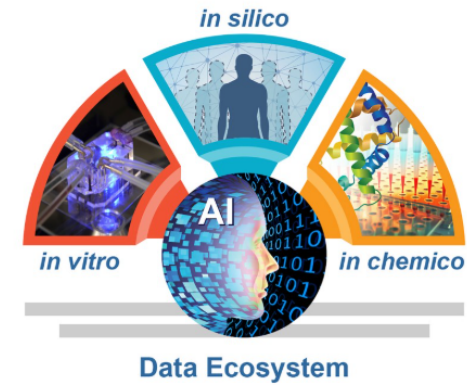




**U.S. FOOD & DRUG**  
ADMINISTRATION



Human-Based New Approach  
Methodologies for Biomedical Research

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# April 10<sup>th</sup>, 2025: FDA Initiative to Reduce Animal Testing

FDA NEWS RELEASE

## FDA Announces Plan to Phase Out Animal Testing Requirement for Monoclonal Antibodies and Other Drugs

**For Immediate Release:** April 10, 2025

Today, the U.S. Food and Drug Administration is taking a groundbreaking step to advance public health by replacing animal testing in the development of monoclonal antibody therapies and other drugs with more effective, human-relevant methods. The new approach is designed to improve drug safety and accelerate the evaluation process, while reducing animal experimentation, lowering research and development (R&D) costs, and ultimately, drug prices.

The FDA's animal testing requirement will be reduced, refined, or potentially replaced using a range of approaches, including AI-based computational models of toxicity and cell lines and organoid toxicity testing in a laboratory setting (so-called New Approach Methodologies or NAMs data). Implementation of the regimen will begin immediately for investigational new drug (IND) applications, where inclusion of NAMs data is encouraged, and is [outlined in a roadmap](#) also being released today. To make determinations of efficacy, the agency will also begin use pre-existing, real-world safety data from other countries, with comparable regulatory standards, where the drug has already been studied in humans.



## Roadmap to Reducing Animal Testing in Preclinical Safety Studies

### Executive Summary

This roadmap outlines a strategic, stepwise approach for FDA to reduce animal testing in preclinical safety studies with scientifically validated new approach methodologies (NAMs), such as organ-on-a-chip systems, computational modeling, and advanced *in vitro* assays. By partnering with federal agencies like NIH and VA through ICCVAM, FDA can accelerate the validation and adoption of these human-relevant methods, improving predictive accuracy while reducing animal use. This transition will enhance public health by streamlining drug development and ensuring safer therapies reach patients faster, while positioning FDA as a global leader in modern regulatory science and innovation.

### Background

There is growing scientific recognition that animals do not provide adequate models of human health and disease.<sup>1</sup> Over 90% of drugs that appear safe and effective in animals do not go on to receive FDA approval in humans predominantly due to safety and/or efficacy issues (1). Animal-based data have been particularly poor predictors of drug success for multiple common diseases including cancer (2), Alzheimer's (3) and inflammatory diseases (4). Some medications which are generally recognized safe in humans, such as aspirin, may have never passed animal testing (5). Conversely, some compounds which have appeared safe in animal models have been lethal in human trials (5). These examples highlight basic physiologic differences between humans and other animal species.

Due to the limitations of animal testing as well as ethical concerns about animals testing, there has been increased focus within the scientific community on New Approach Methodologies (NAMs). NAMs encompass *in vitro* human-based systems, *in silico* modeling, and other innovative platforms that can collectively evaluate immunogenicity, toxicity, and pharmacodynamics in humans and provide an opportunity to improve the predictive relevance of preclinical drug testing while reducing or replacing animal use. NAMs also have enormous cost saving potential (6).

