National Institutes of Health
Division of Program Coordination, Planning, and Strategic Initiatives

NIH PRIORITIZATION OF HUMAN-BASED RESEARCH

WARREN CASEY, PHD, DABT
Executive Director, Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)

NIEHS Division of Translational Toxicology / On Detail to the NIH OD Division of Program Coordination, Planning, and Strategic Initiatives

SCIENTIFIC ADVISORY COMMITTEE ON ALTERNATIVE TOXICOLOGICAL METHODS

SEPTEMBER 11TH , 2025

The Advisory Committee to the NIH Director (ACD)

Accepted by NIH Director in February 2024

The Advisory Committee to the NIH Director (ACD) recommendations to catalyze the development and use of novel alternative methods. Through its Novel Alternative Methods (NAMs) Working Group, the ACD consulted with experts in the field and reviewed input from the community to deliver a final report in December 2023.

ACD Recommendations to Catalyze the Development and Use of NAMs (2024)

1. Prioritize the development and use of **combinatorial NAMs**
2. Establish resources, infrastructure, and collaborations to promote the use of **interoperable, reliable, and well curated/high quality datasets** produced from research using NAMs
3. Promote **effective dissemination and interconnection** of NAMs technologies
4. Invest in **comprehensive training** to bolster continuous advances in NAMs development and use
5. Facilitate **multidisciplinary teams** with expertise across technologies and the lifecycle of NAMs development and use
6. Support and maintain **coordinated infrastructure** to catalyze effective and responsible NAM development and use

Complement-ARIE: Complement Animal Research in Experimentation (2024)

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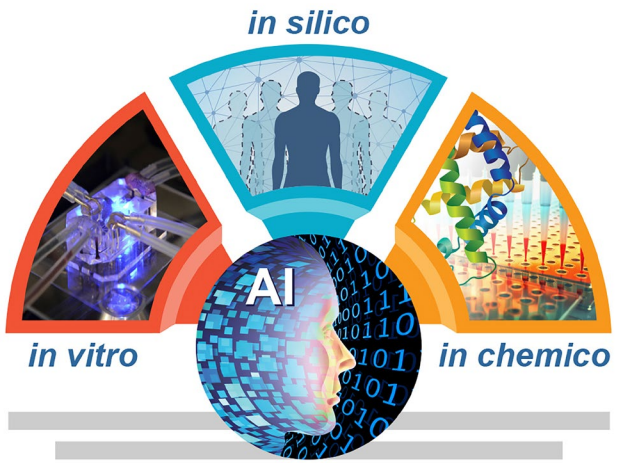
Purpose: To catalyze the development, standardization, validation and use of **human-based new approach methodologies (NAMs)** that will transform the way we do basic, translational, and clinical sciences

Goals:

1. Better model and **understand human health and disease** outcomes **representative of the patient populations**.
2. Develop NAMs that **provide insight into specific biological processes** or disease states.
3. Validate mature NAMs to **support <u>regulatory</u> use** and standardization.
4. Complement traditional models and **make <u>biomedical research</u> more efficient and effective**.



