For those regulations that have specific testing requirements, the Agency has been successful in using its authority to increase flexibility in some cases (e.g., using science policy changes).

Baselines and Metrics to Evaluate Progress

Strategy:

- Build on previously established baselines and metrics for animal use within OCSPP and ORD
- Progressively extend to other EPA offices since baselines and metrics will need to be customized to the specific requirements in each program

Deliverable: Progress and summary metrics reported annually through EPA website starting in Q4 of 2021

Initial Findings:

- Within OCSPP, EPA will initially use the number of animals required for testing under the 40 C.F.R. Part 158 as a baseline to measure and track mammalian use for pesticide actions.
- Within ORD, the average number of mammals used for research purposes between 2016 and 2018 was 8,600 per year.

Establish Scientific Confidence and Demonstrate Application

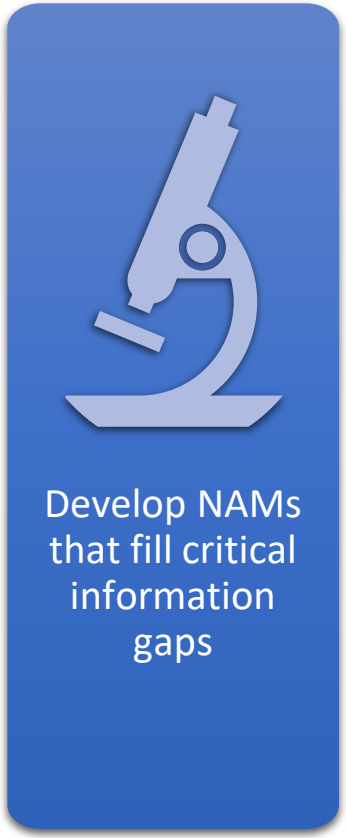
Strategy:

- Characterize the scientific quality and relevance of existing animal tests
- Develop a scientific confidence framework to evaluate the quality, reliability, and relevance of NAMs
- Develop recommended reporting templates
- Demonstrate application of the NAMs to regulatory decisions through case studies

Deliverables:

- NAS report on uncertainties and utility of existing mammalian toxicity tests in Q4 2022.
- Scientific confidence framework to evaluate the quality, reliability, and relevance of NAMs in Q3 2022.
- Reporting templates which may be used by EPA and stakeholders that capture the range of specific NAMs used for Agency decisions in Q4 of 2022.
- Approximately one case study every other year beginning in 2022.

Develop NAMs to Address Scientific Challenges and Fill Important Information Gaps



Strategy:

- Facilitate joint planning of NAM development by EPA research scientists and regulators
- Encourage development and evaluation of NAMs by external parties

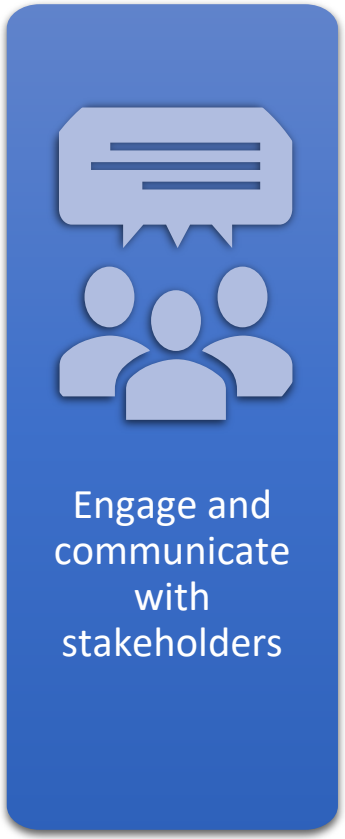
Deliverable:

- Develop EPA Strategic Research Action Plans on a regular 4-year planning cycle
- Encourage development of NAMs through mechanisms such as the STAR grant program and facilitate partnerships with organizations focused on establishing scientific confidence in alternative methods. Ongoing deliverable.

