



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

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## Outline

- + Overview of changes made by the Frank R. Lautenberg Chemical Safety for the 21st Century Act that impact animal testing
- + Describe EPA's implementation process for prioritization, risk assessment and reduction guidance
- + Present potential solutions for maximizing reduction of animal testing

# The Frank R. Lautenberg Chemical Safety for the 21st Century Act:

- + First update to the Toxic Substances Control Act in 40 years
  - + Requires pre-market assessment to determine whether the chemical or significant new use
    - “presents an unreasonable risk”;
    - “information...is insufficient to permit a reasoned evaluation...”;
    - “may present an unreasonable risk; or
    - is “not likely to present an unreasonable risk”
  - + Gives EPA increased authority to ask for information about existing chemicals
    - “resets” current inventory of 86,000 chemicals into “active” and “inactive”
    - Requires EPA to prioritize chemicals for assessment
- Will likely lead to a significant amount of new testing

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

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

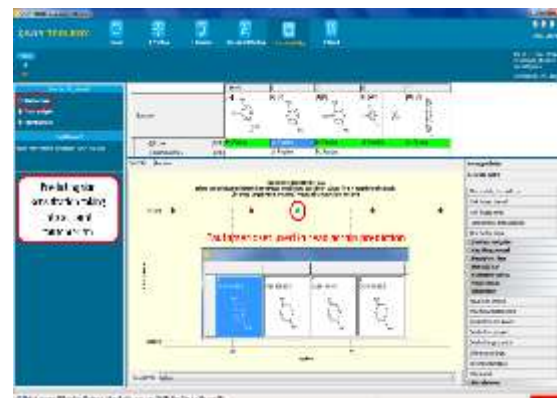
“IN GENERAL —The ***Administrator shall reduce and replace***, to the extent practicable, scientifically justified, and consistent with the policies of this title, ***the use of vertebrate animals in the testing of chemical substances or mixtures under this title***”



# 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

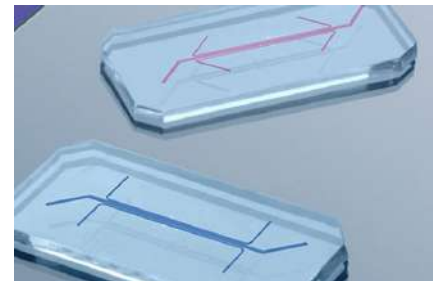


+ Requirement to replace vertebrate testing applies to required and voluntary testing

- “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 of existing chemicals
  - Intention is to prioritize based on **available** information and **focus resources** (testing) on chemicals of highest priority
- + "Data" has been replaced with "information"
  - to create flexibility
- + 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

→ Timelines impact the amount and duration of testing that can be done



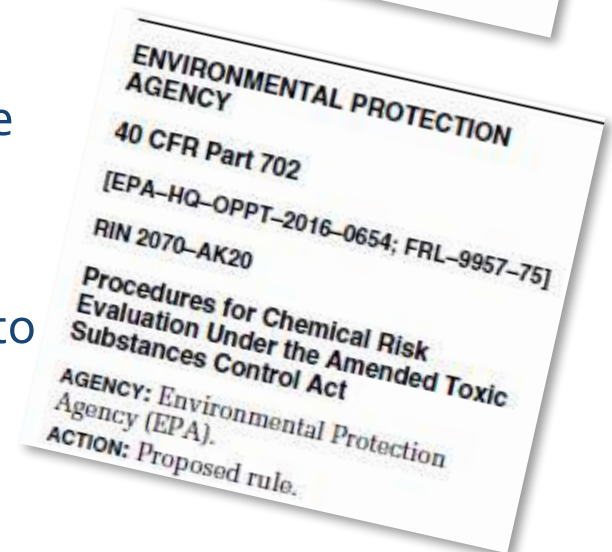
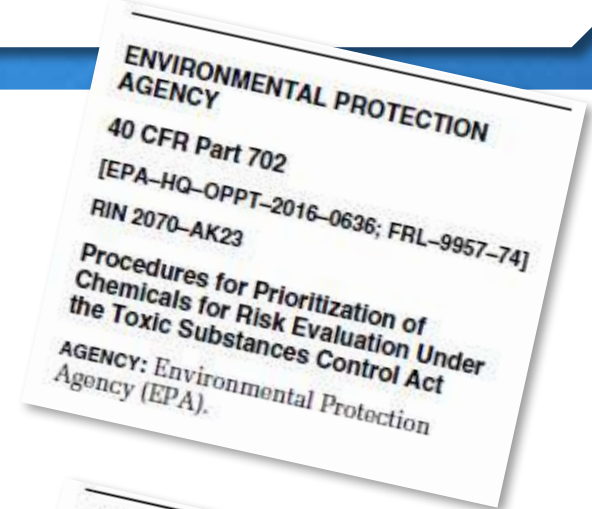