Complement-ARIE website

UNITED STATES ICCVAM Advancing Alternatives to Animal Testing

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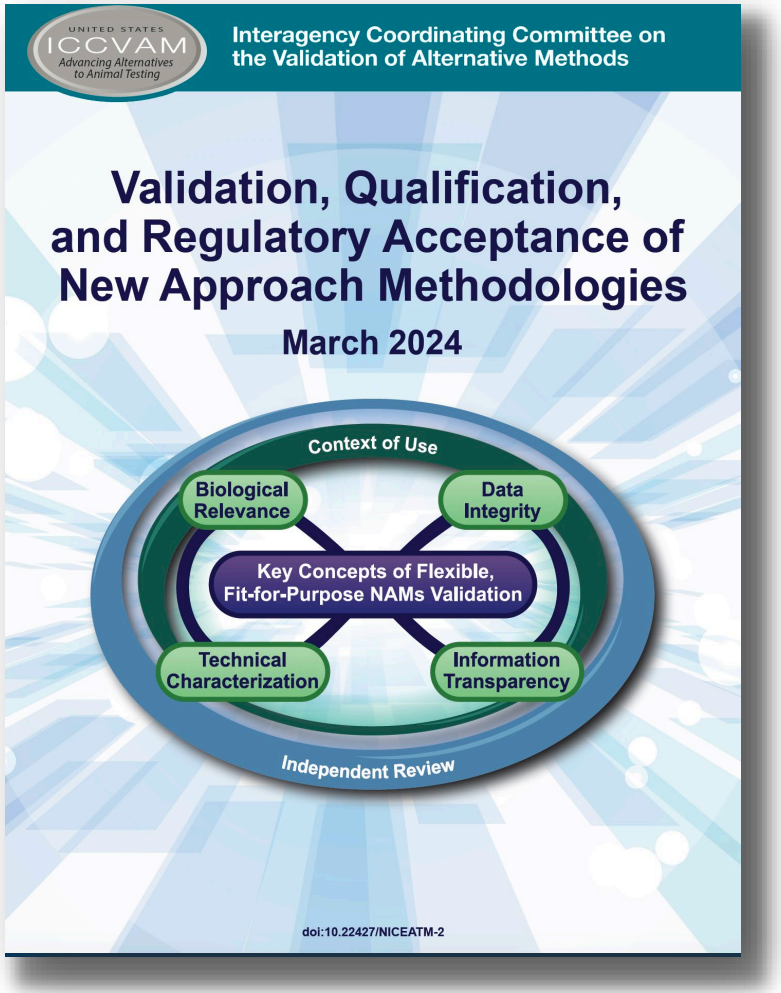
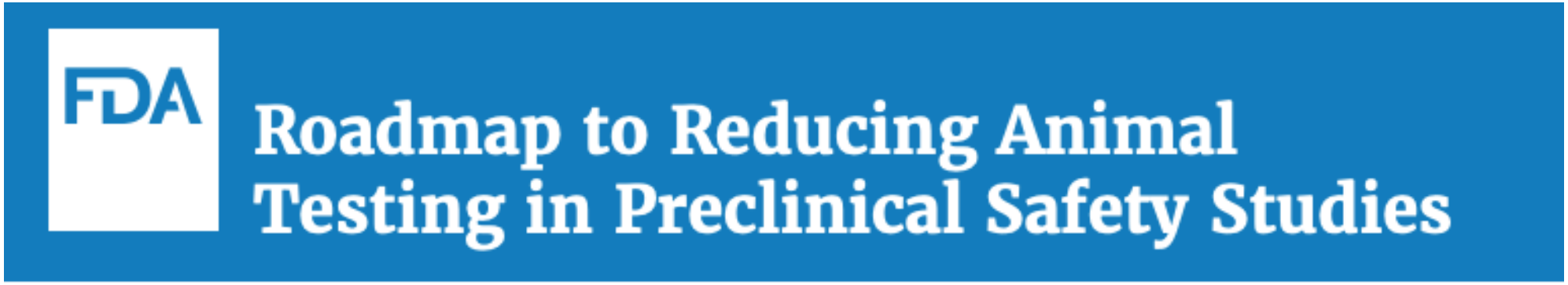
2024



NIH Director's Priorities

1. **Focus on Improving Population Health**: The work of NIH, whether basic or applied, must address the health needs of the American people, including the chronic disease crises that have hampered the well-being of countless Americans.
2. **Reproducibility and Rigor:** The research NIH conducts and supports must be rigorous, reproducible, and unbiased. NIH must address and solve the reproducibility crisis in the biomedical sciences.
3. **Innovation and Collaboration:** NIH must be at the forefront of biomedical innovation. This will involve embracing new technologies, new ideas, and new approaches to old problems.
4. **Research Safety and Transparency:** NIH must ensure that all the experiments we support pose no risk of harm to human populations and meet the highest ethical standards. We must maintain the highest standards of transparency in all our endeavors.
5. **Academic Freedom:** Advances in science require the freedom to think differently from the scientific consensus. NIH will foster an environment where varied perspectives are valued and encouraged at the agency and among the broader scientific community.

