TSCA as Amended by the Frank R. Lautenberg Chemical Safety for the 21st Century Act: The New Future for Alternative Test Methods

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June 7, 2017
Topics Covered

• General Overview of New Law
• How does OPPT Use Test Information?
• Section 4(h) of New TSCA - Alternative Test Methods
• OPPT Activities to Address New Section
• Collaboration with Other Agencies, Stakeholders, etc.
The New Law

• “The Frank R. Lautenberg Chemical Safety for the 21st Century Act”
  – Amends and updates the Toxic Substances Control Act (TSCA)
  – Signed into law on June 22, 2016
  – Effective immediately

• Significance
  – First update to TSCA in 40 years (1976)
  – Sets up program to prioritize and review existing chemicals
  – Requires affirmative determination for each new chemical review
The New Law

Changes Related to New Chemicals

- Requires EPA to make affirmative finding on new chemicals or significant new uses of existing chemicals
- Before the chemical can enter the market, EPA must find that the chemical:
  - “presents an unreasonable risk” and issue a 5(f) order to address such risk;
  - “information...is insufficient to permit a reasoned evaluation...” and issue a 5(e) order;
  - “may present an unreasonable risk” and issue a 5(e) order; or
  - is “not likely to present an unreasonable risk” and publish the determination
The New Law

Changes Related to Existing Chemicals

• Mandatory duty on EPA to evaluate existing chemicals – clear and enforceable deadlines

• Chemical assessment is risk-based, with no consideration of cost or other non-risk factors

• Must consider risks to potentially exposed and susceptible subpopulation

• Unreasonable risks identified in the risk evaluation must be eliminated

• Expanded authority to more quickly require development of chemical information when needed
The New Law  

Additional Changes

• New requirements for substantiating Confidential Business Information (CBI) claims will provide greater public access to critical chemical information

• Source of Funding
  – Provides authority to collect fees from manufacturers and processors for certain activities, i.e., submission of: test data; notification of intent to manufacture; request EPA to conduct risk evaluation – no deadline to promulgate this rule
New Law, New Rules

• TSCA requires EPA to promulgate a number procedural rules (collectively, the “Framework Rules”) to set up or otherwise align EPA’s chemical management program with the new requirements and responsibilities in the law:
  • Prioritization Rule
  • Risk Evaluation Rule
  • Active/Inactive Inventory Reporting Rule
• Must be finalized within 1-year (by June 22, 2017)
How Does OPPT Use Toxicity Information?
New Chemicals – Pre-2016 and Now

Historically (and now):
  – Computational approaches used extensively
    • QSAR and Expert Systems
    • Read-across from Analogs/Categories
  – Tiered-testing approach: requests for higher tiered testing informed by screening results

Now (and in the future):
  – Incorporation of alternative test methods/information?
How Does OPPT Use Toxicity Information?

Existing Chemicals – Pre-2016 and Now

**Historically (and now):**
- To date, have mostly used *in vivo* toxicity testing conducted with established test guidelines and studies published in the scientific literature
- Categories and read-across from analogs used extensively in screening programs (e.g., High Production Volume [HPV] chemicals)
- Categories/clusters used in some TSCA Work Plan assessments

**Now (and in the future):**
- Incorporation of alternative test methods/information (by new law)
The New Future: Section 4(h) and Amended TSCA

• Section 4(h)(1) - “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...”

And, for voluntary testing (that is, not asked for or required by the Administrator) –

• 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...”
### Asking for Information...

<table>
<thead>
<tr>
<th>New Chemical (no information)</th>
<th>Existing Chemical (some information)</th>
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<tr>
<td>• Identify <em>concerns</em> (hazard and/or exposure)</td>
<td>• Identify <em>data needs</em> (hazard and/or exposure)</td>
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<td>• Ask for specific information</td>
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<td>– Analog/read across/in silico</td>
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<td>– In vitro data (specific to the concern)</td>
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<td>• Receptor binding (i.e., ER/AR)</td>
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<td>• Pathways/AOP for certain endpoint</td>
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<td>• Muta...etc.</td>
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<td>– Tiered testing/limited In vivo</td>
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<td>• Prioritization</td>
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Using the Information...

EPA is committed to determining a path toward using alternative test methods for regulatory decisions under the amended TSCA

– In the new chemicals program, EPA uses alternative methods extensively (QSAR, analog and read-across, tiered testing)

– EPA is reviewing various methods proposed in the literature and discussed at various meetings regarding quantitative use of in vitro and other (i.e., in silico) information to make regulatory (i.e., risk assessment) decisions.

– EPA also understands that, as regulators, we are being asked explicitly to better define this question...
The New Future: Requirement for Development of a Strategic Plan Under Section 4(h) of Amended TSCA

Section 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…” (by June of 2018)
Goal/Vision

• **DRAFT TSCA GOAL:** “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.”

  (Direct quote of amended TSCA – Section 4(h)(2)(A))
Scientific Considerations

• Chemistry
  – Defining chemical space for Structure-Activity (similarity indices for endpts, read across, etc.)

• Biology
  – Mapping of biological pathways (AOP) to apical endpoints
  – Developing appropriate approaches to “test guidelines” for alternative methods (performance-based standards, defined approaches – recent OECD developments)
  – Agreement on the science/relevance of in vitro results and in silico predictions

• Implementation – use in hazard/risk assessment
  – Determining hazard value from in vitro/in silico results
  – Uncertainties (different from those in vivo?)
  – Decision Context: prioritization, risk assessments (screening and/or quantitative)
Acceptance Considerations

- Stakeholder acceptance
  - Confidence in what regulators are asking for (in terms of information) – IATA and Defined Approaches (DA)
  - Confidence in decision - MAD
- Various efficiencies – cost, animals, time
- Social Acceptance – communication and translation
- Identify early opportunities for application of alternative test methods to regulatory decisions
- Identify targeted R&D priorities for medium- to longer-term application to regulatory decisions
- Others?
**DRAFT TIMELINE**

- **June – August, 2017**: Solicit, Receive Ideas (Stakeholders)
- **August-September, 2017**: Host Stakeholder Workshop
- **April - May, 2018**: Complete first draft, hold consultation reviews with stakeholders
- **December, 2017 – April, 2018**: Finalize and post for public comment June 22, 2018
Collaboration with Other Agencies, Stakeholders, International Organization, etc

In the US Government:

- **Within EPA** – Office of Research and Development, Office of Pesticide Programs, Office of Science Coordination and Policy (Endocrine Program)
- **EPA Grants** – NCER program/STAR grants on alternative methods
- **Interagency Coordinating Committee for Validation of Alternative Methods (ICCVAM):** Sixteen federal agencies
  
  – **DRAFT VISION:** To facilitate the development and use of new approaches for evaluating the safety of chemicals and medical products in the United States that will increase confidence in alternative methods and improve their relevance to human health, while maintaining a commitment to replace, reduce, and refine animal use.
- **Other** – NIH (including NTP, NICEATM, Tox21)
Collaboration with Other Agencies, Stakeholders, International Organization, etc

Outside of US Government:

- **Industry** – Regulated community, CROs,
- **NGOs** - “traditional”, think tanks, animal rights organizations
- **International** – EU, Canada, OECD, others
- **Academics**
- **The general public**
- **Professional organizations** – such as SOT!
Importance of Collaboration

With the amended TSCA requirement to develop and implement the use of alternative test methods in risk assessments, EPA is reaching out – and considering – all ideas/stakeholders as it builds this new paradigm...

THANK YOU!