# Implementation Process

- + Framework Rules:
  - Prioritization Rule
  - Risk Evaluation Rule
  - Active/Inactive Inventory Reporting Rule
  - Were finalized 1 year after enactment (June 22, 2017)
- + Development of the strategic plan for replacement
  - By June 22, 2018

# Draft prioritization and risk evaluation rules

- + Issued Jan 17, comments were due March 20
  - Requirement to reduce and replace vertebrate animal use is statutory and not subject to rule-making
  - Evaluations will 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*



# Prioritization draft rule

- + EPA proposed a four-step process for prioritization:
  - 1) *pre-prioritization – 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 pre-prioritization phase
  - By-passed legislated deadlines
  - Circumvented legislative intent to:
    - Rapidly identify chemicals that require immediate attention

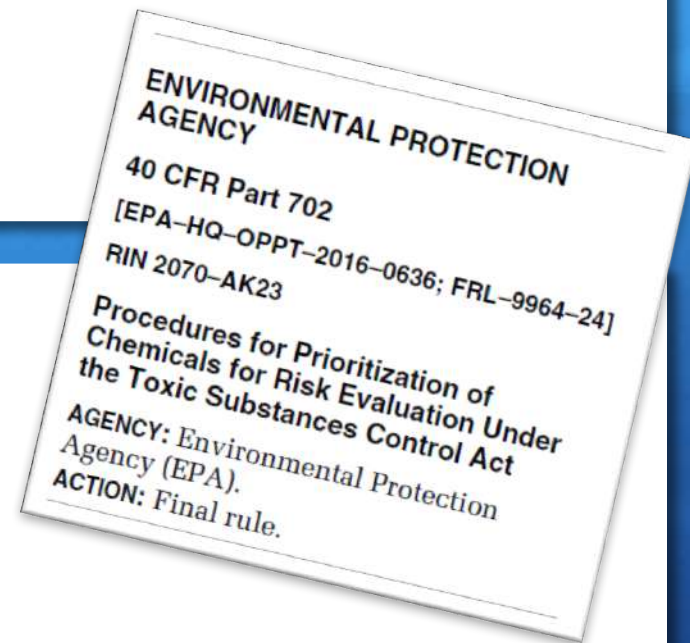
Comments from Humane Society of the United States and Gradient Corp on Proposed Rule: Procedures for Prioritization of Chemicals for Risk Evaluation Under the Toxic Substances Control Act, Docket ID **EPA-HQ-OPPT-2016-0636**