Recent legislative changes have signaled Congress is simultaneously open to regulatory innovation. In late 2022, Congress passed the FDA Modernization Act 2.0,<sup>2</sup> which explicitly authorized the use of non-animal alternatives (cell-based assays, computer models, etc.) to support an investigational new drug (IND) application and "remove[d] a requirement to use animal studies" for biosimilar biologics license application (BLA) (7). This landmark policy empowered FDA to accept NAMs in lieu of animal studies. Then in 2024, the

# Media Attention: Nature Reviews Drug Discovery, WBUR On Point



AN AUDIENCE WITH | 15 May 2025

## Is the FDA's plan to phase out animal toxicity testing realistic?

**Lorna Ewart, Chief Scientific Officer at Emulate, discusses the new opportunities and remaining challenges facing organs on chips.**

By [Asher Mullard](#)



Lorna Ewart has long been frustrated by the mismatch between animal and human toxicity data. All too often preclinical studies in rats and dogs will suggest a drug is safe, only for clinical trial data to raise a red flag. In 2012, in the early days of organ-on-a-chip technology, she pitched a project to her colleagues at AstraZeneca to assess whether an engineered system that

[Home](#) / [Radio](#) / [On Point](#)



## Is animal testing even needed anymore?

June 04, 2025 By [Will Walkey](#) and [Meghna Chakrabarti](#)





# The industry trusts & uses NAMs

- Listening Tour
- Speaking Tour



**Date:** July 7, 2025

**Time:** 10:00 a.m. - 2:00 p.m. ET



The image is a YouTube video player thumbnail. At the top left is the FDA logo. To its right, the text "FDA & NIH Workshop on Reducing Animal Testing" is displayed. Below this, a dark blue banner contains the text "From a US national health authority" followed by a right-pointing arrow. The main title "FDA-NIH WORKSHOP Reducing Animal Testing" is prominently displayed in large, dark blue, serif font. A red YouTube play button icon is centered over the word "Testing". The background features faint, light blue line-art icons of laboratory equipment: a microscope, a flask with blue liquid, and a rack of test tubes with blue liquid. At the bottom left, a dark blue bar contains the text "Watch on" followed by the YouTube logo and the word "YouTube". At the top right, there is a share icon and the word "Share".

FDA & NIH Workshop on Reducing Animal Testing

From a US national health authority >

# FDA-NIH WORKSHOP

## Reducing Animal Testing

Watch on YouTube

# FDA-NIH collaboration

## MOU 225-25-012

### Domestic MOUs

[MOU 225-22-024](#)

[MOU 225-22-026](#)

[MOU 225-22-029](#)

[MOU 225-23-001](#)

[MOU 225-23-003](#)

[MOU 225-20-007](#)

[MOU 225-23-008](#)

[MOU 225-23-009](#)

[MOU 225-23-012](#)

MEMORANDUM OF UNDERSTANDING  
BETWEEN  
DEPARTMENT OF HEALTH AND HUMAN SERVICES  
NATIONAL INSTITUTES OF HEALTH  
AND  
THE FOOD AND DRUG ADMINISTRATION  
CONCERNING

Coordinated Efforts on NIH COMPLEMENT-ARIE PROGRAM ("PROJECT")

### I. PURPOSE

This Memorandum of Understanding (MOU) sets forth an overarching framework of partnership between the National Institutes of Health (NIH) and the Food and Drug Administration (FDA; collectively referred to as the "Parties"). To effectuate this purpose, the Parties enter into a non-exclusive, non-binding Memorandum of Understanding to promote the advancement of New Approach Methodologies (NAMs), sometimes referred to as Novel Alternative Methods, New Alternative Methods, or Non-Animal Models. These Parties share common interests and goals in developing NAMs to complement animal research in experimentation and catalyze the development, standardization, validation, qualification and use of human-based NAMs that will transform the way basic, translational, and nonclinical sciences are done. To this extent, this MOU will focus on collaboration among the Parties to advance the goals of the NIH Common Fund's [Complement Animal Research in Experimentation \(Complement-ARIE\) Program](#). The purpose of Complement-ARIE is to accelerate the development, standardization,

