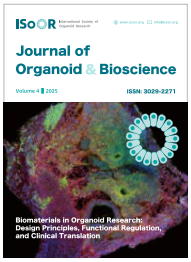
ISoOR International Society of Organoid Research

Journal of Organoid & Bioscience Volume 4 (2025), page 31-38

Journal of Organoid & Bioscience

Official Journal of ISoOR: www.jobs.isoor.org



Industry News

NIH Shift Away from Animal-Only Research Signals a Major Opportunity for Organoids

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Abstract

In April 2025, the U.S. National Institutes of Health (NIH) announced a landmark shift that will reshape biomedical research for decades: the agency will no longer issue Notices of Funding Opportunities (NOFOs) that rely exclusively on animal models. Instead, all future funding calls must include—or explicitly permit—the use of non-animal methods (NAMs), including organoids, microphysiological systems, computational models, human-derived tissues, and advanced in vitro approaches. This policy, formalized at the first FDA-NIH "Workshop on Reducing Animal Testing" on July 7, 2025, marks an unprecedented reorientation of federal funding priorities toward human-relevant, ethical, and translationally predictive model systems. For the organoid field, the implications are vast: expanded funding, accelerated standardization, infrastructure scaling, enhanced regulatory relevance, and deeper integration into drug development and precision medicine. Yet the shift also presents scientific and practical challenges, including issues of reproducibility, biological complexity, and global regulatory acceptance. This article analyzes the motivations behind the NIH decision, its transformative significance for organoid science, the challenges ahead, and the role of standards such as ISoOR-ISOB and the newly funded Standardized Organoid Modeling (SOM) Center in shaping the next era of biomedical research.

Keywords

Organoids; New Approach Methodologies (NAMs); NIH policy; animal research reduction; microphysiological systems; FDA toxicology modernization; organoid biobanking; translational modeling; precision medicine; regulatory science.

1. Introduction

The April 29, 2025, announcement by the U.S. National Institutes of Health (NIH) that it will no longer solicit or fund new research proposals relying solely on animal models represents a turning point

in the history of biomedical science. Elaborated and formalized at the inaugural FDA-NIH "Workshop on Reducing Animal Testing" on July 7, 2025, this policy—championed by Acting NIH Deputy Director for Program Coordination, Planning, and Strategic Initiatives Dr. Nicole Kleinstreuer—has implications that extend far beyond administrative policy. It signals a profound reshaping of the scientific ecosystem, one that places human-relevant model systems such as organoids at the center of research innovation.

This decision reflects a longstanding recognition of two realities. First, animal models carry inherent ethical, logistical, and regulatory burdens. Second, and perhaps more importantly, animal models often fail to predict human outcomes reliably, particularly in oncology, immunology, neurology, toxicology, and emerging therapeutic modalities.

In this context, organoid technologies and other non-animal methods (NAMs) are no longer alternative or supplementary—they are becoming foundational to the future of biomedical discovery. As Dr. Kleinstreuer stated during the workshop, "All new NIH funding opportunities moving forward should incorporate language on consideration of NAMs... NIH will no longer seek proposals exclusively for animal models."

For organoid researchers, this policy shift is more than an endorsement; it is a structural repositioning that will accelerate adoption, standardization, and regulatory integration. It marks a new chapter in which organoids are poised to move from innovative niche tools to mainstream pillars of biomedical science. With the NIH committing to prioritize human-focused approaches across its $47 billion annual budget, organoid-centric proposals stand to gain a competitive edge, potentially unlocking billions in funding for scalable, reproducible models that better mirror human biology.

2. The Policy Shift: What NIH Actually Changed

2.1 End of Animal-Only Research Solicitations

Under the new NIH framework, as of July 2025:

- No Notice of Funding Opportunity (NOFO) may mandate exclusively animalbased research.
- Investigators are required to justify their model selection scientifically, rather than defaulting to historical norms such as rodent or primate models.
- This requirement is not merely bureaucratic; it represents a deep rethinking of the assumptions underpinning decades of preclinical and translational research practice.

