CLIENT ALERT | May 20, 2025

FDA and NIH Announce Initiatives to Reduce Animal Testing and Encourage Alternative Methodologies

The initiatives reflect the latest measures from federal agencies to reduce and ultimately replace animal testing in drug development and biomedical research.

Key Points:

- FDA and NIH recently announced initiatives outlining specific actions each agency will take to encourage greater adoption of new and emerging technologies to reduce the need for — and potentially replace — animal testing.
- FDA's roadmap has identified monoclonal antibodies (mAbs) as the first promising area for reducing animal use in preclinical safety testing. FDA intends to expand the roadmap to other biological molecules and eventually new chemical entities.
- FDA plans to solicit stakeholder input on its implementation of the roadmap, providing sponsors with an opportunity to further inform the actions FDA may take to phase out animal testing.
- NIH intends to establish a new Office of Research, Innovation, and Application (ORIVA) to coordinate NIH-wide efforts to develop, validate, and scale the use of non-animal approaches across the agency's biomedical research portfolio.

In recent weeks, the US Food and Drug Administration (FDA) and National Institutes of Health (NIH) have announced certain measures as part of a broader Department of Health & Human Services (HHS) initiative to reduce and eventually eliminate the use of laboratory animals in drug testing. On April 10, 2025, FDA published a roadmap outlining a "strategic, stepwise approach" for FDA to reduce, refine, and replace animal testing in preclinical safety studies with scientifically validated new approach methodologies (NAMs),[1] such as organ-on-a-chip systems, computational modeling, and advanced in vitro assays.[2] Several weeks later, on April 29, 2025, NIH announced it intends to establish the Office of Research, Innovation, and Application (ORIVA) as part of a coordinating initiative to expand innovative, human-based science while reducing animal use in research.[3]

The newly announced initiatives advance a longstanding effort within HHS to encourage the adoption of NAMs in preclinical safety studies and biomedical research.[4] According to FDA, there is growing scientific recognition that animals do not provide adequate models of human health and disease, and animal-based data have been particularly poor predictors of drug success for common diseases including cancer, Alzheimer's, and inflammatory diseases.[5] FDA asserts, for example, that a majority of drug development failures "are due to lack of efficacy or unexpected safety issues that were not evident in animal tests."[6]

FDA states that the adoption of "human-relevant" NAMs will improve the predictive accuracy of preclinical safety studies and "get safer treatments to patients faster and more reliably, while also reducing R&D costs and drug prices."[7] NIH similarly stated that the increased adoption of NAMs in biomedical research will "expand the toolbox for researchers to answer previously difficult or unanswerable biomedical research questions."

FDA identified monoclonal antibodies (mAbs) as a promising area of drug development for reducing animal use in preclinical safety testing. FDA believes that animal testing of mAbs has proven particularly challenging for sponsors because of the number and cost of animals, such as non-human primates (NHPs), used to develop safety data for these programs.[8] Nevertheless, FDA currently mandates repeat-dose toxicity studies in animals for the development of mAbs.[9] FDA will therefore focus its initial efforts under the roadmap on replacing animal testing in the development of mAbs. FDA intends to then expand the roadmap to other biological molecules and eventually new chemical entities and medical countermeasures.

Building on this effort, NIH's newly established ORIVA will coordinate NIH-wide efforts to develop, validate, and scale the use of non-animal approaches across NIH's biomedical research portfolio. It will also expand funding for, and training in, the use of non-animal approaches, and simultaneously raise awareness of the value of non-animal approaches in translational success to humans.

Collectively, these initiatives represent a significant step in the broader HHS initiative to phase out the use of animal testing and encourage the adoption of NAMs.

Early Efforts to Encourage the Adoption of NAMs

For years, FDA has participated in interagency and international standards organization efforts aimed at reducing the use of NAMs.[10]

FDA has also been active at the center level. Researchers in the Division of Applied Regulatory Science in the Center for Drug Evaluation and Research developed cellular microsystems platforms that replicate human physiology to advance FDA's ability to model drugs' effects on the liver and heart.[11] The Center for Devices and Radiological Health (CDRH) also developed in vitro and in silico methods to predict and assess health risks from exposure to medical device extractables and leachables, such as color additives, to support biocompatibility evaluations of medical devices without requiring that such tests be conducted on animals.[12] And in 2023, CDRH and the Center for Biologics Evaluation and Research (CBER) published a guidance document stating that the centers agreed with a revision to the International Organization for Standardization's (ISO's) standard for biological evaluation of medical devices (ISO 10993) regarding biocompatibility testing.[13] This revision is intended to reduce the "number and exposure of test animals by giving preference to *in vitro* models and to chemical, physical, morphological, and topographical testing, in situations where these methods yield equally relevant information to that obtained from *in vivo* models."[14]