Content current as of:  
08/27/2025

| Endpoint                       | FDA Center | Test Article      | Current Animal Test Guideline/Guidance:<br>animals per test                                                | Alternative Method                                                                                                                     | Validation / Performance                                                              | Regulatory Acceptance Status                                                                        | Key Steps to Finalize                                                                                               |
|--------------------------------|------------|-------------------|------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| Pyrogenicity                   | CDRH       | Implanted devices | ISO 10993-1:2013 (tests for pyrogenicity):<br>rabbits per test material, minimum                           | Recombinant Bacterial Endotoxin Test (rBET)                                                                                            | accepted in Europe, which will phase out RPT by January 2026.                         | context of uses in medical devices (dental bone screws)                                             | device test alternatives. Potentially PSCI/NICEATM 2018 workshop on p                                               |
| Acute Oral Systemic Toxicity   | CDRH       | Medical devices   | ISO 10993-11:2017 (new guidance drafted):<br>10 rats                                                       | BALB/3T3 mouse fibroblast and human epidermal keratinocyte <i>in vitro</i> tests. Collaborative Acute Toxicity Modeling Suite (CATMoS) | <i>in vitro</i> assays should be conducted prior to animal assays                     | Accepted and active. Test can be waived.                                                            | Continue validation and bench                                                                                       |
| Acute Dermal Systemic Toxicity | CDRH       | Medical devices   | 20 rats, rabbits, or guinea pigs                                                                           | In-silico QSAR and 3T3 cytotoxicity                                                                                                    | Showed high sensitivity and low false negative rate when coupled to prediction model. | Accepted and active as part of Weight-of-Evidence assessment. Test can be waived.                   | Continue validation and bench                                                                                       |
| Vaginal Irritation             | CDRH       | Medical devices   | 3 rabbits                                                                                                  | EpiVaginal (MatTek) human tissue model                                                                                                 | Developers (PSCI) building data under narrow context of use; early ISO WG discussions | Not yet accepted; MDDT pathway seen as ineffective to date                                          | Co-develop study/analysis plans with consultation path; publish                                                     |
| Skin Sensitization             | CDRH       | Medical devices   | 12–30 mice or guinea pigs per ISO 10993-10                                                                 | Defined approaches (OECD TG 497); In silico and in chemico (OECD TG 442C-E)                                                            | OECD TGs. Outperforms animal assays.                                                  | Validated; OECD TGs                                                                                 | Update guidance for biomedical dev. Survey FDA centers to understand v sensit                                       |
| Eye Irritation / Corrosion     | CDRH       | Medical devices   | 1-3 rabbits                                                                                                | OECD TGs 437 (BCOP); 467 (DA); 492/492B (RhCE); 438 (ICE); 460 (FL); 491 (STE); 494; 496                                               | Validated and ready for use according to OECD Guidelines                              | Accepted and active                                                                                 | Survey FDA centers for contact le understand where animal test                                                      |
| Skin irritation for devices    | CDRH       | Medical devices   | ISO 10993 -23 Tests for Irritation: 5 rabbits per test minimum if well-defined redness or swelling present | Reconstructed human epidermis (RhE; OECD TG 439)                                                                                       | 16-lab interlab study including FDA demonstrated robustness                           | Preferred method in ISO 10993 and recognize in EU, AU, JP, CN. US lagging in formal policy adoption | 1-2 day meeting with FDA CDRH, I results from the workshop and under guidance recognizing ISO 10993-2 irritation re |

# Why have we not made more progress at FDA?

- Largest manufacturers default to include animal testing for FDA
- Communication with FDA prior to application submission can be a challenge
- Sponsors worried about not including animal testing even when they do not think it adds value



# Why have we not made more progress at FDA?

- No incentive to include NAMs data in applications (proprietary, may be more sensitive to toxicity)
- Misunderstanding that NAMs must be pre-qualified or pre-validated by FDA
  - IStand program is slow
  - Gives impression “qualification” is necessary to include NAMs data