The policy builds on the NIH's April 29, 2025, initiative to prioritize human-based research technologies, ensuring that all NOFOs related to animal model systems also support human-focused approaches like clinical trials, real-world data, or NAMs. NOFOs excluding animal use entirely may also be issued, allowing institutes to tailor calls to emerging priorities. As Dr. Kleinstreuer emphasized at the July 7 workshop, "The intent is to ensure investigators consider the models most appropriate for understanding human states of health and disease and are not constrained by the NOFO."

2.2 Inclusion and Encouragement of NAMs

All future NOFOs must include language that encourages the use of NAMs such as:

- Organoids and organ-on-chip systems
- Tissue-derived human in vitro models
- Computational/AI-based biological modeling
- Real-world human data
- Advanced microphysiological systems

By embedding NAMs directly into funding language, NIH is signaling institutional commitment to human-based model systems across the research pipeline. Examples of NAMs explicitly highlighted include ex vivo human-based approaches like perfused organs and precision-cut tissue slices, alongside in vitro methods such as organoids and computational tools. This shift is projected to redirect a significant portion of the NIH's extramural research budget—historically over $20 billion annually—toward proposals incorporating these technologies, fostering innovation while addressing the 90% failure rate of preclinical candidates in human trials.

2.3 Establishment of ORIVA and Agency-Wide Coordination

NIH will establish the Office of Research Innovation, Validation, and Application (ORIVA), a centralized effort aimed at the development, benchmarking, validation, and dissemination of NAMs. Its responsibilities include:

- Creating validation frameworks
- Coordinating inter-institute efforts
- Supporting scale-up of human-based models
- Facilitating interactions with regulatory agencies

As proposed in the April 29 announcement and elaborated at the July 7 workshop, ORIVA will formalize NIH's commitment to NAM integration, partnering with the FDA and other agencies to streamline validation processes. Complementing ORIVA, the September 25, 2025, award of $87 million in contracts for the Standardized Organoid Modeling (SOM) Center—housed at the Frederick National Laboratory for Cancer Research (FNLCR) under the National Cancer Institute (NCI)—will develop reproducible organoid protocols using AI and robotics, initially focusing on liver, lung, heart, and intestine models, with expansion to brain and thymus systems. Together, these reforms demonstrate NIH's commitment to transforming the research infrastructure—not just revising its policies—ensuring affordable, open-access protocols under FAIR principles for NIH-funded researchers nationwide.

3. Why the Policy Matters: Ethical, Scientific, and Translational Drivers

3.1 Ethical and Regulatory Pressures

Animal research has long been challenged by ethical concerns, heightened regulatory scrutiny, and increasing public expectations for humane science. The use of nonhuman primates, in particular, has faced growing legal, societal, and economic pressure. By encouraging alternatives, NIH aligns itself with global scientific and ethical momentum. Aligning with FDA's April 10, 2025, phase-out of mandatory primate testing for monoclonal antibodies—further detailed in the December 2, 2025, draft guidance on waiving six-month non-human primate (NHP) toxicity studies for monospecific antibodies—this policy reduces the ethical burden of using over 100 NHPs per typical monoclonal antibody program, at costs exceeding $50,000 per animal.

3.2 Scientific Limitations of Animal Models

Animal models often fail to:

- Reflect human tumor microenvironments
- Model complex neurological disorders
- Capture patient-specific heterogeneity
- Recapitulate human immune responses
- Predict human toxicity or drug metabolism

These shortcomings have contributed to high attrition rates in drug development and have driven researchers toward human-derived model systems, particularly organoids. Up to 90% of drugs succeeding in animals fail in humans, as highlighted by FDA workshop discussions in July 2025. Efficacy and safety issues account for 52% and 24% of Phase II/III failures, respectively, underscoring the translational gap.

