

U.S. EPA Strategic Plan to Promote the Development and Implementation of Alternative Test Methods: Status and Update

Louis Scarano, US EPA

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NIH, Bethesda, MD



Statutory Mandate - Background

The Toxic Substances Control Act (TSCA) was originally enacted in 1976.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:

- new requirements and deadlines for actions related to the regulation of new and existing chemical substances.
- new subsection under Section 4 (*Testing of Chemical Substances and Mixtures*); particularly, Section 4 (h) entitled *Reduction of Testing on Vertebrates*



Statutory Mandate: Section 4(h) – *Reduction of Testing on Vertebrates*

- Section 4(h)1 – General
- Section 4(h)2 – Develop Strategic Plan
- Section 4(h)3 – Voluntary Testing



Statutory Mandate: Section 4(h)(1)

- 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 – The Strategic Plan (Due June, 2018)

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 and provide information of equivalent or better scientific quality and relevance for assessing risks of injury to health or the environment of chemical substances or mixtures through, ...”



Statutory Mandate – Section 4(h)(3)(A)

“In General—Any person *developing information for submission under this title on a voluntary basis and not pursuant to any request or requirement by the Administrator* shall first attempt to develop the information by means of an alternative test method or strategy identified by the Administrator pursuant to paragraph (2)(C)....before conducting new vertebrate animal testing”