**What are we doing to  
address these  
challenges?**

# Why have we not made more progress?

- Largest manufacturers default to include animal testing for FDA
  - Require NAMs submission instead of animal data when
    - NAMs data already accepted by the FDA
      - Make prior drug applications searchable
    - NAMS already recognized as validated by other US or international regulators
    - Accompanying data provided to reviewers

# FDA list of Qualified Drug Development Tools

| A                                | B                                                                                                                               | C                                             | D                                                                                                | E | F | G |
|----------------------------------|---------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|--------------------------------------------------------------------------------------------------|---|---|---|
| <a href="#">DDT-AMQ-000006</a>   | Qualification of the Cynomolgus Macaque ( <i>Macaca fascicularis</i> ) Model of Pneumonic Tularemia                             | FQP - Full Qualification Package -- Qualified | National Institutes of Health/National Institute of Allergy and Infectious Diseases              |   |   |   |
| <a href="#">DDT-BMQ-000028</a>   | Prognostic biomarker with patient age and baseline glomerular filtration rate for Autosomal Dominant Polycystic Kidney Disease  | FQP - Full Qualification Package -- Qualified | Polycystic Kidney Disease Outcomes Consortium                                                    |   |   |   |
| <a href="#">DDT-BMQ-000021</a>   | Prognostic biomarker used with other characteristics to enrich for COPD exacerbations                                           | FQP - Full Qualification Package -- Qualified | Chronic Obstructive Pulmonary Disease Biomarker Qualification Consortium                         |   |   |   |
| <a href="#">DDT-BMQ-000014</a>   | Safety biomarker panel to aid in the detection of kidney tubular injury in phase 1 trials in healthy volunteer                  | FQP - Full Qualification Package -- Qualified | FNIH Biomarker Consortium Kidney Safety Project and C-Path Predictive Safety Testing Consortium  |   |   |   |
| <a href="#">DDT-BMQ-000004</a>   | Safety serum/plasma cardiotoxicity biomarkers as assessed by immunoassay                                                        | FQP - Full Qualification Package -- Qualified | PJ O'Brien, WJ Reagan, MJ York and MC Jacobsen                                                   |   |   |   |
| <a href="#">DDT-BMQ-000003</a>   | Safety biomarker to be used with traditional indicators to indicate renal injury in rat as measured by assayed serum creatinine | FQP - Full Qualification Package -- Qualified | International Life Sciences Institute (ILSI)/ Health and Environmental Sciences Institute (HESI) |   |   |   |
| <a href="#">DDT-BMQ-000044</a>   | Monitoring biomarker informs initiation of treatment with anti-malarial drug following controlled human malaria challenge       | FQP - Full Qualification Package -- Qualified | University of Washington Department of Laboratory Medicine                                       |   |   |   |
| <a href="#">DDT-BMQ-000002</a>   | Safety biomarker to be used with traditional indicators to indicate renal injury in rat as measured by assayed serum creatinine | FQP - Full Qualification Package -- Qualified | C-Path Predictive Safety and Testing Consortium                                                  |   |   |   |
| <a href="#">DDT-BMQ-000001</a>   | Diagnostic biomarker used with other clinical and host factors to identify patients with Invasive Aspergillus                   | FQP - Full Qualification Package -- Qualified | Mycoses Study Group                                                                              |   |   |   |
| <a href="#">DDT-COA-000110</a>   | WHO Risk Drinking Levels of Alcohol Consumption                                                                                 | FQP - Full Qualification Package -- Qualified | The Alcohol Clinical Trials Initiative (ACTIVE)                                                  |   |   |   |
| <a href="#">DDT-COA-000084</a>   | Kansas City Cardiomyopathy Questionnaire (KCCQ)                                                                                 | FQP - Full Qualification Package -- Qualified |                                                                                                  |   |   |   |
| <a href="#">DDT-COA-000017</a>   | Evaluating Respiratory Symptoms in Chronic Obstructive Pulmonary Disease (E-RS: COPD)                                           | FQP - Full Qualification Package -- Qualified | Evidera                                                                                          |   |   |   |
| <a href="#">DDT-COA-000009</a>   | Non-Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ)                                                         | FQP - Full Qualification Package -- Qualified | Critical Path Institute: Patient- Reported Outcome (PRO) Consortium                              |   |   |   |
| <a href="#">DDT-COA-000008</a>   | Symptoms of Major Depressive Disorder Scale (SMDDS)                                                                             | FQP - Full Qualification Package -- Qualified | Critical Path Institute: Patient- Reported Outcome (PRO) Consortium                              |   |   |   |
| <a href="#">DDT-COA-000006</a>   | Asthma Daytime Symptom Diary (ADSD) and Asthma Nighttime Symptom Diary (ANSDD)                                                  | FQP - Full Qualification Package -- Qualified | Critical Path Institute: Patient- Reported Outcome (PRO) Consortium                              |   |   |   |
| <a href="#">DDT-COA-000005</a>   | Diary of Irritable Bowel Syndrome Symptoms - Constipation (DIBSS-C)                                                             | FQP - Full Qualification Package -- Qualified | Critical Path Institute: Patient- Reported Outcome (PRO) Consortium                              |   |   |   |
| <a href="#">DDT-COA-000003</a>   | Exacerbations of Chronic Pulmonary Disease Tool (EXACT)                                                                         | FQP - Full Qualification Package -- Qualified | Evidera                                                                                          |   |   |   |
|                                  |                                                                                                                                 |                                               |                                                                                                  |   |   |   |
| Qualified Drug Development Tools |                                                                                                                                 |                                               |                                                                                                  |   |   |   |