3.3 NAMs as Scientifically Superior Alternatives

By formalizing support for NAMs, NIH acknowledges the increasing evidence that organoids, tissue chips, and human-derived in vitro models offer:

- Greater mechanistic fidelity
- Enhanced translational predictiveness
- Relevance to patient-specific biology
- Capacity for high-throughput drug screening
- Potential to reduce ethical burdens

This scientific reasoning underpins the shift as much as ethical considerations, with NAMs projected to cut preclinical costs by up to 30% while improving success rates.

4. Implications for Organoid Research

The NIH policy shift opens a new frontier for organoid science.

4.1 Expansion of Funding Opportunities

Organoid-based proposals are likely to:

- Gain a competitive advantage
- Receive increased funding allocation
- Attract multi-institute initiatives
- Integrate more deeply into clinical and translational pipelines

Fields likely to see the greatest growth include oncology, toxicology, developmental biology, precision medicine, and immunology. With NIH's $47 billion budget, organoid projects could capture 10–15% more extramural funds by 2027, especially through targeted NOFOs like those under ORIVA.

4.2 Infrastructure and Standardization

A major bottleneck for organoids is inconsistency across laboratories. The NIHfunded Standardized Organoid Modeling (SOM) Center is positioned to address this by:

- Developing standardized protocols
- Establishing national biobanking infrastructure
- Creating reproducibility frameworks
- Supporting cross-laboratory quality control
- Facilitating data governance and metadata standards

Awarded $87 million on September 25, 2025, and housed at the Frederick National Laboratory for Cancer Research (FNLCR) under NCI, SOM will use AI and robotics for real-time protocol optimization, starting with liver, lung, heart, and intestine models before expanding to brain and thymus. Open-access under FAIR principles, it ensures minimal-cost access for NIH-funded researchers, aligning with FDA for regulatory validation. This infrastructure will enable scalable production and data sharing, addressing reproducibility gaps that currently affect 40–60% of organoid studies.

4.3 Enhancing Interdisciplinary Collaboration

The organoid field increasingly intersects with:

- Bioengineering
- Single-cell and spatial omics
- Machine learning

- Immunology and oncology
- Regulatory science

NIH's new policy encourages these interdisciplinary collaborations by placing NAMs at the forefront of federal funding, with ORIVA coordinating cross-institute efforts and SOM integrating AI for protocol refinement.

5. Regulatory and Translational Impact

The NIH announcement aligns with recent FDA toxicology modernization decisions, including the April 10, 2025, phase-out of mandatory primate testing for monoclonal antibodies and the December 2, 2025, draft guidance waiving six-month NHP toxicity studies for monospecific antibodies (using three-month data from NHPs, dogs, or mini-pigs supplemented by weight-of-evidence assessments). The July 7 workshop committed to publishing NAM "use cases" for IND/BLA submissions, potentially integrating organoid data into safety assessments.

Together, NIH and FDA reforms may transform:

- IND submission expectations
- Preclinical safety assessment
- Mechanistic toxicology
- Early-phase drug development strategies

In the future, organoid-derived data may become an expected component of translational pipelines, rather than an optional supplement, reducing the 90% preclinical-to-clinical attrition rate.

6. Challenges, Limitations, and Scientific Realities

Despite the optimism, experts warn of several challenges.

6.1 Biological Complexity

Organoids still lack:

- Fully functional vasculature
- Mature immune components
- Endocrine cross-talk
- Systemic metabolic interactions

For certain studies—particularly systemic toxicology—animal systems currently offer capabilities that NAMs cannot yet match. As noted by experts at the July 2025 workshop, NAMs like organoids are "very premature" for complex multi-system studies (e.g., Eliza Bliss-Moreau, UC Davis: "too simplistic for multi-system toxicology").

