Presentation Abstracts and Background Materials

SCIENTIFIC ADVISORY COMMITTEE ON ALTERNATIVE TOXICOLOGICAL METHODS

Session I: Updates, Roadmaps, and Collaboration
Thursday, September 11, 2025

Session IA: Updates

NICEATM and ICCVAM

Presenter: Dr. Warren Casey, ICCVAM; National Institute of Environmental Health Sciences (NIEHS) Division of Translational Toxicology (DTT)

This talk will share information about recent and upcoming events and activities of the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) and ICCVAM.

Background

- NICEATM Website
- Webpage: About ICCVAM
- Webpage: ICCVAM Public Forum: July 2025 (Slides and video from the Public Forum will be available on this page. An announcement will be sent via NICEATM News when they are posted.)
- Webpage: NICEATM & ICCVAM Publications and Presentations

NIH Prioritization of Human-based Research Technologies

Presenter: Dr. Warren Casey, ICCVAM; NIEHS DTT

The National Institutes of Health (NIH) is launching a new initiative to advance innovative, human-based science while reducing the use of animals in research. Developing and applying cutting-edge, non-animal research models aligns with the U.S. Food and Drug Administration's (FDA's) recent initiative to reduce animal testing. This talk will provide an overview of some of the ongoing and planned efforts to develop, validate, and scale the use of non-animal approaches across the agency's biomedical research portfolio, and to serve as a hub for interagency coordination and regulatory translation to protect public health.

Background

- NIH News Release: NIH to prioritize human-based research technologies (April 29, 2025)
- A Strategic Roadmap for Establishing New Approaches to Evaluate the Safety of Chemicals and Medical Products in the United States

Session IB: Roadmaps and Collaboration

FDA Roadmap Implementation to Reducing Animal Testing in Preclinical Safety Studies

Presenter: Dr. Tracy Beth Høeg, FDA

The FDA's 2025 "Roadmap to Reducing Animal Testing in Preclinical Safety Studies" released April 10th outlined a strategic shift toward replacing animal-based studies with scientifically validated new approach methodologies (NAMs),

such as organ-on-a-chip systems, computational models, organoids, and advanced in vitro assays. The initiative aims to reduce and hopefully eventually eliminate animal testing in drug development with more accurate and predictive human-centric technologies. Currently over 90% of drugs that advance to Phase 1 clinical trials do not end up being approved for use in humans. Industry has increasingly relied on NAMs data to predict toxicity and efficacy in lieu of animal models. Since the publication of the roadmap, the FDA has continued to publicly signal its interest in sponsors submitting applications with new approach methodologies data used to reduced or replaced animal testing. This was made clear to the public at a live-streamed workshop on July 7th, which the FDA co-hosted with NIH. The FDA will partner with NIH to revise guidances, provide education and support to reviewers, increase data sharing, and track progress on NAMs acceptance and reductions in animal testing using artificial intelligence (AI). This effort aligns with the FDA Modernization Act 2.0, which clarified animal testing is not required for Investigational New Drugs (INDs) and biosimilars, and is supported by new legislative proposals and NIH initiatives such as the Office of Research Innovation, Validation, and Application. Ultimately, the roadmap seeks to usher in a new era of faster, more cost effective, more accurate and more ethical drug development which moves away from reliance on animal testing.

Background

- FDA's Roadmap to Reducing Animal Testing in Preclinical Safety Studies
- FDA News Release: FDA Announces Plan to Phase Out Animal Testing Requirement for Monoclonal Antibodies and Other Drugs (April 10, 2025)
- FDA-NIH Workshop: Reducing Animal Testing (July 7, 2025)

FDA's ISTAND (Innovative Science and Technology Approaches for New Drugs) Program

Presenter: Dr. Vanitha Sekar, FDA

Launched in November 2020, ISTAND provided a dedicated pilot qualification pathway outside of existing drug development tools (DDTs) programs to enable innovative DDTs, such as microphysiological systems (e.g., tissue chips), novel nonclinical pharmacology/toxicology assays, AI-based algorithms, and digital health technologies like wearables and digital endpoints. As of 2025, ISTAND has transitioned from a pilot program to a permanent DDT Qualification Program, continuing to support innovative, science-driven approaches that improve drug development and regulatory decision-making. It follows a three-step submission process—Letter of Intent, Qualification Plan, and Full Qualification Package, with transparency provisions under the 21st Century Cures Act requiring public disclosure of accepted submissions and their status (Innovative Science and Technology Approaches for New Drugs (ISTAND) Program | FDA). Since its inception, ISTAND has accepted eight submissions: three AI-based tools, two tools that assess preclinical safety without using animals, two novel methods involving tissues, and one novel statistical approach. Once a tool is qualified, it becomes available for use in regulatory submissions (e.g., INDs, New Drug Applications, Biologic License Applications) within its defined context of use, without requiring tool re-evaluation. ISTAND's activities complement other FDA initiatives to expedite drug development, including efforts to reduce, replace, and refine the use of animal testing.

