U.S. Environmental Protection Agency (EPA) Office of Pollution Prevention and Toxics (OPPT) Strategic Plan for Developing and Implementing Alternative Test Methods and Strategies to Reduce, Refine, or Replace Vertebrate Animal Testing for Chemical Substances or Mixtures

Draft Considerations for the Development of the Strategic Plan

for

Docket Posting and Presentation at November 2, 2017 Meeting

Topics

- Statutory Mandate
- Regulatory Context
- Strategic Plan –
  - Goals and Objectives
- Charge questions to Experts and the Public
- Timeline

Statutory Mandate - Background

The Toxics Substances Control Act (TSCA) was originally enacted on October 11, 1976 and serves as the nation's primary chemicals management law. On June 22, 2016, TSCA was amended by the Frank R. Lautenberg Chemical Safety for the 21st Century Act. The Office of Pollution Prevention and Toxics (OPPT) is responsible for carrying out the mandate of TSCA; which includes new requirements and deadlines for actions related to the regulation of new and existing chemical substances. It also includes a new subsection under Section 4 (Testing of Chemical Substances and Mixtures); specifically, Section 4 (h) entitled *Reduction of Testing on Vertebrates*.

Statutory Mandate

- Section 4(h)1 -

“In General - The Administrator shall reduce and replace, to the extent practicable, scientifically justified, and consistent with the policies of this title, the use of vertebrate animals in the testing of chemical substances or mixtures…”

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—***

Are Six Points…..

Statutory Mandate – What is Required in the Strategic Plan

1. 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***…"

2. 4(h)(2)**(B)** – "as practicable, ensure that the strategic plan developed under subparagraph (A) is reflected in the development of requirements for testing under this section;"

Statutory Mandate – What is Required in the Strategic Plan

3. 4(h)(2)**(C)** - Requirement for “a list...of particular alternative test methods or strategies the Administrator has identified that do not require new vertebrate animal testing…”

4. 4(h)(2**(D)** – “provide an opportunity for public notice and comment on the contents for the plan developed under subparagraph (A), including the criteria for considering scientific reliability and relevance of the test methods and strategies that may be identified...”

Statutory Mandate – What is Required in the Strategic Plan

5. 4(h)(2)**(E)** beginning on the date that is 5 years after the date of enactment of the Frank R. Lautenberg Chemical Safety for the 21st Century Act, and every 5 years thereafter, submit to Congress a report that describes the progress made in implementing the plan…and goals for future alternative test methods and strategies implementation;

6. 4(h)(2)**(F)** - Prioritize and carry out performance assessment, validation and translational studies to accelerate the development of alternative methods/strategies

Statutory Mandate – Submitting Information Voluntarily*

Section 4(h)(3)(A) – “Any person developing information for submission…shall first attempt to develop the information by means of an alternative test method or strategy…”

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*Or, information not requested by the Agency