6.2 Reproducibility and Standardization Gaps

Variability in:

- Culture conditions
- Donor tissue quality
- Differentiation protocols
- Analytical methods

can significantly affect reproducibility. Without coordinated standards, organoid data may be difficult to compare across institutions. FASEB's July 14, 2025, comments urged greater transparency in NOFO implementation to address these gaps.

6.3 Regulatory Pathways Still Evolving

Regulators worldwide are cautious. Many jurisdictions still require animal data for:

- Long-term toxicity
- Pharmacokinetics
- Developmental and reproductive toxicology

Thus, organoids must undergo rigorous validation before obtaining universal regulatory acceptance. The FDA's December 2 draft guidance represents progress but applies only to monospecific mAbs, leaving broader scopes for future action.

7. The Role of ISoOR, ISOB, and Global Standardization

International collaboration is essential. Organizations such as:

- ISoOR
  (International Society of Organoid Research)
- ISoOR-ISOB
  (International Standards for Organoid Biobanking)

are creating standards for:

- Culture reproducibility
- Biobanking and cryopreservation
- Data annotation
- Cross-lab comparability
- Regulatory-ready documentation

ISoOR's September 12, 2025, ILAC Stakeholder status enhances this effort, providing access to global accreditation networks for ISO/IEC 17011 alignment and future MRA recognition. ISoOR-ISOB, building on ISO 20387 with pilot validations, ensures organoid data meets reproducibility thresholds critical for NIH/FDA integration.

These frameworks will be critical to ensuring that organoids move from research tools to validated preclinical systems, bridging the translational gap that contributes to 90% of drug failures.

8. Implications for Cancer Research and Precision Oncology

Oncology stands to benefit immensely. Organoids offer:

- Patient-specific tumor modeling
- Accurate representation of tumor heterogeneity
- Co-culture with immune cells and stroma
- Real-time drug sensitivity profiling
- Analysis of resistance mechanisms
- Exploration of rare cancer subtypes

Given the high failure rate of oncology drugs in clinical trials—up to 95% attrition from preclinical to Phase III, with animal models succeeding in only 8% of cases that reach humans—NIH's new funding environment may accelerate the integration of patient-derived tumor organoids (PDTOs) into precision oncology workflows. Supported by NCI's leadership in the SOM Center for tumor microenvironment modeling, PDTOs could reduce oncology's 52% efficacy failure rate by enabling personalized screening before trials.

9. A Call to Action for the Organoid Community

To seize the opportunity, the field must:

1.Expand organoid infrastructure through biobanks, automation, quality control, and scalable production.

2.Strengthen interdisciplinary collaboration to integrate organoids with computational, engineering, and clinical frameworks.

3.Develop and adopt global standards to support reproducibility and regulatory acceptance.

4.Engage regulators early to co-design validation and qualification pathways.

5.Acknowledge limitations transparently and use complementary models where necessary.

This shift demands leadership, coordination, and scientific rigor. With SOM's $87 million investment and ORIVA's coordination, the community has unprecedented resources to act.

10. Conclusion

The NIH's decision to eliminate animal-only research solicitations and elevate NAMs marks an inflection point in biomedical science. It reflects an evolving understanding that human-relevant, ethical, and mechanistically faithful models—especially organoids—are essential to advancing translational research. The April 29 announcement, workshop formalization, ORIVA proposal, and SOM Center award collectively redirect resources toward innovation, addressing the 90% preclinical failure rate that has plagued drug development.

For the organoid field, the implications are transformative. With increased funding, strengthened infrastructure, deeper regulatory engagement, and global standardization initiatives like ISoOR-ISOB, organoids are now positioned to become a cornerstone of 21st-century biomedical research. The transition will be complex, but the opportunity is unparalleled. As organoids become more physiologically integrated—incorporating vasculature, immune components, multi-organ interactions, and computational modeling—their capacity to replace or complement animal models will only grow.

The age of organoid-centered biomedical innovation has begun, and the NIH's 2025 policy shift marks the official start of this new scientific era.