FDA Roadmap Announcement, April 10



Executive Summary

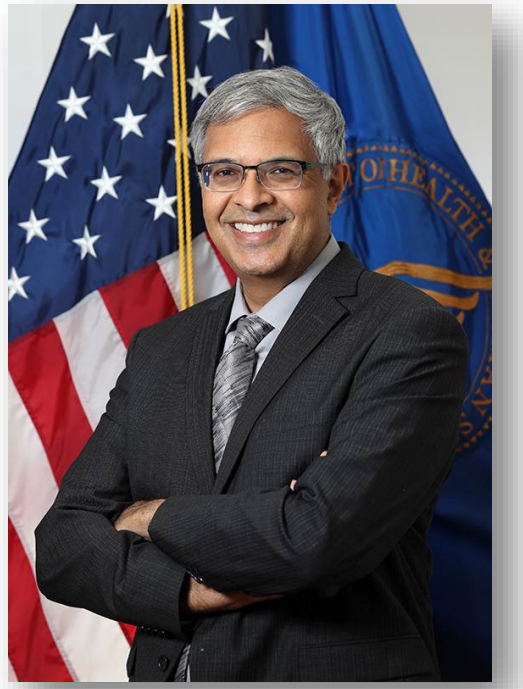
This roadmap outlines a strategic, stepwise approach for FDA to reduce animal testing in preclinical safety studies with scientifically validated new approach methodologies (NAMs), such as organ-on-a-chip systems, computational modeling, and advanced *in vitro* assays. By partnering with federal agencies 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.

Tuesday, April 29, 2025

NIH to prioritize human-based research technologies

New initiative aims to reduce use of animals in NIH-funded research.

"For decades, our biomedical research system has relied heavily on animal models. With this initiative, NIH is ushering in a new era of innovation. By integrating advances in data science and technology with our growing understanding of human biology, we **can fundamentally reimagine the way research is conducted—from clinical development to real-world application**. This human-based approach will **accelerate innovation, improve healthcare outcomes, and deliver life-changing treatments**. It marks a critical leap forward for science, public trust, and patient care."



Jay Bhattacharya, M.D., Ph.D.
Director, NIH

NIH Announcement April 29th, 2025

The National Institutes of Health (NIH) is adopting a **new initiative to expand innovative, human-based science while reducing animal use in research**. Developing and using cutting-edge alternative nonanimal research models **aligns with the U.S. Food and Drug Administration's (FDA) recent initiative to reduce testing in animals in preclinical safety studies.**

NIH Announcement April 29th, 2025

"To integrate innovative human-based science, the NIH intends to **establish the Office of Research Innovation, Validation, and Application (ORIVA)** within NIH's Office of the Director"

NIH Announcement April 29th, 2025

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STATEMENT Friday, August 15, 2025