Most recently, in October 2024, the Science Board to the Food and Drug Administration, which is an advisory committee to FDA, developed six recommendations to encourage greater adoption of NAMs.[15] These recommendations include creating a uniform framework for FDA to qualify the use of NAMs, compiling a central NAMs database for all of FDA to use, and establishing a transparent and scientifically rigorous review process for incoming product applications that rely on NAMs to demonstrate efficacy and/or safety.[16]

Congress also recently took steps to empower FDA to permit a drug to enter clinical trials without first undergoing animal testing. In late 2022, Congress amended the Federal Food, Drug, and Cosmetic Act (FDCA) to expressly authorize drug sponsors to use nonclinical tests, such as cell-based assays and computer modeling, to support an Investigational New Drug application.[17]

Recently Announced FDA and NIH Initiatives

FDA's Plans to Phase Out Animal Testing

As part of its April 2025 announcement, FDA stated that it will accept a range of NAMs sponsors to evaluate the safety of mAbs in lieu of animal studies. To determine efficacy, FDA states in the announcement that it will "begin use [of] pre-existing, real-world safety data from other countries, with comparable regulatory standards, where the drug has already been studied in humans," although FDA does not offer additional detail in the announcement or roadmap on how the use of such data would accomplish this objective.[18]

FDA also published a roadmap outlining a strategic, stepwise approach to reduce animal testing in preclinical safety studies. The roadmap details several types of NAMs potentially suitable for assessing the safety, efficacy, and pharmacology of drugs and therapeutics without traditional animal models. FDA believes widespread adoption of the following NAMs, most of which are expressly identified as examples of permissible nonclinical tests under FDCA Section 505(z), will provide "'faster and more accurate risk assessments'" of drugs while reducing animal use:

- Miniature organ units or "organ-on-a-chip" devices
- Computer models and in silico tools, including machine learning and artificial intelligence predictive models
- Donated human organs and tissues
- Human-cell-based assays using robotic screening methods to profile the effects of a product on human cells

The roadmap includes several other proposed actions designed to make animal studies "the *exception* rather than the norm for pre-clinical safety/toxicity testing."[19] FDA will consider identifying critical endpoints and use cases for NAMs, supporting targeted development of NAM technologies, establishing validation and qualification pathways for NAMs, developing regulatory guidance and standards for NAMs, training FDA reviewers and scientists on these new approaches promoting the acceptability of NAMs in the scientific community, and monitoring outcomes to enable refinements over time.[20]

FDA announced it will also continue with interagency efforts to accelerate the validation and adoption of NAMs, and will host a public workshop later this year to discuss the roadmap and gather stakeholder input on these efforts. FDA also intends to launch a pilot program allowing select mAb developers to use a primarily non-animal-based testing strategy, under close FDA consultation.[21] FDA has also established the Innovative Science and Technology Approaches for New Drugs (ISTAND) pilot program, and it recently accepted the Emulate Liver-Chip S1 — an organ-on-a-chip technology — into the program to study drug-induced liver injury for certain drug candidates.[22] According to FDA, findings from this study will inform broader policy changes and guidance updates, which FDA expects to roll out in phases.

NIH's Initiative to Prioritize Human-Based Research Technologies

NIH adopted a complementary initiative to expand the use of NAMs while reducing animal use in research.[23] Under this initiative, NIH intends to establish ORIVA within NIH's Office of the Director.[24] According to NIH, ORIVA will coordinate NIH-wide efforts to develop, validate, and scale the use of non-animal approaches across NIH's biomedical research portfolio.[25] NIH intends for ORIVA to expand funding and training in non-animal approaches and to increase awareness of NAMs' value in translational success.[26] New funding opportunities will reportedly include evaluation criteria that assess NAMs based on their suitability for the research question, context of use, translatability, and human relevance.[27] NIH also plans to train grant review staff to address possible biases against non-animal studies.[28]

Conclusion

FDA and NIH's recently announced initiatives are the latest in a series of actions by federal agencies to promote NAMs in medical product development and biomedical research. FDA believes its efforts to move sponsors away from animal studies and promote alternative nonclinical research methods could enable more agile product development. Sponsors that wish to use non-animal testing alternatives should therefore consider participating in FDA's planned pilot programs and providing feedback on FDA's roadmap, among other opportunities for engagement. FDA's evolving approach toward the use of NAMs may present opportunities for sponsors to engage in targeted discussions on incorporating the use of these technologies into their development programs, potentially streamlining product development and reducing costs in the process.

Contacts

Nathan A. Beaton
nathan.beaton@lw.com
+1.202.637.1062
Washington, D.C.