Regulatory Context Under TSCA

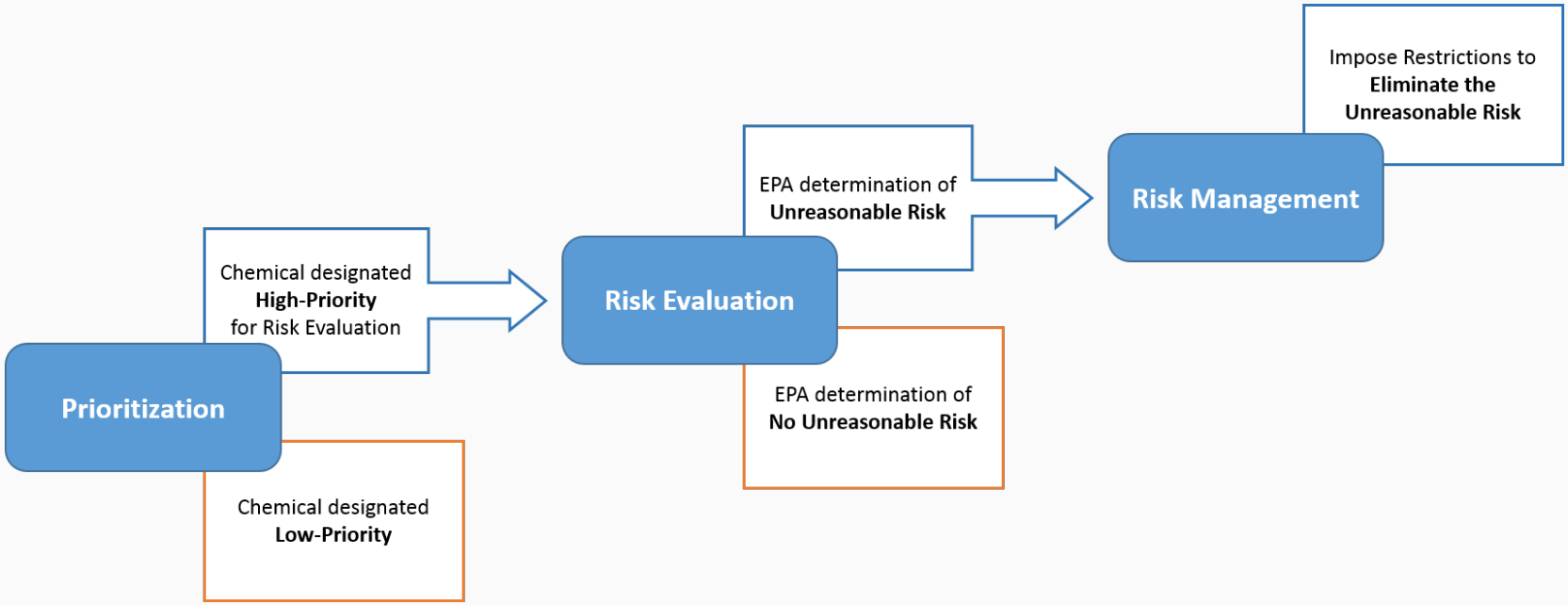
There are many alternative test methods and strategies currently available and potentially useful for some regulatory purpose. Under TSCA, the major needs are for risk-based decision making for both new and existing chemicals, and prioritization of existing chemicals for eventual risk evaluation. Combinations of actual test methods, computer models and tiered testing/evaluation approaches all play important roles given the regulatory context.

Evaluating Risks For New Chemicals: *NAMs* Already Heavily Used*

- Use analog(s), category/read-across analyses, In silico predictions (e.g., OncoLogic for cancer in humans and ECOSAR for ecological receptors)
- EPA may request hazard or exposure information…

**For clarity/brevity – the term New Approach Methodologies (NAMs) will be used to mean alternative test methods and strategies*

Evaluating Risks of Existing Chemicals



Overarching Considerations Important to the Strategic Plan (1 of 2)

- Understanding the concept expressed throughout the law of implementing NAMs – **"to the extent practicable (and) scientifically justified"**
- Identifying and promoting **advances in science and NAMs** (including training)
- **Fostering collaboration** with domestic and international stakeholders inside and outside the government on NAMs
- **Global harmonization**

Overarching Considerations Important to the Strategic Plan (2 of 2)

- **Communication and education of the public**
- The need to **identify appropriate information to replace vertebrate animal testing**
- **Enhance and harmonize IT systems** to maximize the use of existing information and assessments.
- To **develop a new risk evaluation paradigm for human health and the environment** for new and existing chemicals in US commerce which uses non-animal alternative test methods and strategies.

Strategic Plan - Goals and Objectives

- The goals are the six statutory requirements under Section 4(h)(2)
- Both Goals and Objectives will be specific to TSCA needs (i.e., new and existing chemical regulation in the US)

Strategic Plan - Goals and Objectives

Strategic Considerations

- Incremental - Easiest first, increasing difficulty over time
- Iterative - Learn by doing; revisit, revise, improve
- Transparent - Be inclusive, open, and make results publicly available
- Best Available Science - Follow principles as described in Section 26 of TSCA

And will be identified for both new and existing chemicals

GOALS

- Goal 1: Promote the development and implementation of alternative test methods and strategies (4(h)(2)(A)) - G1

- Goal 2: Ensure that the strategic plan is reflected in the development of requirements for testing (4(h)(2)(B)) – G2

- Goal 3: Requirement for a list of particular alternative test methods or strategies 4(h)(2)(C)) – G3

GOALS

- Goal 4: Criteria for considering scientific reliability and relevance of the test methods and strategies that may be identified (4(h)(2)(D)) – G4

- Goal 5: Every 5 years from 2016, submit to Congress a report that describes the progress made in implementing the plan, with goals for future alternative test methods and strategies implementation (4(h)(2)(E)) – G5

- Goal 6: Prioritize and carry out performance assessment, validation and translational studies to accelerate the development of alternative methods/strategies (4(h)(2)(F)) – G6

OBJECTIVES: New Chemicals (Link to Goals Provided)

Near Term (2018-2020)

