The role of non-animal safety assessment methods in implementation of the new TSCA

Catherine Willett
Humane Society of the United States
Humane Society International

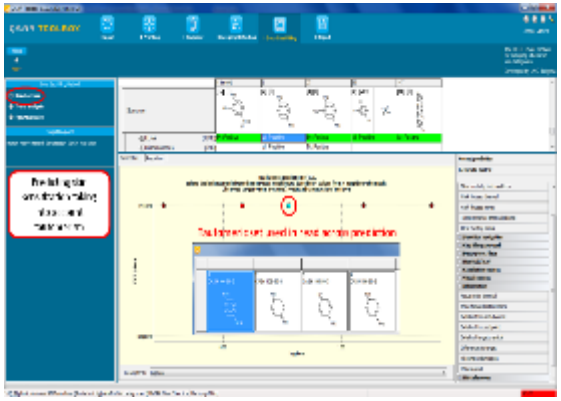
The Frank R. Lautenberg Chemical Safety for the 21st Century Act: Reduction of Testing on Vertebrates

Sec. 4(h):Reduction of Testing on Vertebrates:

"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 under this title***"

The Frank R. Lautenberg Chemical Safety for the 21st Century Act: Reduction of Testing on Vertebrates

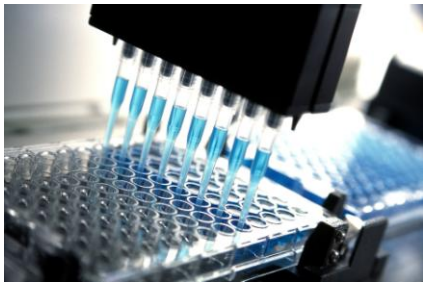
- " prior to making a request or adopting a requirement for testing using vertebrate animals… taking into consideration…"
  - reasonably available existing information
  - scientifically valid test methods and strategies not using vertebrate animals
  - chemical grouping
  - the formation of industry consortia

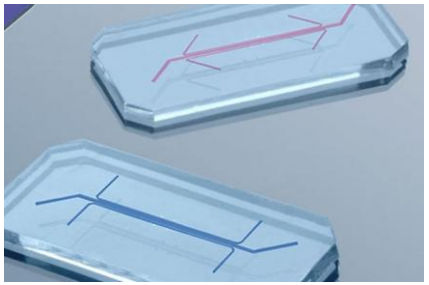


- Requirement to replace vertebrate testing applies to required and voluntary testing
  - "*Any person* developing information for submission under this title on a voluntary basis and not pursuant to any request or requirement by the Administrator shall first attempt to develop the information by means of an alternative test method or strategy"

Implementation of Alternative Methods

- "To promote the development and timely incorporation of new scientifically valid test methods and strategies that are not based on vertebrate animals" the EPA shall:
  - Create a strategic plan to promote the development and implementation of alternative test methods and strategies
    - Within two years of implementation (by June 22, 2018)
  - Prioritize the development and implementation of methods and approaches not using vertebrate animals





Other elements impacting animal testing

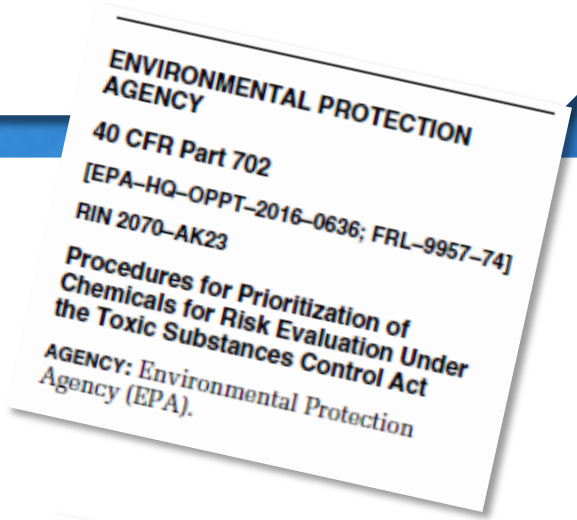
- Decisions are risk based
  - prioritization and evaluation are **risk**, not hazard, based for both new and for existing chemicals
  - data requirements should be related to exposure/use
- Prioritization of existing chemicals
  - EPA has one year to establish a risk-based screening process to determine whether existing chemicals are low or high priority
  - Intention is to prioritize based on **existing** information and **focus resources** (testing) on chemicals of highest priority
- Requirement for tiered screening and testing
  - When requesting any new information, the EPA must employ a tiered screening and testing process
  - Intention is **focus resources** on information necessary for regulation