Background

- ISTAND Program Website

Engaging NAMs for Toxicant REgulation and Effects (ENTRÉE): A Draft Pilot Program for US FDA Human Foods Program (HFP) - How to Qualify a New Approach Method (NAM) for Food Safety Use

Presenter: Dr. Steven Hermansky, FDA

For HFP to reach sound regulatory decisions regarding the safety of chemicals found in foods, and to maintain the public's trust, it must have: 1) high quality data; 2) a thorough, unbiased, and transparent scientific review process; and 3) confidence in the tools and methods relied upon to assess the safety of those chemicals based on the level of consumer dietary exposure. Formal approaches to validation involve lengthy and expensive processes that may not be necessary for all uses of a particular NAM. As an alternative to validation, the process HFP will use to evaluate NAMs for regulatory use is called "qualification." Qualification involves establishing the scientific rigor by which a NAM must be judged, based on its intended Context of Use, which is the manner and purpose of a particular application of a NAM (e.g., when and how it will be used). Once a NAM is qualified by HFP for a specific Context of Use, it can be used by industry and other stakeholders for the qualified purpose, and HFP can be confident in its utility without the need to re-review the data supporting the suitability of the NAM for toxicological assessment within that context.

To facilitate the development and qualification of NAMs for assessing the toxicity of chemicals and contaminants in the U.S. food supply, HFP is piloting a program called **ENTRÉE** (Engaging NAMs for Toxicant Regulation and Effects). HFP invites potential sponsors of new methods who wish to have their NAM qualified via ENTRÉE to have initial discussions with us. If recommended for submission to the program, HFP will request a Letter of Intent to initiate the ENTRÉE process. The letter of intent should include a discussion of the following: (1) the Context of Use, (2) Biological Relevance, (3) Technical Characterization, (4) plans for Data Integrity and information Transparency, (5) a Qualification Plan and (6) any plans for an Independent Review. HFP is committed to realizing the goals of developing more predictive human relevant models while allowing us to reduce, refine, and replace the use of animal testing for assessing the safety of chemicals found in foods. The ENTRÉE pilot program provides a roadmap to qualify NAMs by delineating the initial data and information needed to develop performance standards by which HFP can evaluate new methods for use in assessing the safety of chemicals found in foods.

Requests for informal discussions, submissions of Letters of Intent, and questions about this pilot program should be sent to HFPNAMS@fda.hhs.gov.

Background

- None.

ICCVAM Roadmap and Increased Opportunities

Presenter: Dr. Helena Hoegberg-Durdock, NICEATM, DTT, NIEHS

ICCVAM's "A Strategic Roadmap for Establishing New Approaches to Evaluate the Safety of Chemicals and Medical Products in the United States" provides a framework for better communication between stakeholders, emphasizing flexibility in establishing confidence and promotes adoption and implementation. The roadmap consists of three strategic goals: 1) connect end users with developers of NAMs, 2) foster the use of efficient, flexible, and robust practices to establish confidence in new methods, and 3) encourage the adoption and use of new methods and approaches by federal agencies and regulated industries.

Here are some examples of ICCVAM's and NICEATM's recent efforts to address these. The Method Developers Forums were established to provide an opportunity for NAMs developers to present their methods and regulatory issues with

relevant stakeholders. The update of the Validation, Qualification, and Regulatory Acceptance of New Approach Methodologies describes a more flexible approach to NAMs validation that reflects modern toxicity testing and integrating results from multiple approaches. To encourage the adoption of NAMs, NICEATM has developed defined approaches, integrated approaches to testing and assessment, and computational tools that simplify the analysis and interpretation of NAMs data in addition to supporting Organisation for Economic Co-operation and Development programs.

NICEATM and ICCVAM have over the years made major progress in replacing the “six-pack” of acute toxicity tests that were discussed by SACATM in 2023. In concordance with SACATM’s recommendations, we have since incorporated more complex endpoint, such as developmental neurotoxicity and carcinogenicity. In 2025, several agencies announced an expansion in innovative, human-based science while reducing animal use in research and risk assessment. This exciting progress increases NICEATM’s and ICCVAM’s opportunities to strengthen collaborations, fostering new partnerships, and broadening our role.

Background

- NIH News Release: NIH to prioritize human-based research technologies (April 29, 2025)
- NIH Extramural News: How Does the NIH Initiative to Prioritize Human-Based Research Affect Research Proposing the Use of Laboratory Animals? (July 18, 2025)
- A Strategic Roadmap for Establishing New Approaches to Evaluate the Safety of Chemicals and Medical Products in the United States
- FDA News Release: FDA Announces Plan to Phase Out Animal Testing Requirement for Monoclonal Antibodies and Other Drugs (April 10, 2025)