August 15th, 2025

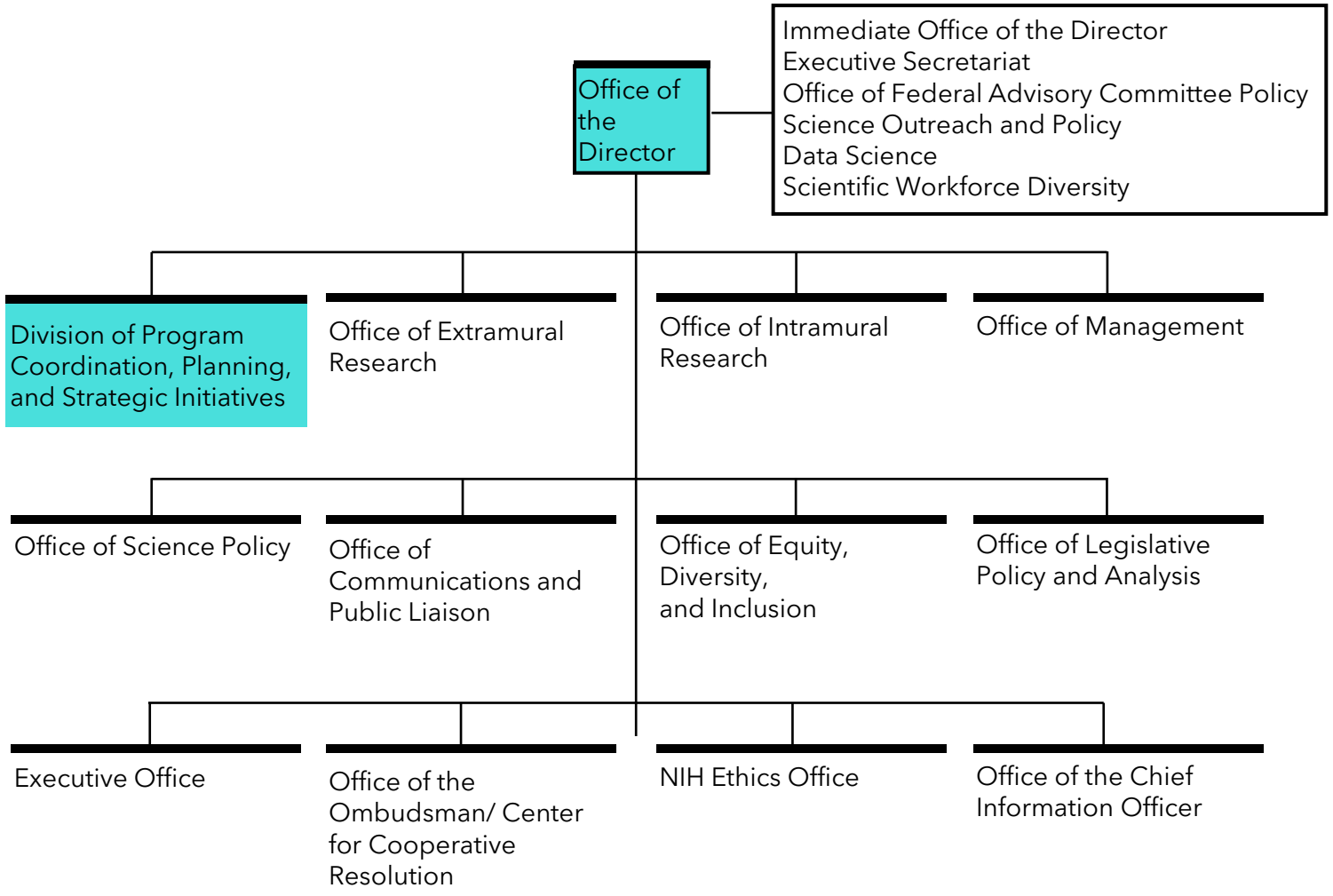
Advancing NIH's Mission Through a Unified Strategy

Priorities include:

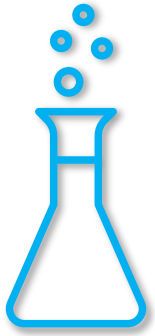
Alternative testing models

NIH is establishing the **Office of Research Innovation, Validation, and Application (ORIVA)** under the Division of Program Coordination, Planning, and Strategic Initiatives, to develop, validate, and scale the use of human-biology-based new approach methodologies (NAMs) to complement animal models and enhance investigations.

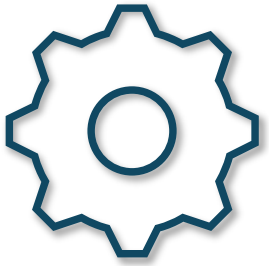
NIH Office of the Director



What Does DPCPSI Do?



Aligns & Catalyzes Science



Develops Resources

Facilitates Strategic Coordination

HOW?

DPCPSI, leading through synergistic **coordination** of its Offices and through vital IC partnerships, **identifies** and **catalyzes** research to address scientific gaps and opportunities, **fosters** collaborations, **develops** methods to enable research goals, and **serves** as an experimental testbed for innovative NIH-wide activities to improve the health of the Nation.