Other impacting elements

- Tight timelines
  - EPA has one year to establish a risk-based screening process to determine whether existing chemicals are low or high priority
  - Prioritization process: 6 - 9 months
  - Risk evaluation determination: 3 yrs + 6 months possible extension
  - EPA has two years to develop the strategy for reducing and replacing vertebrate animal testing

EPA interpretation and proposals

- Draft rules issued Jan 17, comments due March 20, Final rules due June 22,2017
  - Requirement to reduce and replace vertebrate animal use is statutory and not subject to rule-making
  - Risk must encompass all known, intended and reasonably foreseen exposure scenarios (one assessment per chemical)
  - EPA will not initiate chemical prioritization until it has all of the information it expects to need for a full risk assessment


ENVIRONMENTAL PROTECTION AGENCY

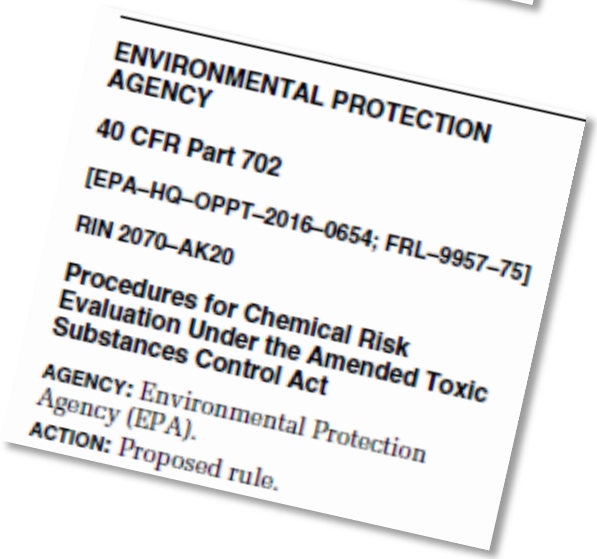
40 CFR Part 702

[EPA–HQ–OPPT–2016–0636; FRL–9957–74]

RIN 2070–AK23

Procedures for Prioritization of Chemicals for Risk Evaluation Under the Toxic Substances Control Act

AGENCY: Environmental Protection Agency (EPA).


ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 702

[EPA–HQ–OPPT–2016–0654; FRL–9957–75]

RIN 2070–AK20

Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act

AGENCY: Environmental Protection Agency (EPA).

ACTION: Proposed rule.

Prioritization draft rule

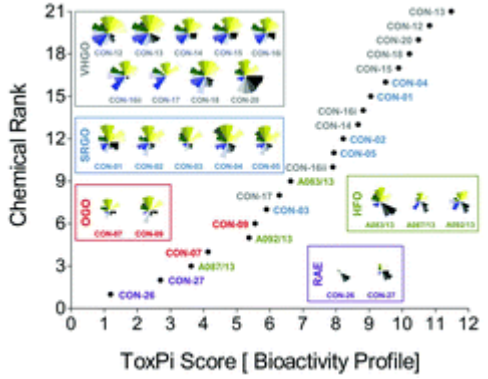
- EPA is proposing a four-step process for prioritization:
  - 1) *pre-prioritization – most data will be generated here*
  - 2) initiation (public comment) – clock starts ticking: 6 – 9 months
  - 3) proposed designation (public comment)
  - 4) final designation: moves directly to risk assessment
- High-Priority designation: "may present an unreasonable risk…because of a potential hazard and a potential route of exposure"
  - "a fairly low bar"
  - all chemicals lacking sufficient information will default to "high priority"
- Low-Priority designation requires sufficient information for all conditions of exposure
  - "a fairly high bar"