Anton Lesaca
anton.lesaca@lw.com
+1.202.521.5824
Washington, D.C.

Trevor Thompson
trevor.thompson@lw.com
+1.202.350.5177
Washington, D.C.

Endnotes

[1] FDA has also referred to these as "New Alternative Methodologies" or "New Approach Methodologies." *See* FDA, *Advancing New Alternative Methodologies at FDA* (Jan. 2021), https://www.fda.gov/media/144891/download ("Animal Testing White Paper"); FDA, *Potential Approaches to Drive Future Integration of New Alternative Methods for Regulatory Decision-Making* (Oct. 2024), https://www.fda.gov/media/182478/download ("Science Board Report").

[2] FDA, *Roadmap to Reducing Animal Testing in Preclinical Safety Studies* (Apr. 10, 2025), https://www.fda.gov/news-events/press-announcements/fda-announces-plan-phase-out-animal-testing-requirement-monoclonal-antibodies-and-other-drugs ("Roadmap to Reducing Animal Testing").

[3] NIH, NIH News Release, *NIH to prioritize human-based research technologies* (Apr. 29, 2025), https://www.nih.gov/news-events/news-releases/nih-prioritize-human-based-research-technologies ("NIH Announcement").

[4] *See* supra note 1.

[5] Roadmap to Reducing Animal Testing at 1.

[6] *Id.* at 2.

[7] FDA, FDA News Release, *FDA Announces Plan to Phase Out Animal Testing Requirement for Monoclonal Antibodies and Other Drugs* (Apr. 10, 2025), https://www.fda.gov/news-events/press-announcements/fda-announces-plan-phase-out-animal-testing-requirement-monoclonal-antibodies-and-other-drugs#:~:text=The%20FDA%27s%20animal%20testing%20requirement,Approach%20Methodologies%20or%20NAMs%20data ("April 2025 Announcement").

[8] Roadmap to Reducing Animal Testing at 2.

[9] *Id.*

[10] The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) has led efforts to encourage the adoption of NAMs. ICCVAM is an interagency committee that coordinates technical reviews of alternative test methods and cross-agency activities relating to validation, acceptance, and harmonization of test methods (see Animal Testing White Paper at 27). ICCVAM also facilitates the development, validation, and regulatory acceptance of test methods that replace, reduce, or refine the use of animals in testing. FDA representatives participate in ICCVAM's monthly meetings, public forums, and Scientific Advisory Committee on Alternative Toxicological Methods meetings and work groups. FDA has promoted the development of NAMs in other ways as well. In 2019, FDA established an Alternative Methods Working Group to develop a targeted strategy for the use of NAMs for regulatory testing. In 2021, the Alternative Methods Working Group published a white paper addressing FDA's steps toward integrating alternative testing approaches into the agency's regulatory programs (*Id.* at 6).

[11] FDA, *Impact Story: Evaluating the Potential of Microengineered Human Cellular Systems to Predict Drug Effects in the Clinic* (Feb. 5, 2019), https://www.fda.gov/drugs/regulatory-science-action/impact-story-evaluating-potential-microengineered-human-cellular-systems-predict-drug-effects-clinic.

[12] Animal Testing White Paper at 17.

[13] FDA, Guidance for Industry and Food and Drug Administration Staff, *Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process'* (Sep. 8, 2023), at 16, https://www.fda.gov/media/142959/download.

[14] *Id.* at 16.

[15] Science Board Report at 4.

[16] *Id.*

[17] Consolidated Appropriations Act, 2023, Pub. L. No. 117-328, § 3209, 136 Stat. 5821, 5822 (2022) (codified as amended at 21 U.S.C. § 355(i)(1)(A)). Specifically, Congress amended FDCA section 505 to replace references to "preclinical tests (including tests on animals)" with "nonclinical tests," which it defines as a "test conducted in vitro, in silico, or in chemico, or a nonhuman in vivo test, that occurs before or during the clinical trial phase of the investigation of the safety and effectiveness of a drug."

[18] April 2025 Announcement.

[19] Roadmap to Reducing Animal Testing at 6.

[20] *Id.* at 6-8.

[21] April 2025 Announcement.

[22] FDA, *FDA's ISTAND Pilot Program accepts a submission of first organ-on-a-chip technology designed to predict human drug-induced liver injury* (DILI) (Sep. 24, 2024), https://www.fda.gov/drugs/drug-safety-and-availability/fdas-istand-pilot-program-accepts-submission-first-organ-chip-technology-designed-predict-human-drug.

[23] NIH Announcement.

[24] *Id.*

[25] *Id.*

[26] *Id.*

[27] *Id.*

[28] *Id.*