DPCPSI Director's Priorities

1. **Transformative Science via Strategic Investments**: Identify/accelerate emerging areas of biomedical research (e.g., NAMs) with strong potential for public health impact through cross-NIH initiatives that focus on scientific excellence and innovation.
2. **Stronger Partnerships to Amplify NIH Mission**: Cultivate and strengthen collaborations across ICOs, federal agencies, and external stakeholders on initiatives that are responsive to national health priorities and leverage shared expertise and resources.
3. **Data-Driven Decision-Making:** Integrate real-time data, performance metrics, and horizon scanning into DPCPSI processes to inform resource allocation and program planning and evaluation.
4. **Workforce Development and Programmatic Leadership**: Promote innovative training, cross-disciplinary career development, and leadership opportunities that reflect the evolving needs of DPCPSI, NIH, and science and society at large.
5. **Accelerate Translation through Practical Solutions**: Ensure research funded/coordinated by DPCPSI leads to practical, scalable solutions for disease prevention, diagnosis, and treatment by promoting translational readiness, implementation science, and stakeholder engagement.

National Institutes of Health
Division of Program Coordination, Planning, and Strategic Initiatives

Office of Research Innovation, Validation, and Application (ORIVA)

- **Coordinate NIH-wide efforts** to develop, validate, and scale innovative human-based NAMs to improve public heath
- Promote the **development and application of 3Rs principles** (replacement, refinement, reduction) for NIH-funded research
- Create a hub for **interagency coordination and regulatory translation**
- Expand **funding and training** for human-based approaches
- Enhance **awareness of the value** of NAMs in translational research
- Expand **NAMs infrastructure** to improve accessibility
- **Train grant review staff** to address possible bias towards animal studies and integrate NAMs experts into study sections
- **Publicly report on research spending** to measure progress

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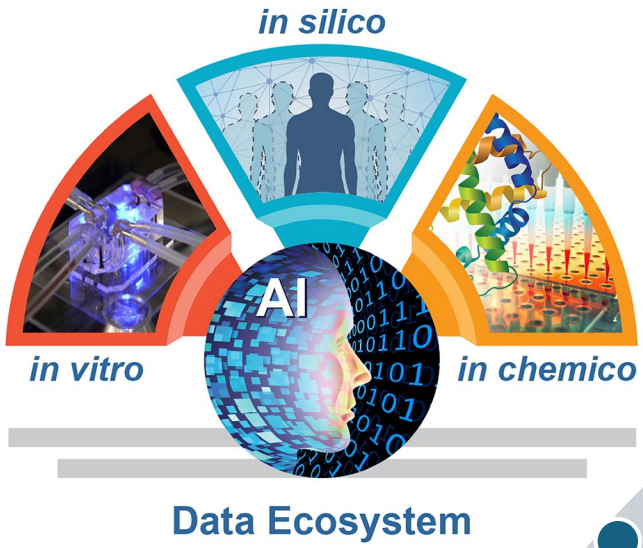


Biomedical Research

Validation/ Qualification

Regulatory Implementation

etc.

ICATM

ICH harmonisation for better health

OECD

The NAMs Confidence Continuum:
from *Biomedical Research* to *Toxicological Application* and *Regulatory Implementation*

NIH-FDA Coordinated Efforts to Advance Goals of Complement-ARIE

- The NIH and FDA have established an MOU to collaborate and coordinate efforts that will promote and accelerate the translational use of NAMs. Efforts include:
  - Providing **regulatory expertise** (FDA) to help support, refine, and advance projects with regulatory potential within Complement-ARIE
  - Holding regular joint **NIH-FDA workshops and meetings** to ensure progress in goals and to develop new policies and initiatives as needed.
  - Engaging **in activities to promote development, adoption, and uptake of NAMs** that may have applicability for FDA regulatory use.
- A similar MOU has also been established with the EPA.

The Standardized Organoid Modeling (SOM) Center

National Mission: A Federally Funded Resource for Standardized Organoid-based New Approach Methodologies (NAMs) for Next Generation Organoid Development

Why the SOM Center?

Standardizing Organoid Technology for Translational Impact

Organoid Power:
Miniaturized human tissue models for disease modeling, drug discovery, toxicity testing.

Major challenges
Current organoid research suffers from *inconsistencies* in protocol → poor reproducibility across labs → research silos

Result
Delays in clinical translation, limited use in regulatory pathways.

SOM Solution
A national resource for standardized organoid-based NAMs across key tissues: liver, heart, lung, intestine.