- 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

# Final prioritization rule

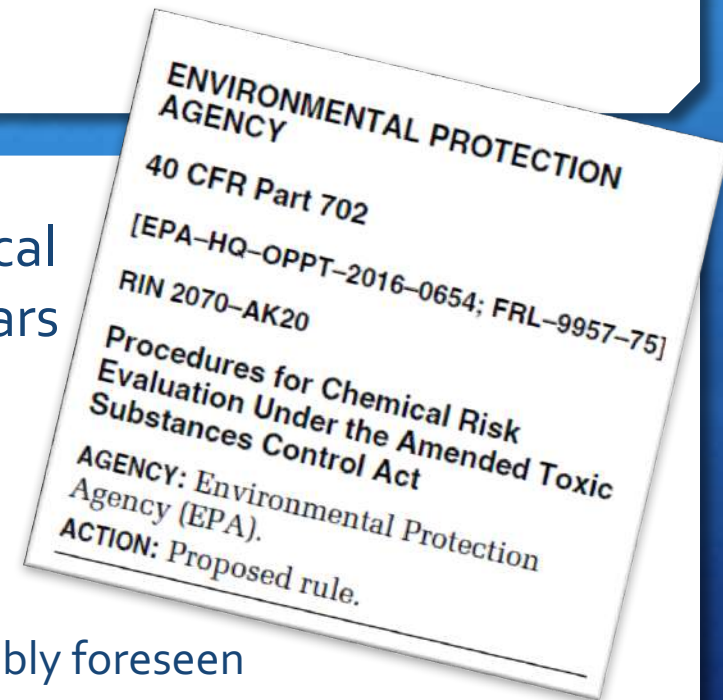
+ Issued June 22, 2017

- EPA will not initiate chemical prioritization until it has all of the information it expects to carryout ***prioritization, avoiding "excessive" data gathering before priority designation.***
- Clarified that "reasonably available information" includes new testing, as long as it can be done in a relatively short time-frame (removed the word "existing"), but within the time constraints
- Chemicals lacking information will still default to high priority but that language, and mention of high and low bars has been removed.
- ***Description of pre-prioritization has been deferred and will likely be a separate rulemaking process.***



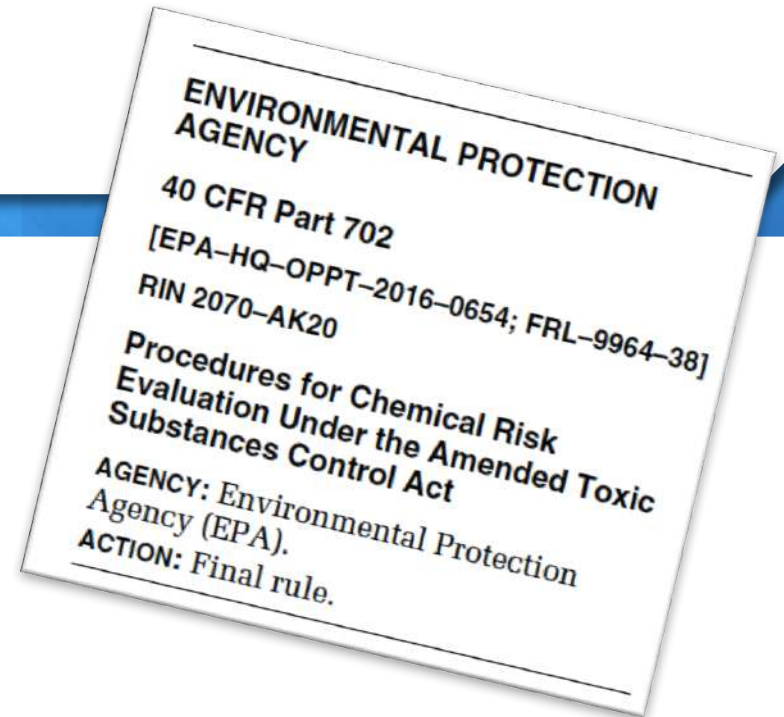
# Risk evaluation draft rule

- + LSCA: must determine whether a chemical presents “unreasonable risk” within 3 years with possible 6 month extension
- + 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      Using largely existing guidance



# Risk evaluation final rule

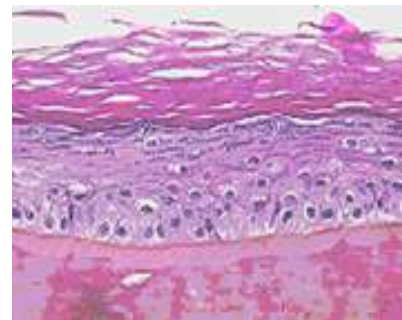
- + EPA has discretion to determine covered circumstances of use and may exclude some uses
- + “Reasonably available” information includes short-term, but not longer-term testing
- + Clarifies definitions of “best available science,” “weight of the scientific evidence,” “systematic review” and other elements
- + But not “sufficiency of information” or “unreasonable risk”
- + Description of “fit-for-purpose” evaluations