- Incorporate NAMs in evaluation of priority TSCA new chemical category(ies) (G1, G2)
- Identify most requested/needed studies for new chemicals (G1, G2)
- Identify available existing OPPT CBI information (NAMs and animal test data)(G1, G2, G3, G6)
- Work with partners to identify research gaps and promote advances in NAMs relevant to TSCA needs (G1, G3, G4, G6)
- Work with partners to accelerate the use of NAMs where possible– Accelerating the Pace of Chemical Risk Assessment (APCRA) activity (G6)

OBJECTIVES: New Chemicals (Link to Goals Provided)

Mid Term (2020-2022)

- Determine most appropriate NAMs for studies identified above (G1, G2, G3, G4, G6)
- Work with partners to identify research gaps and promote advances in NAMs relevant to TSCA needs (G1, G3, G4, G6)
- Incorporate NAMs as part of new chemicals testing plan, either side-by-side with animal or as a replacement (G2)
- Begin using NAMs (where possible) for quantitative or qualitative risk evaluation for new chemicals (G1, G6)

OBJECTIVES: New Chemicals (Link to Goals Provided)

Long Term (2022 and beyond)

- Standard use of NAMs as first-tier screen for new chemicals testing (G2, G6)
- Work with partners to identify research gaps and promote advances in NAMs relevant to TSCA needs (G1, G3, G4, G6)
- Continue expanding the use NAMs for quantitative or qualitative risk evaluation for new chemicals (G1, G6)

OBJECTIVES: Existing chemicals (Link to Goals Provided)

Near Term (2018-2020)

- Use NAMs to identify candidates for prioritization (G1, G2, G3, G6)
- As prioritization candidates are identified, consider NAMs to fill data gaps (G2)
- Work with partners to identify research gaps and promote advances in NAMs relevant to TSCA needs (G1, G3, G4, G6)

OBJECTIVES: Existing chemicals (Link to Goals Provided)

Mid Term (2020-2022)

- Use NAMs in developing and improving priority existing chemical category(ies); e.g., PFCs (G1, G2, G3, G6)
- Use NAMs (where possible) for qualitative use in risk evaluation(G1, G6)
- Work with partners to identify research gaps and promote advances in NAMs relevant to TSCA needs (G1, G3, G4, G6)

OBJECTIVES: Existing chemicals (Link to Goals Provided)

Long Term (2022 and beyond)

- Use NAMs (where possible) for quantitative use in risk evaluation(G1, G6)
- Work with partners to identify research gaps and promote advances in NAMs relevant to TSCA needs (G1, G3, G4, G6)

Draft Timeline for Development of Strategic Plan

June – November, 2017
Create draft outline, solicit Ideas

November-December, 2017
Expert and Public Discussions

December, 2017 – February, 2018
Develop first draft

March-April, 2018
Solicit Public Comment

May-June, 2018
Finalize Plan

Post by June 22, 2018

Charge Questions: 1 of 3

1. Review and comment on the draft goals and objectives presented in the draft PowerPoint.
   a. Is there anything missing?
   b. Did the Agency appropriately identify near-, mid- and long-term objectives?
   c. Are there additional objectives the Agency should consider important to achieving the goals identified?

2. Regarding the use of NAMs, what should the Agency consider in terms of process and content for "…providing information of equivalent or better scientific quality and relevance that will support regulatory decisions…" (as stated in 4(h)(2)(A) and elsewhere)?

Charge Questions: 2 of 3

3. Please provide ideas for criteria for reliability and relevance of NAMs that may be used under TSCA (4(h)(2)(D); considering the different contexts (regulatory – prioritization, screening risk evaluation, robust risk evaluation; and type of NAM – computer predictions, in vitro, organs-on-a-chip, etc.)

4. Please provide suggestions for which NAMs may be useful to meet our Goal 3 (requirements for a list of NAMs). Are there existing lists that EPA should preferentially draw from? Existing lists that EPA are considering includes those from OECD, ICCVAM and ECVAM (links provided in separate document)

5. Please provide examples of implementation (in a non-regulatory or regulatory setting) of the use of NAMs for the purpose of evaluating risk to human health or the environment. This can be for chemicals, medical devices/products, pesticides, etc.

Charge Questions: 3 of 3

6. Collaboration and identifying and promoting the use of the new science will be a key to success. What are steps the Agency can take to ensure this happens?

7. As mentioned in TSCA (Sections 4(h)(1)(B)(iii) and 4(h)(2)(A)(viii)), please provide ideas for how to form industry consortia?

8. What research and method development needs remain to achieve long-term TSCA objectives?
   a. What are the best approaches for the Agency in identifying gaps in science and encouraging research and development in those areas?

9. How should the Agency ensure that the strategic plan developed is reflected in the development of requirements for testing?

THANK YOU FOR YOUR INPUT!