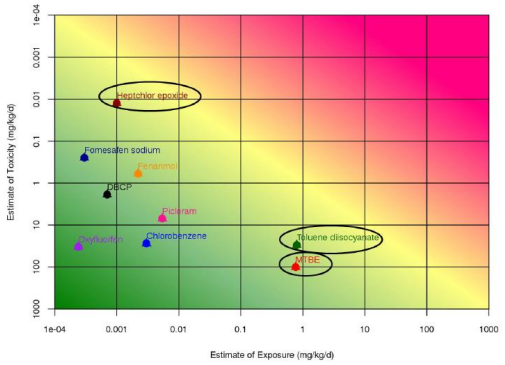
Prioritization draft rule: consequences

- Proposed new phase of pre-prioritization
  - By-passes legislated deadlines
  - Circumvents legislative intent to:
    - Rapidly identify chemicals that require immediate attention
    - Prioritize using largely existing information
    - Increase public confidence about large numbers of "untested" chemicals
  - Does not actually prioritize chemicals
    - Most chemicals likely will be designated high-priority
  - Hazard information will likely be gathered on most chemicals
    - Could result in REACH-like levels of testing (as a part of prioritization)
    - Does not focus resources on chemicals of most potential risk
  - Public (and regulated) communities left in the dark regarding the vast majority of chemicals

Prioritization draft rule: suggestions

- Pre-Prioritization could instead:
  - Initially focus on chemicals on existing lists of concern
  - Including EPA's own TSCA work plan
  - 90 chemicals in 2014 update
  - And of these, data rich chemicals should be prioritized for initiation
  - This approach would give EPA ample time to develop a comprehensive and transparent prioritization process



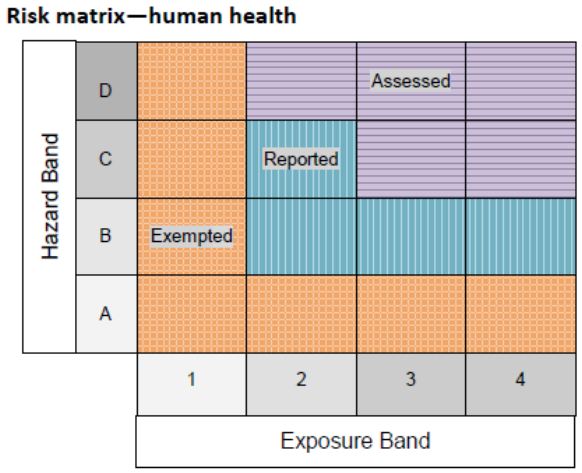


Comments from Humane Society of the United States and Gradient Corp on Proposed Rule: Procedures for Prioritization of Chemicals for Risk Evaluation Under the Toxic Substances Control Act, Docket ID EPA-HQ-OPPT-2016-0636

Prioritization draft rule: suggestions

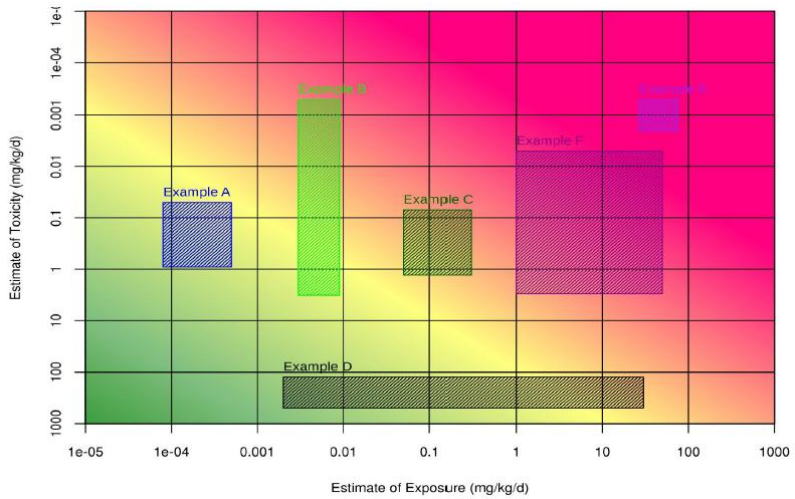
Adapting existing process:

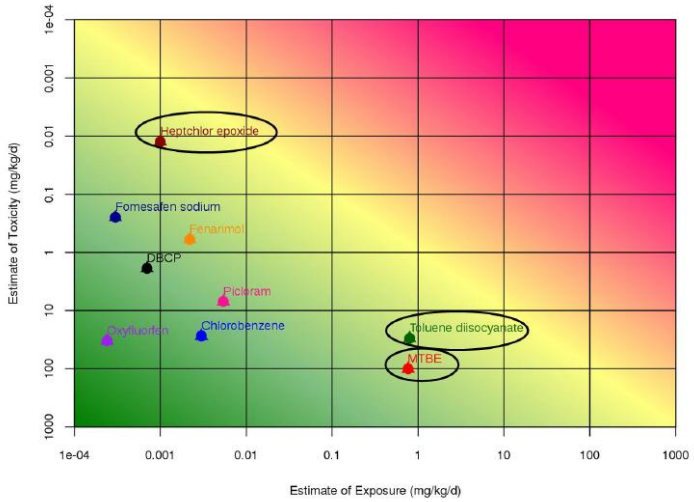
- Canada's Chemical Management Program (CMP)
- Australia's National Industrial Chemicals Notification and Assessment Scheme (NICNAS)
- ILSI/HESI's RISK21 matrix
- Pre-Prioritization process should require no or very little new information generation or new vertebrate animal testing



Prioritization draft rule: suggestions

- *RISK21 Decision Matrix*





- Matrix is decision context-dependent
- Map chemicals based on existing information/prediction
- Includes uncertainty estimate
- Readily identifies where additional information would reduce uncertainty
- Tiered data gathering focused on reducing uncertainty

www.risk21.org

International Life Sciences Institute/Health and Environmental Sciences Institute (ISLI/HESI) Risk21 project
Doe et al. Critical Reviews in Toxicology 2015.
Wolf et al. Critical Reviews in Toxicology 2014.

Prioritization draft rule: suggestions

- *This type of approach would:*
  - Allow transparent communication of relative risk of chemicals in the active TSCA inventory
  - Enhance public confidence that priority chemicals were being addressed first
  - Focus resources (and testing) on priority chemicals
  - Provide industry with an incentive to provide information (especially exposure) to reduce uncertainty

