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

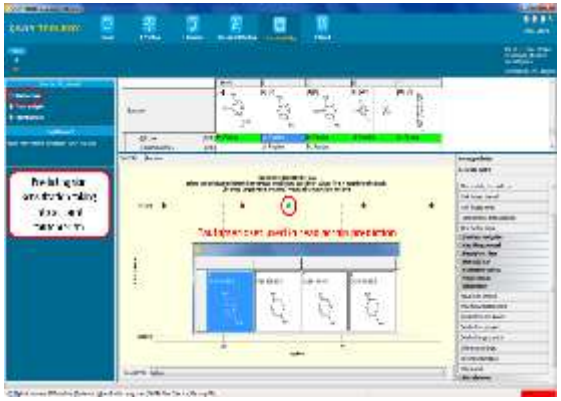
The Frank R. Lautenberg Chemical Safety for the 21st Century Act: Reduction of Testing on Vertebrates

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

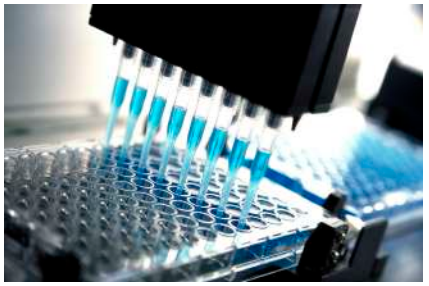
- " prior to making a request or adopting a requirement for testing using vertebrate animals… taking into consideration…"
  - reasonably available ***existing*** information
  - scientifically valid test methods and strategies not using vertebrate animals
  - chemical grouping
  - the formation of industry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

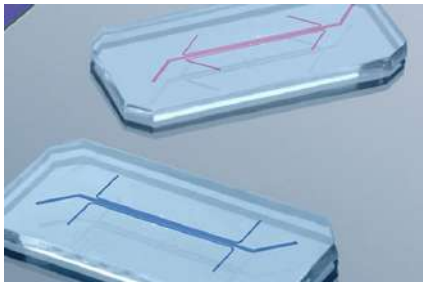


- Requirement to replace vertebrate testing applies to required and voluntary testing
  - "*Any person* developing information for submission under this title on a voluntary basis and not pursuant to any request or requirement by the Administrator shall first attempt to develop the information by means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


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 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"

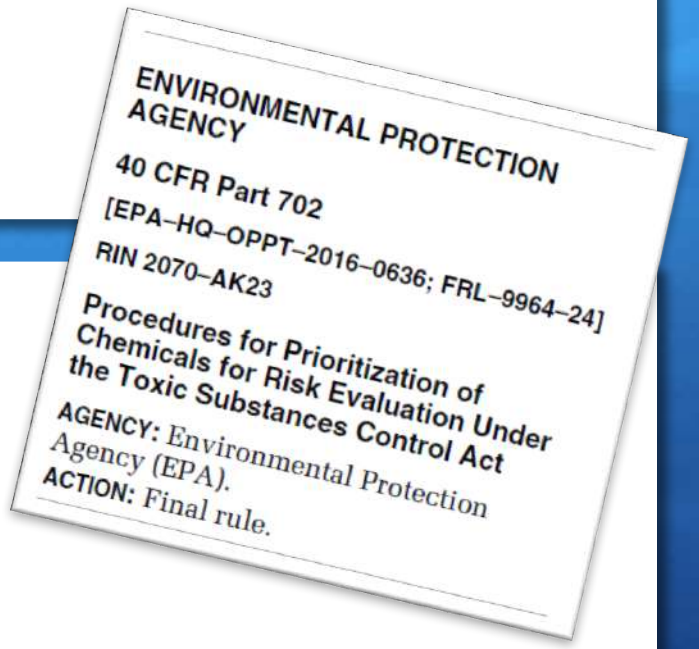
Prioritization draft rule: consequences

- 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


ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 702

[EPA–HQ–OPPT–2016–0636; FRL–9964–24]