# Why have we not made more progress?

- Communication with FDA prior to application submission can be a challenge
  - In CEO listening tour we learned communication is better with private HRECs (Australian IRBs) and this is attracting more Phase 1 applications and more NAMs data
  - Held/are holding meetings with Australia/Australian HRECs to understand their process
  - Low vs high risk application types?
  - Making center directors aware so they can discuss with reviewers

# Why have we not made more progress?

- Sponsors worried about not including animal testing even when they do not think it adds value
  - Speaking publicly about not needing to do so
  - New regulations/guidance
  - Encourage early communication of sponsors with centers when they believe they have clear rationale to not use/reduce animal testing
  - Plan to publicize success cases
  - Reviewer training in NAMs/NAMs hotline

# Why have we not made more progress?

- No incentive to include NAMs data in applications (proprietary, may be more sensitive to toxicity)
  - Safe Harbour like EMA (met with congressional staffers)
  - Priority Review?
  - ? Ask to include NAMs when animal data are insufficient

# Why have we not made more progress?

- Misunderstanding that NAMs must be pre-qualified or pre-validated by FDA
  - I STAND program is slow
    - Streamlining or modifying the three-step submission process mandated by the 21st Century Cures Act
  - Gives impression “qualification” is necessary to include NAMs data
    - Communicating to sponsors (and reviewers) that qualification is not required

# Additional

- Ask Congress to amend Section 351(a) of the PHS Act for biologics, to include a pathway that mirrors the 505(b)(2) pathway for drugs under the FD&C Act. This new pathway will substantially reduce use of NHPs by allowing the sponsors to rely on the safety information from the labels of approved products and/or from published articles
- Flexibility- does testing in 2 animals add useful or necessary information?



# Develop internal FDA model to predict toxicity

Currently under development- ARPA-H,  
NIH, ? Private partnership/s



## A win-win initiative

- Improve toxicity and efficacy testing (better products for Americans)
- Save time and money
- Ethical treatment of animals