References

[1] National Institutes of Health (NIH). NIH Funding Announcements to Align with NIH Initiative to Prioritize Human-based Research. Extramural Nexus, July 8, 2025. https://grants.nih.gov/news-events/nih-extramural nexusnews/2025/07/nih-funding-announcements-to-align -with-nih-initiative-toprioritize-human-based-research

[2] FDA and NIH. Workshop on Reducing Animal Testing, July 7, 2025. Full recording and agenda: https://www.fda.gov/science-research/fda-scienceforum/fda-nih-workshop-reducing-animal-testing-07072025

[3] Physicians Committee for Responsible Medicine (PCRM). In Landmark Shift, NIH Announces It Will No Longer Solicit Animal-Only Research. News Release, July 8, 2025. https://www.pcrm.org/news/news-releases/landmarkshift-nih-announces-no-more-exclusive-funding-animal-experiments

[4] Applied Policy. FDA and NIH Initiatives Part of Move Away From Animal Testing. June 28, 2025. https://www.appliedpolicy.com/fda-and-nihinitiatives-part-of-move-away-from-animal-testing/

[5] Federation of American Societies for Experimental Biology (FASEB). New NIH Policy Announced at Joint FDA-NIH Workshop on Reducing Animal Testing. Washington Update, July 24, 2025. https://www.faseb.org/journalsand-news/washington-update/new-nih-policy-announced-at-joint-fda-nihworkshop-on-reducing-animal-testing

[6] NIH Extramural Nexus. Standardized Organoid Modeling Center to Reduce Reliance on Animal Modeling. September 25, 2025. https://grants.nih.gov/news-events/nih-extramural-nexusnews/2025/09/standardized-organoid-modeling-center-to-reduce-reliance-onanimal-modeling

[7] U.S. Food and Drug Administration (FDA). FDA Releases Draft Guidance on Reducing Testing on Non-Human Primates for Monoclonal Antibodies. Press Release, December 2, 2025. https://www.fda.gov/news-events/pressannouncements/fda-releases-draft-guidance-reducing-testing-non-humanprimates-monoclonal-antibodies

[8] Fierce Biotech. NIH Earmarks $87M for New Organoid Center as Pivot Away from Animal Testing Continues. September 29, 2025. https://www.fiercebiotech.com/biotech/nih-earmarks-87m-new-organoidcenter-pivot-away-animal-testing-continues

[9] BioPharm International. New Draft Guidance Highlights FDA Push Toward Human-Relevant Safety Models. December 3, 2025. https://www.biopharminternational.com/view/new-draft-guidance-highlightsfda-push-toward-human-relevant-safety-models

[10] Mak IW, Evaniew N, Ghert M. Lost in translation: animal models and clinical trials in cancer treatment. Am J Transl Res. 2014;6(2):114-118. PMID:24489990; PMCID: PMC3902221.

[11] International Society of Organoid Research (ISoOR). ISoOR-ISOB: International Standards for Organoid Biobanking. March 2025. https://www.isoor.org/isoor-isob

[12] FASEB. FASEB Comments on Joint FDA-NIH Workshop on Reducing Animal Testing. July 16, 2025. https://www.faseb.org/journals-andnews/latest-news/faseb-comments-on-joint-fda-nih-workshop-on-reducinganimal-testing

[13] TheWell Bioscience. Tracking Progress: Key Milestones Toward Animal-Free Research with NAMs. September 30, 2025. https://www.thewellbio.com/news/tracking-progress-key-milestones-towardanimal-free-research-with-nams/

[14] BioPharma Dive. FDA Details Plan to Scale Back Animal Tests for Some Antibody Drugs. December 2, 2025. https://www.biopharmadive.com/news/fda-non-human-primate-testingmonoclonal-antibodies-guidance/806779/

[15] OncoDaily. FDA Issues Draft Guidance to Reduce Non-Human Primate Testing for Monoclonal Antibodies. December 3, 2025. https://oncodaily.com/industry/fda-3