Initial Findings:

- The next EPA research planning process begins Summer 2021
- EPA partners with a broad range of external organizations on NAM development and application
- EPA encouraging the development of NAMs by external entities is the award of $4.25 million to five universities through its STAR Program

Engage and Communicate with Stakeholders



Strategy:

- Develop centralized portal for releasing EPA-related NAM Information
- Actively solicit comment and feedback associated with deliverables
- Develop training courses, workshops, and conferences for stakeholders on NAMs

Deliverable:

- Centralized EPA NAM website (www.epa.gov/nam) and email address for feedback.
- Public webinars when deliverables are released.
- Training, opportunities for scientific exchange, and progress updates through Agency sponsored and partners events.

Initial Findings:

- Two annual NAM conferences have been held and conference reports have been posted.
- Public webinars on NAM work plan.

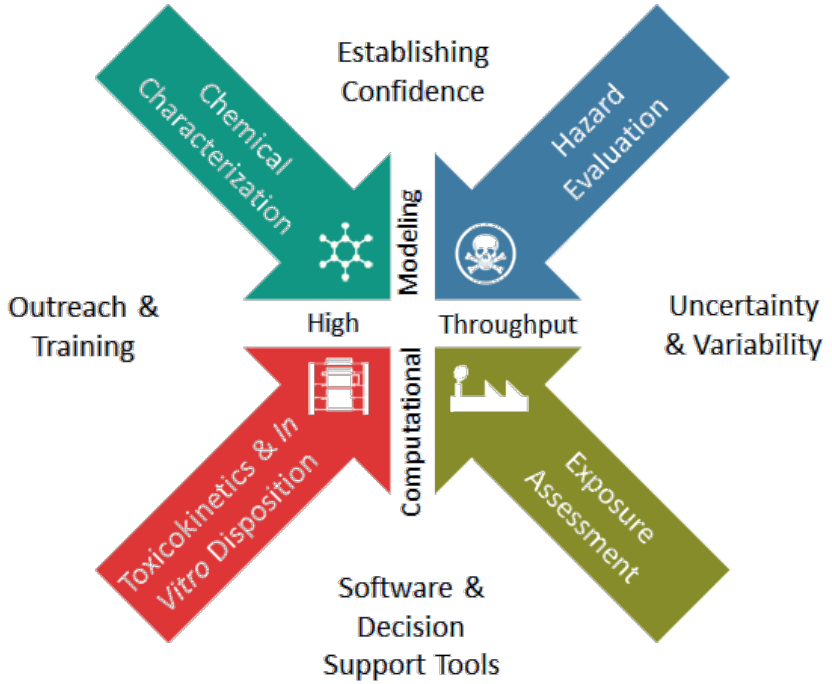
EPA's Integrated Research and Development Efforts are Operationalizing the NAM Work Plan

- DSSTox
- Chemical library
- Systematic Read across
- SAR/QSAR modeling
- Chemotypes
- TTC

- OECD/ APCRA Case Studies
- NAM Work Plan
- Reference Materials
- Reporting Templates

- Eco/HH HTS (HTTr, HTPP, ToxCast)
- Tiered testing
- Organotypic models
- Addressing limitations (metabolism, chemical space)
- Statistical and Biologically-based Modeling
- AOPs

- Communities of Practice
- ToxCast Owners Manual
- Training courses/ videos



- SEEM
- ToxBoot
- HTTK
- ToxRefDB

- HTTK assays (metabolism, bioavailability, binding)
- Partition coefficients
- HTTK R package
- Multi-route models
- Model verification (e.g., CvT)
- In vitro disposition

- CompTox Chemicals Dashboard
- RapidTox
- Factotum
- ECOTOX
- SeqAPASS

- ExpoCast
- NTA/SSA
- ENTACT
- Product emissivity

EPA
United States
Environmental Protection
Agency

Thank you for your attention!