RIN 2070–AK23

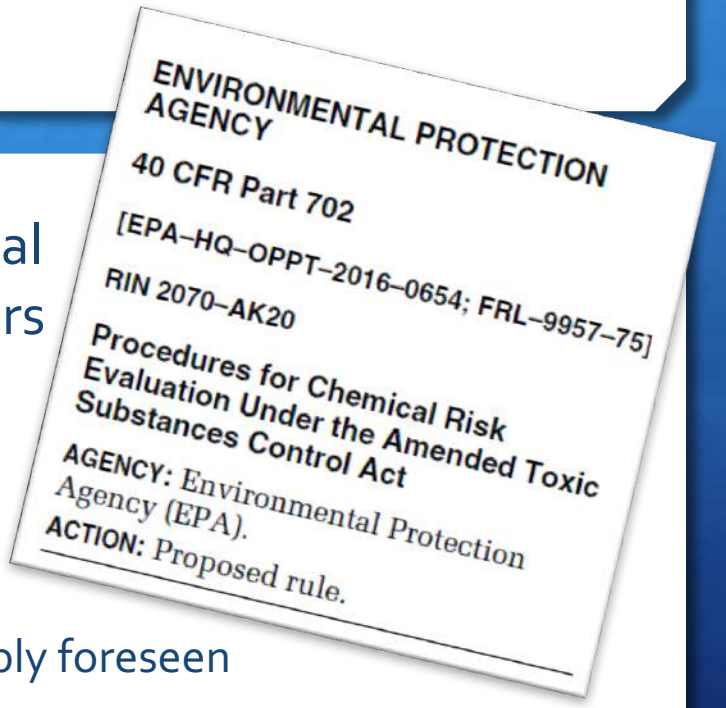
Procedures for Prioritization of Chemicals for Risk Evaluation Under the Toxic Substances Control Act

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final 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


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

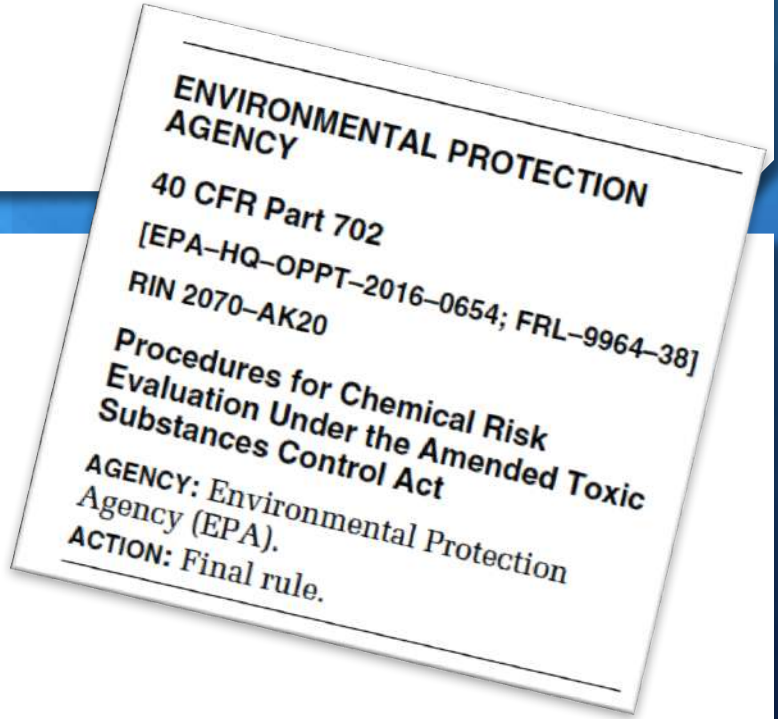
AGENCY: Environmental Protection Agency (EPA).

ACTION: Proposed rule.

- 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


ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 702

[EPA–HQ–OPPT–2016–0654; FRL–9964–38]

RIN 2070–AK20

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

AGENCY: Environmental Protection Agency (EPA).