# Strategic Plan: to promote development and implementation of alternative test methods and strategies

- + Draft outline presented to OECD in June
- + Goal Statement (directly from legislation):  
“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...**”
- + Organized following the legislation
- + Will have near-, mid- and long-term goals for each type of methodology or strategy
- + Strong emphasis on collaboration: intra-EPA, inter-agency, international, with stakeholders





# Strategic Plan



From G. Scarano, SOT webinar, June 2017

# Pre-prioritization: suggestions

## Adapt existing processes:

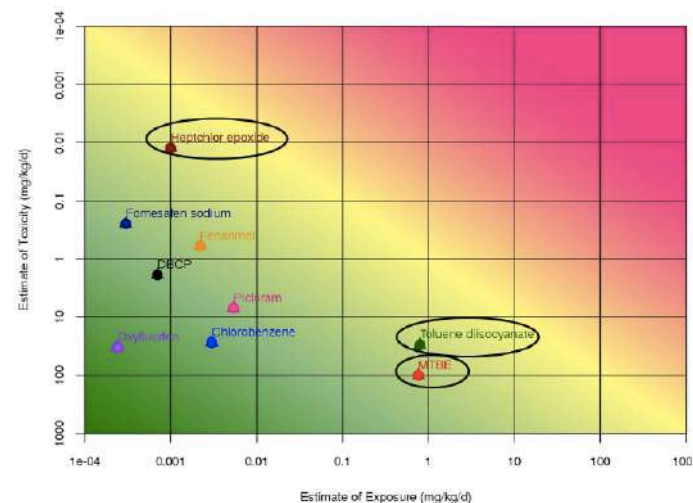
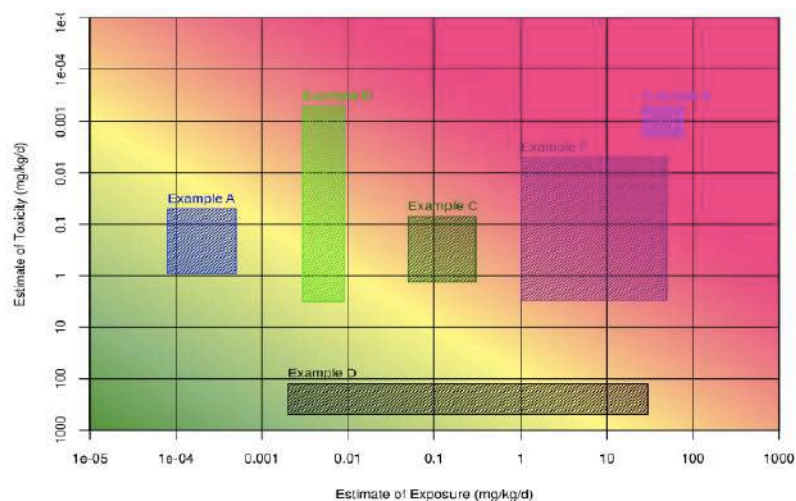
- + Canada's Chemical Management Program (CMP)
- + Australia's National Industrial Chemicals Notification and Assessment Scheme (NICNAS)
- + ILSI/HESI's RISK<sub>21</sub> matrix
- + Pre-Prioritization process should require no or very little new information generation or new vertebrate animal testing

Risk matrix—human health

Hazard Band	D			Assessed	
	C		Reported		
	B	Exempted			
	A				
		1	2	3	4
		Exposure Band			

# Pre-prioritization: suggestions

## + RISK<sub>21</sub> 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](http://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.