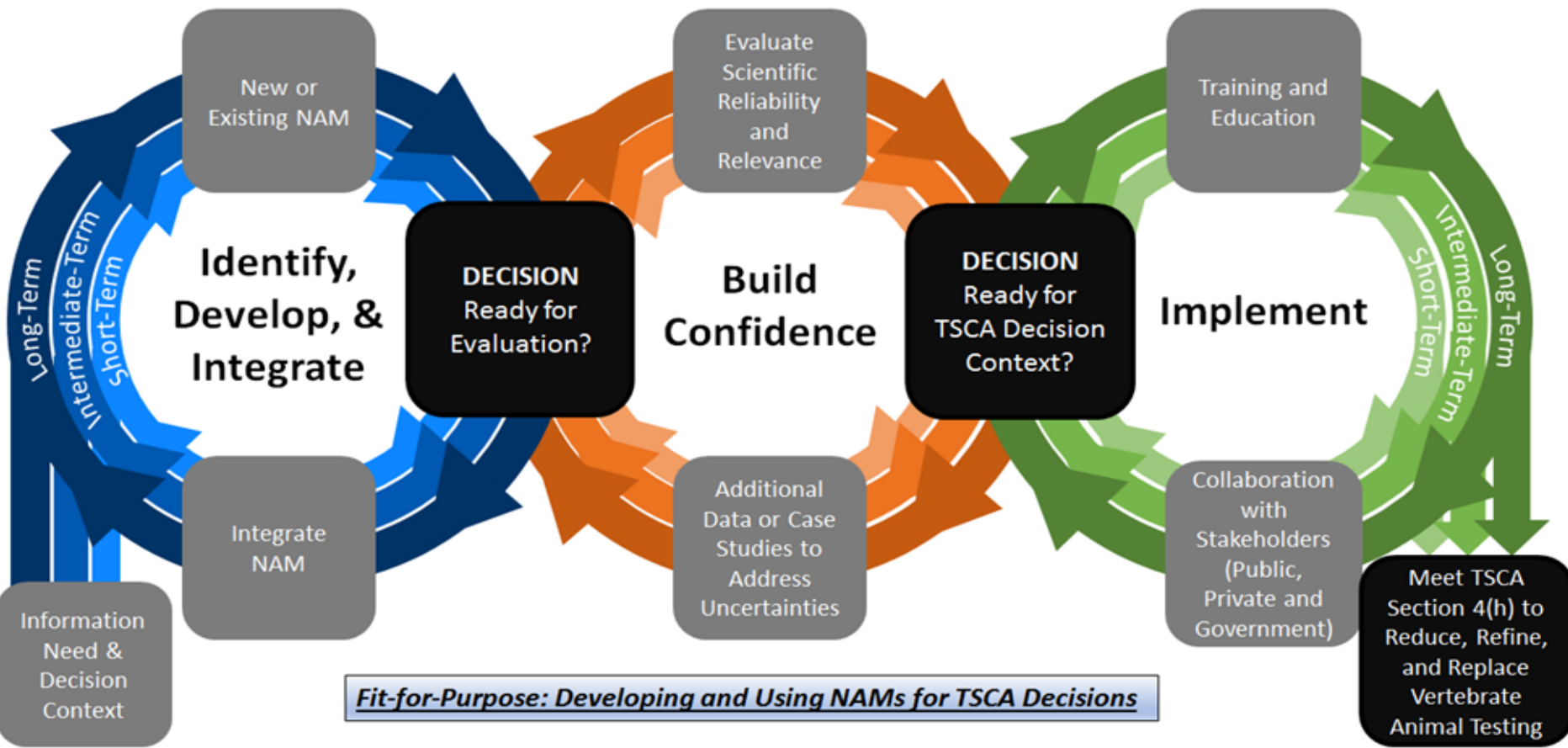


Overview of Draft Strategic Plan

1. Identification, Development and Integration of New Approach Methodologies (NAMs)*
2. Establishing Scientific Relevance, Reliability and Confidence
3. Importance of Training, Education and Collaboration
4. Implementation of NAMs Under TSCA
 - Commitment of time and resources through the establishment of the TSCA NAM Team (TNT)

** EPA views the term New Approach Methodologies as equivalent to alternative test methods and strategies*

Fig. 1 Core Components of EPA Strategic Plan to Develop and Implement New Approach Methodologies (NAMs) in TSCA





Use of NAMs for TSCA –Decision Context

The importance of Fit-for-Purpose :

- New chemicals program has been using NAMs for years
 - ECOSAR, OncoLogic, EPISuite, New Chemical Categories Document, SAR/QSAR/Read-Across
- EPA will consider NAMs for:
 - Screening candidates for prioritization
 - Prioritization
 - Risk evaluation



New Chemicals

Presents an
unreasonable
risk

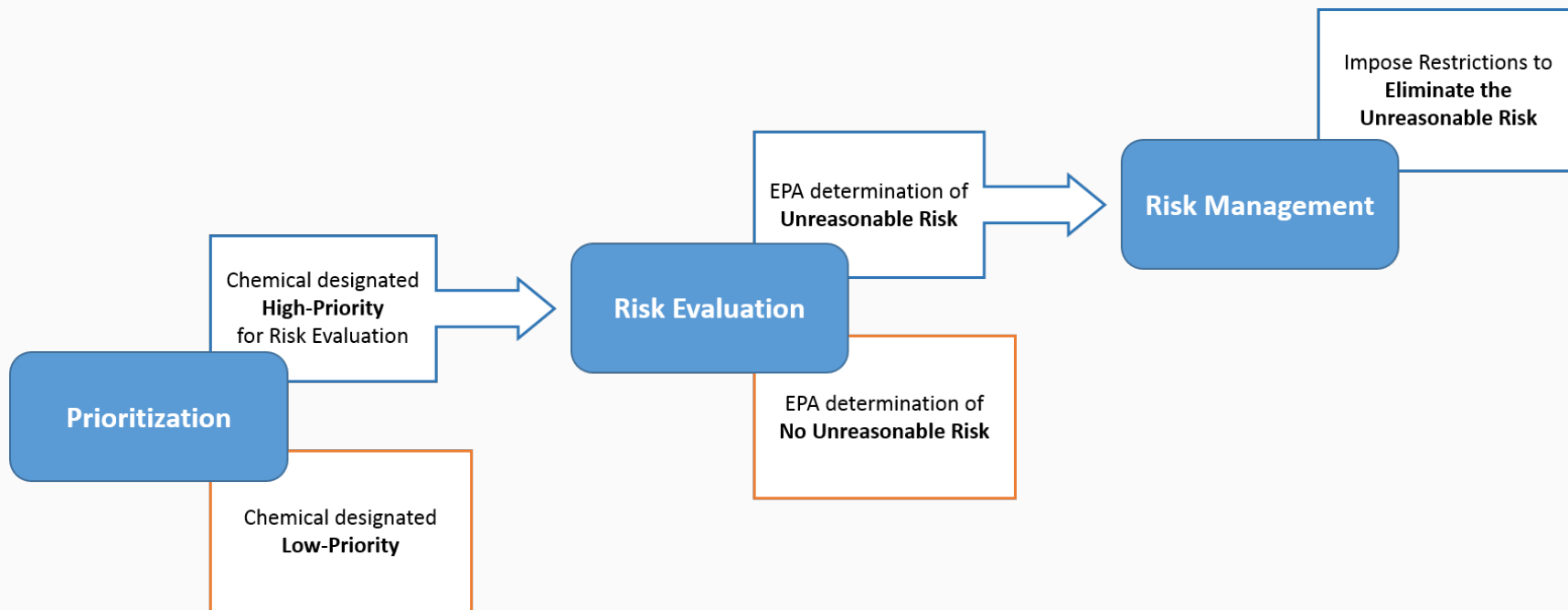
May present
an
unreasonable
risk

Is not likely to
present an
unreasonable
risk

Information is
insufficient to
permit a
reasoned
evaluation of
the risk.