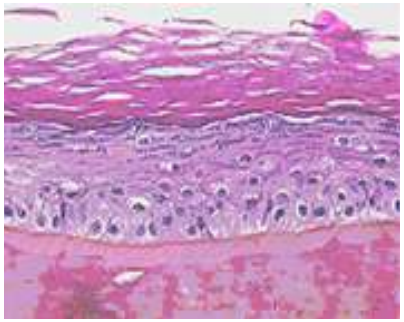
ACTION: Final rule.

- 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



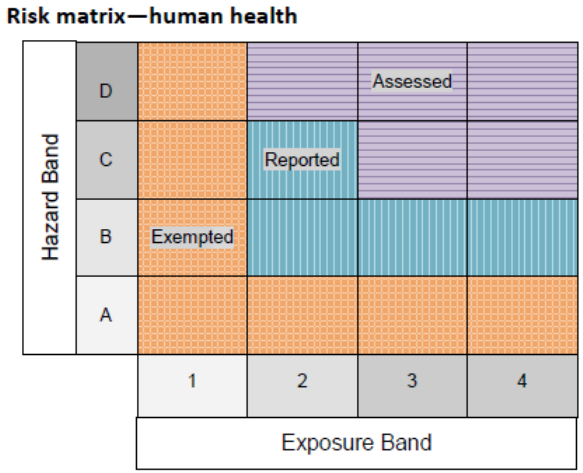
Strategic Plan

From G. Scarano, SOT webinar, June 2017

Pre-prioritization: suggestions

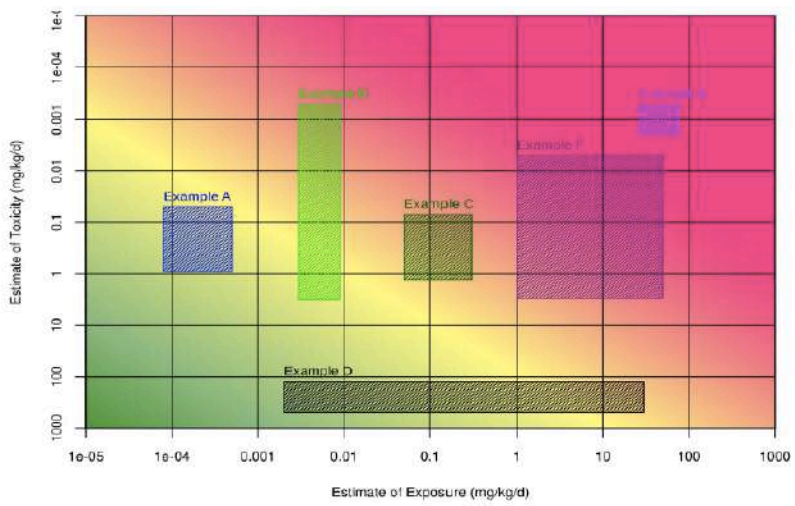
Adapt existing processes:

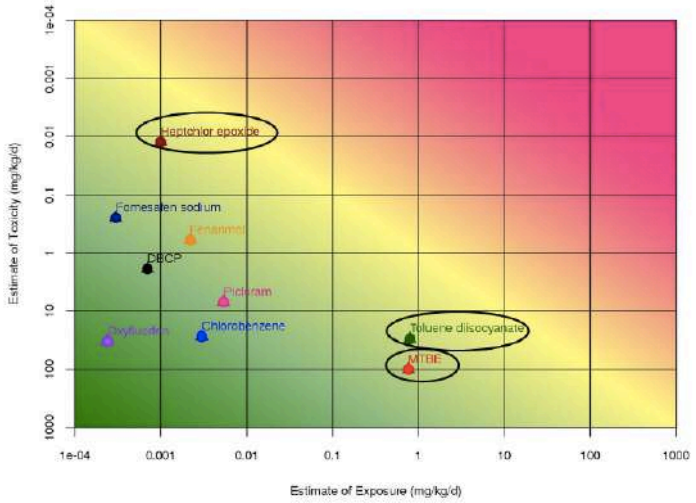
- Canada's Chemical Management Program (CMP)
- Australia's National Industrial Chemicals Notification and Assessment Scheme (NICNAS)
- ILSI/HESI's RISK21 matrix
- Pre-Prioritization process should require no or very little new information generation or new vertebrate animal testing



Pre-prioritization: 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.