# Pre-prioritization: suggestions

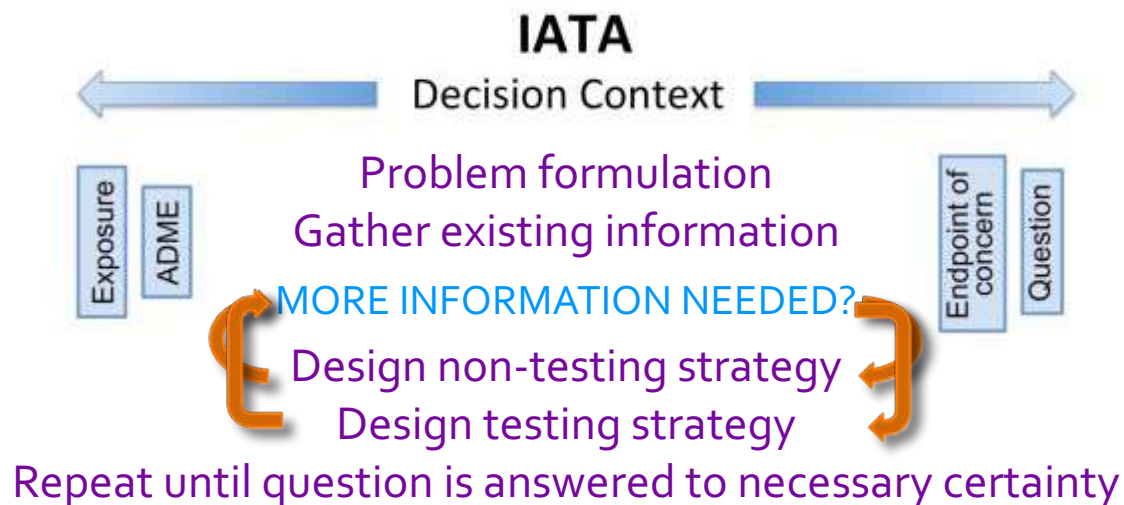
## + *This type of approach would:*

- 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 suggestions

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

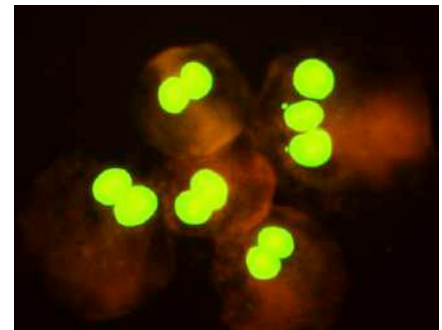
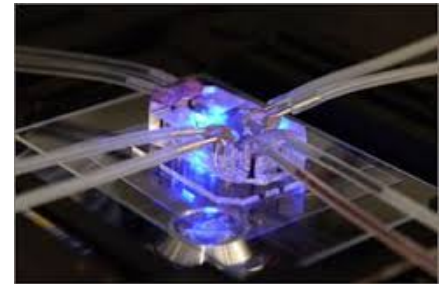
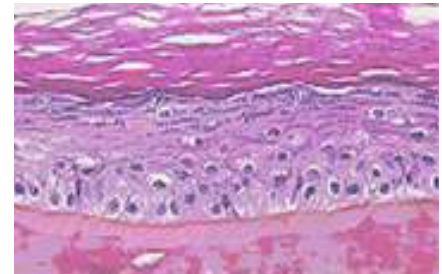
*"a structured approach that strategically integrates and weights all relevant data to inform regulatory decisions regarding potential hazard and/or risk and/or the need for further targeted testing and therefore optimising and potentially reducing the number of tests that need to be conducted."*



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, e.g.
    - 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
  - Adopt OECD test guidelines, guidance documents, IATA strategies



# Implications/Opportunities: summary

- + Develop transparent, efficient pre-prioritization process
  - 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

# Summary

- + New authority *will* increase testing
- + Language to reduce testing on vertebrates will mitigate this increase and provide incentive for developing new replacement methods
- + Opportunity for streamlined, efficient pre-prioritization process
- + Prioritization will use “reasonably available information” including short-term testing; deadlines limit amount and duration
- + Risk evaluation process sounds a lot like OECD IATA process in risk evaluation – will be “fit-for-purpose,” iterative, and tailor testing to information needed to make a decision
- + Strategic Plan: to promote alternative test methods and strategies provides an opportunity to accelerate development and implementation of alternative methods



# Thank you!

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