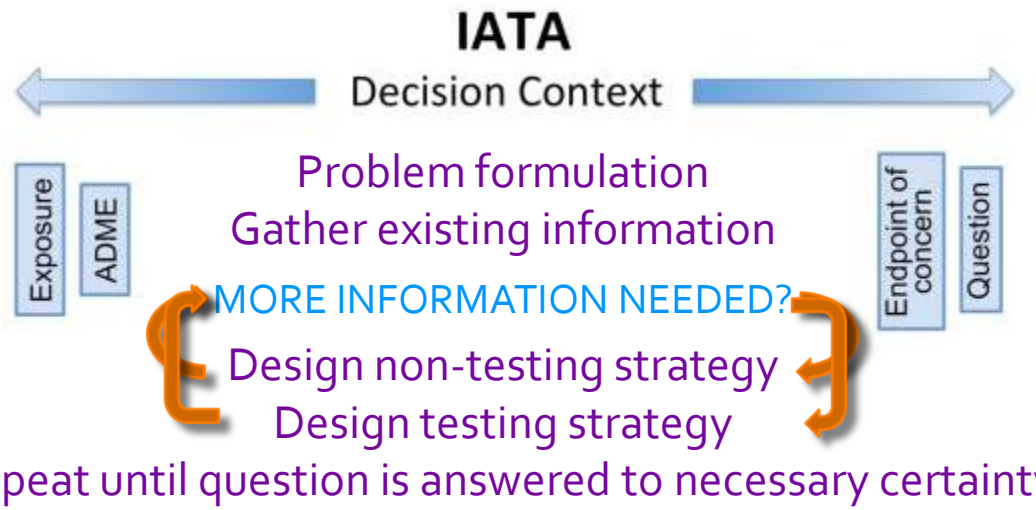
Risk evaluation draft rule

- Must determine whether a chemical presents "unreasonable risk" within 3 years with possible 6 mo. Extension
- Must have 20 assessments in process by 2019, and 20 ongoing thereafter: at least 50% from 2014 TSCA work plan
  - + 20 – 50% manufacturer-requested
- Risk evaluation
  - Scoping (6 mo. after start of RA)
    - affected populations
    - spectrum of known, expected and reasonably foreseen exposures (public comment)
  - Hazard assessment
    - Broad potential considerations
    - no description of how information requests relate to risk assessment (other than general "fit for purpose")
    - Includes dose-response information
  - Exposure assessment
  - Risk characterization

Risk evaluation draft rule

- Proposed process is similar to existing approaches to integrated testing and assessment, e.g. OECD IATA

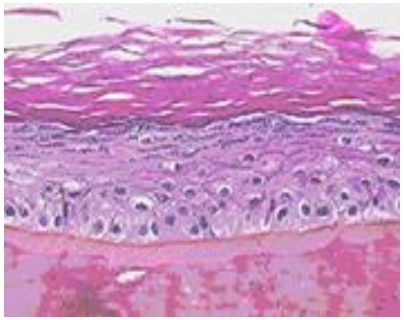
> *"a structured approach that strategically integrates and weights all relevant data to inform regulatory decisions regarding potential hazard and/or risk and/or the need for further targeted testing and therefore optimising and potentially reducing the number of tests that need to be conducted."*

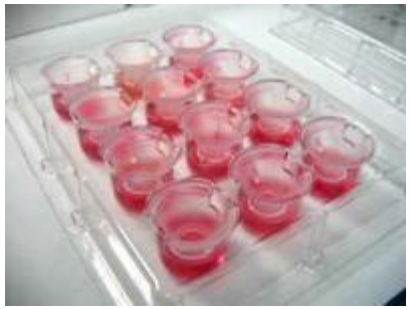


Report of the Workshop on a Framework for the Development and Use of IATA. 2015. OECD Series on Testing and Assessment No. 215

Avoiding vertebrate testing in risk evaluation

- Build on existing and developing approaches
  - Adoption of all available alternatives
    - Acute toxicity: reduction, waiving, bridging, cell-based
    - Skin and eye corrosion and irritation: complete replacements
    - Sensitization: nearing complete replacement
    - Collaborate with OPP and international efforts
    - OECD test guidelines, guidance documents, IATA strategies
  - Applies to industry supplied information as well as requests from EPA





Implications/Opportunities: summary

- Develop transparent prioritization process
  - Initial focus on existing priority chemicals
  - Adapt existing risk matrix to prioritize chemicals for initiation
- Adapt OECD IATA process in risk evaluation
- Immediate adoption of available alternative assessment methods
  - Build on OPPTS long practice of appropriate use of non-test methods
  - Adopt all available accepted alternatives
  - Coordinate with other offices on programs on development and acceptance of additional alternative methods

Thank you!

Catherine Willett, PhD
Director, Regulatory Testing
Risk Assessment and Alternatives
Humane Society of the United States
Humane Society International

Coordinator, Human Toxicology Project Consortium

kwillett@humanesociety.org

THE HUMANE SOCIETY OF THE UNITED STATES

HUMANE SOCIETY INTERNATIONAL
国际人道对待动物协会

HUMAN TOXICOLOGY PROJECT CONSORTIUM