Evaluating Risks of Existing Chemicals





Identification, Development and Integration of NAMs

- Identification and Development of NAMs
 - Chemical Characterization
 - Hazard Identification and Characterization
 - Dosimetry and In Vitro-In vivo Extrapolation (IVIVE)
 - Characterizing Exposure to Humans and the Environment
- Integration of NAMs: Frameworks and Weight of Evidence
 - Section 26(h) and (i) – use of Weight of Evidence (WoE) and Best Available Science
 - Section 4(h) – “information of equivalent or better scientific quality” (than traditional animal models)
 - Various frameworks for Integrating or combining NAMs



Establishing Scientific Relevance, Reliability and Confidence of NAMs

- Framework (OECD Guidance Document 34):
 - **Relevance** – regulatory need/usefulness and associated limitations
 - **Reliability** - reproducibility
 - Transparency (i.e., release of data sets and performance characteristics)
- Eight Criteria (largely based on Casati et al., 2017)



Education, Training and Collaboration

- NAMs and the new advancements in science (biology, chemistry, non-vertebrate animal test methods) need to be understood for proper application under TSCA
- Ensuring that EPA scientists, the regulated community, and interested stakeholders are properly training to understand and use NAMs is critical to the success of implementing Section 4(h) of TSCA (including public outreach)
- EPA will continue to collaborate with multiple domestic and international partners on the development and use of NAMs for regulatory purposes.



Implementation: Near-Term (Next Three Years) – Building a TSCA NAM Foundation

- i. Continue to Implement NAMs to Evaluate Hazard, Exposure and Environmental Fate for New and Existing Chemicals

Ongoing

- ii. Review Existing NAMs and Create and Maintain a List as required.

1. Publish list – June 2018

Appendix B has six separate tables: - DRAFT AND SNAPSHOT IN TIME

1. EPA (TSCA) Specific NAMs
2. OECD Test Guidelines (Health)
3. OECD Guidance and Review Documents - Non-Testing Methods
4. OECD Guidance and Review Documents – Testing for Human Health
5. OECD Guidance and Review Documents – Testing for Endocrine Disruption
6. OECD Guidance and Review Documents – Performance Standards

2. Review other existing NAMs according to Chapter 5 criteria

First Quarter 2019



Implementation: Near-Term (Next Three Years) – Building a TSCA NAM Foundation (cont.)

- iii. Identify and Maintain Most Requested/Needed Studies for New and Existing Chemicals – Retrospective Analysis

Second Quarter 2019

- iv. Identify and Curate Available Existing TSCA Information on NAMs (and Traditional Test Data) – CBI; TSCA In-House Inventory Analysis

Second Quarter 2019



Implementation: Near-Term (Next Three Years) (cont.)

- v. Use of NAMs to identify candidates for prioritizing existing chemicals
Ongoing

- vi. Begin development of Scientific Information Technology (IT) Platform
Ongoing

- vii. Collaborate with partners and stakeholders to identify NAMs for further development (including case studies through TNT)
Ongoing



Implementation: Intermediate-Term Objectives (3-5 years)

- i. Progress towards use of NAMs for prioritization and risk evaluation - several possibilities identified: toxicological threshold of concern (TTC); encouraging voluntary submitters to use NAMs; possible use of NAMs in designing safer chemicals.
- ii. Maintaining the expansion of the TSCA NAM List
- iii. Developing and maintaining educational and outreach goals for regulatory scientists, end-users and the public
- iv. Continue collaboration with partners and stakeholders to identify NAMs for further development



Implementation: Long-Term

- EPA's long-term goal is to move towards making TSCA decisions (conducting prioritization and risk evaluations for new and existing chemicals) with NAMs in order to reduce and eventually eliminate vertebrate animal testing for TSCA.



Next Steps

- Draft Strategic Plan released on **March 7th** , Public Meeting held **April 10th** in Washington, DC
- Comments on the Plan closed on **May 11th**
 - Received 32 substantive comments (all publicly available in the docket – EPA-HQ-OPPT-2017-0559 at www.regulations.gov) – next slide
- Final will be published by **June 22, 2018**



Who Submitted the Substantive Comments

Submitter Type	Number
Animal Welfare/Animal Protection Organizations	10
Individual Citizens (not form letters)	8
Environmental NGOs	4
Industry Trade Organizations	3
Chemical Company	1
Professional Society	1
Academic	1
Foundation	1
Other	2



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