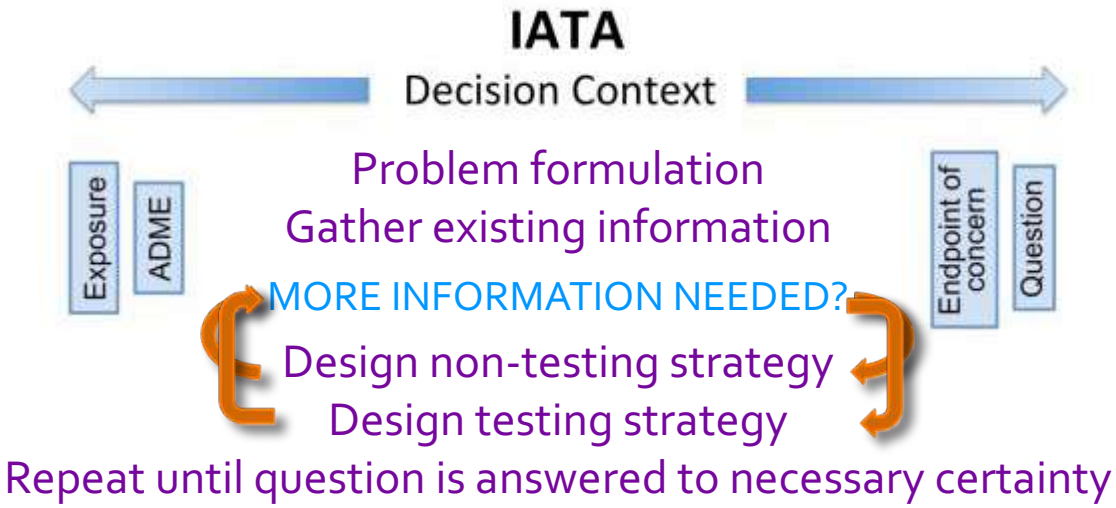
Pre-prioritization: suggestions

- *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

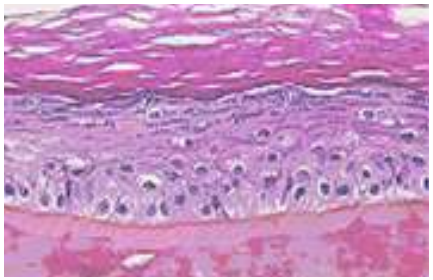
> *"a structured approach that strategically integrates and weights all relevant data to inform regulatory decisions regarding potential hazard and/or risk and/or the need for further targeted testing and therefore optimising and potentially reducing the number of tests that need to be conducted."*

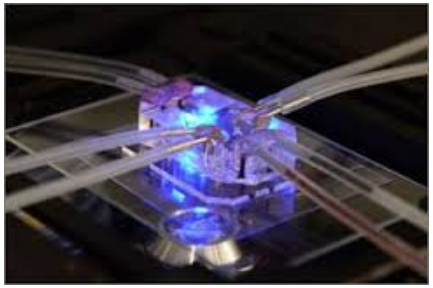


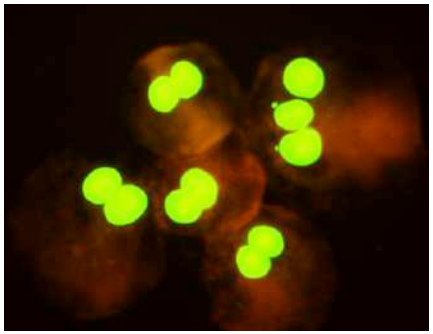
Report of the Workshop on a Framework for the Development and Use of IATA. 2015. OECD Series on Testing and Assessment No. 215

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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