Communicating Progress in Advancing Alternative Methods for Regulatory Use at the FDA

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FDA’s Mission

Protect and advance public health by:

- Ensuring the safety of our food supply, cosmetics, and products that emit radiation
- Fostering development of medical products to respond to deliberate and naturally emerging public health threats
- Ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices
- Regulating the manufacturing, marketing, and distribution of tobacco products

Key Point: FDA’s mission is diverse, carried out by multiple Centers under different statutory authority and regulations
Fulfilling FDA’s Mission

FDA reviews data submitted by product developers or obtained in other ways to establish
Under what conditions (e.g., dose, population, patient monitoring) a new medical product can be safely administered to patients (human or animal)
Whether some new medical product carries an increased risk for developmental and reproductive toxicity or an increased cancer risk
Whether a new ingredient for food is safe for consumption
The potential risks associated with tobacco products including electronic nicotine delivery systems (ENDS)

This includes evaluating endpoints that cannot be collected or ethically obtained in humans
For example:
- Histopathological evaluations
- Effects on embryofetal development
- Carcinogenic potential

Animal studies have played a critical role to meet these needs and bring safe and effective products to the market

FDA has a long-standing commitment to replace, reduce and refine (“3Rs”) animal testing
FDA has a long-standing commitment to replace, reduce and refine ("3Rs") animal testing – an incomplete timeline.

Start of ICH guidances related to nonclinical


53 FR 39650
LD<sub>50</sub> test is not an FDA required procedure

ICH

NIH – FDA Joint Leadership Council
Advancing Regulatory Science Program
Heart-Lung Micromachine

NCATS Tissue Chip Program

OECD BCOP
How can FDA demonstrate contribution to 3Rs and implementation of alternative methods?

• Collate and provide a list of FDA research, policy, guidance and qualified methods related to 3Rs and alternative methods
• Communicate how these efforts impact 3Rs and alternative methods
• Provide and track training in these efforts
Collate FDA research, policy and guidance related to 3Rs and alternative methods and Communicate.
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FDA’s Predictive Toxicology Roadmap
2018 Annual Report
Prepared by the Food and Drug Administration’s Toxicology Working Group

Workshop:
Implementing FDA’s Predictive Toxicology Roadmap: An Update of FDA Activities
September 18, 2019
Collect FDA research, policy and guidance related to 3Rs and alternative methods and Communicate

Advancing Alternative Methods at FDA

Read about the activities FDA scientists are undertaking to spur the development of new regulatory approaches that can help improve predictivity—and potentially replace, reduce and/or refine animal testing.
Advancing Alternative Methods at FDA

**Website content**

- FDA’s Alternative Method Working Group
- FDA Webinar Series on Alternative Methods
- FDA Definitions – Microphysiological Systems, Organ-on-a-chip
- Publications, Presentations, Guidances
  - Publications Co-authored by FDA on Alternative Methods
  - Presentations by FDA Scientists on Alternative Methods
  - Guidances List: Alternative Methods
- Resources for You
## Seminars Sponsored by the Alternative Methods Working Group

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List of qualified tools includes “Nonclinical Assessment Models”
**FDA Tool Development Programs**

**Drug Development Tool (DDT) Qualification Programs**

**Spotlight Events & Announcements**

To locate a project or a qualified biomarker, go to [CDER & CBER’s DDT Qualification Project Search database](#).

**DDT Funding Announcement**

***DDT Grant cycle is now closed for FY2021. The next submission deadline is May 17, 2022***

**Regulated Product(s)**

- Drugs
- Drug Development Tools

**Topic(s)**

- Research
- Drug Development Tools
- Law(s) & Regulation(s)
- 21st Century Cures Act of 2016

**Guidance**

- [Qualification Process for Drug Development Tools – Guidance for Industry and FDA Staff](#)

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**Innovative Science and Technology Approaches for New Drugs (ISTAND) Pilot Program**
A transparent process – so all stakeholders are aware of tools in development, stage, and FDA determinations/recommendations
FDA Drug Development Tool Program – A Transparent Process

Similar list would be created of those methods qualified through ISTAND
Future FDA efforts to implement alternative methods and communicate those efforts
The FY2023 President’s Budget proposes new funding to implement a cross-agency New Alternative Methods Program to:

- Spur the adoption of new alternative methods for regulatory use that can replace, reduce and refine animal testing and improve predictivity of nonclinical testing to:
  - Streamline development of FDA-regulated products
  - Bring products to US public and patients more rapidly and more efficiently
  - Ensure products are safe, effective, and that patients can depend on them
FDA’s Proposed New Alternative Methods Program

• Centrally coordinated through FDA’s Office of the Chief Scientist with FDA Centers implementing Agency-wide programmatic objectives

• If this initiative is funded, FDA hopes to
  – Expand processes to qualify alternative methods for regulatory use
  – Provide guidance to external stakeholders developing alternative methods
  – Fill information gaps with applied research to advance new policy and guidance development

• Collaborations with external stakeholders are vital
  – Federal partners, public-private partnerships, international regulators
What are Potential Guidances to Stakeholders Developing Alternative Methods?

- Guidance on qualification process
- Topical guidance on specific safety or development areas
- Guidances on assessing credibility of specific types of alternative methods or what to include in regulatory submissions – examples:

  - Role for microphysiological systems-related general considerations guidance?

Guidance on qualification process 
Topical guidance on specific safety or development areas 
Guidances on assessing credibility of specific types of alternative methods or what to include in regulatory submissions – examples:

Guidance Document: Assessing the Credibility of Computational Modeling and Simulation in Medical Device Submissions
Draft Guidance for Industry and Food and Drug Administration Staff
December 2021

Guidance Document: Physiologically Based Pharmacokinetic Analyses – Format and Content Guidance for Industry
September 2018

Role for microphysiological systems-related general considerations guidance?
Future communication efforts

Improve Advancing Alternative Methods at FDA website

- make more user-friendly
- add interpretative language to explain significance of some publications
- add information about collaborations with external groups
- provide additional links to resources for the regulated industry (e.g., to tool qualification programs)

Write more publications specifically related to alternatives