Mission: Combine AI/ML and expert biology to launch organoids into clinical research and therapeutic validation

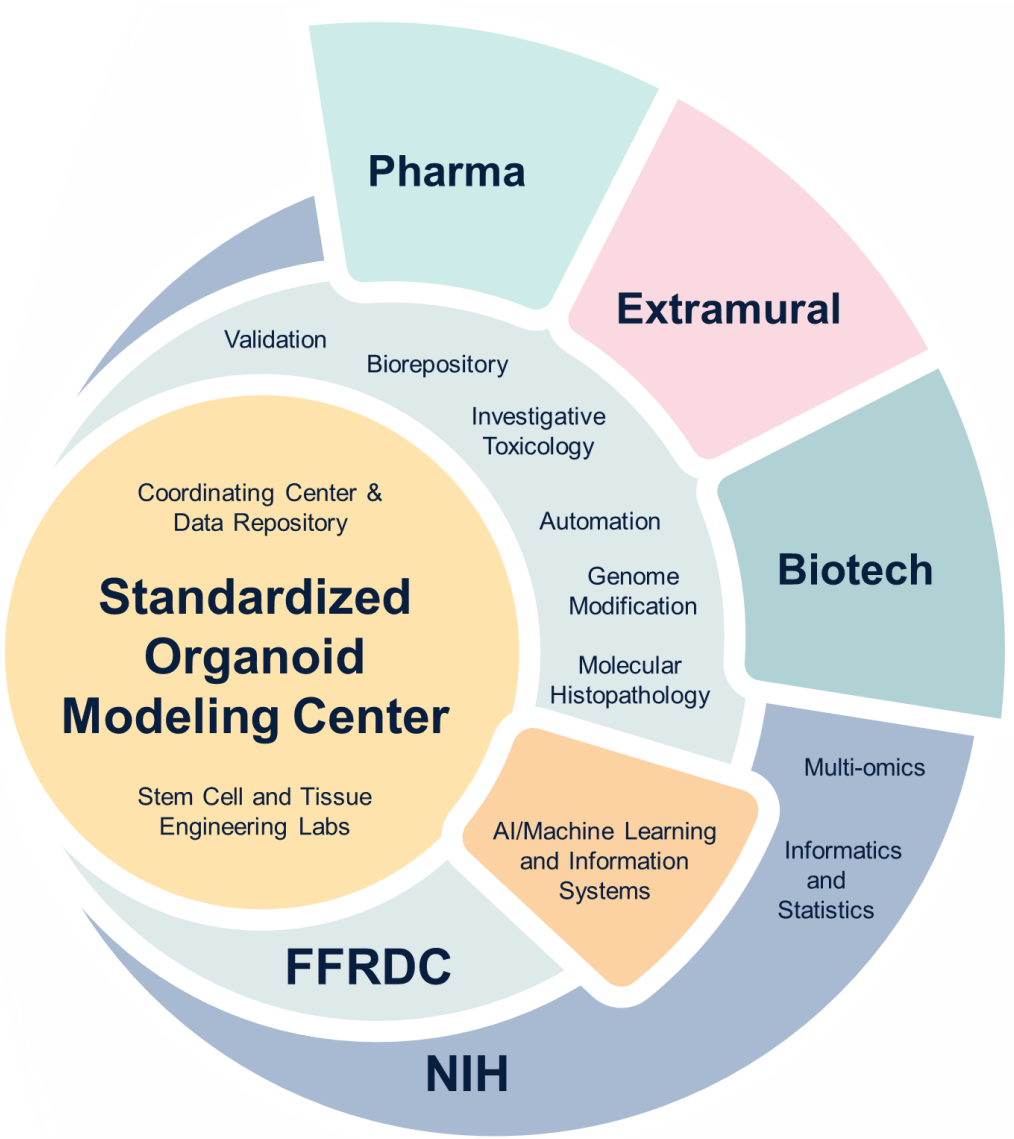
Vision: Standardize/validate Organoid culture for scalable, and reproducible biomedical use to deliver robust, reproducible, and patient-centered solutions transforming drug discovery, disease modeling, and toxicity testing while advancing precision medicine and regulatory science

The NIH's FFRDC

Home for the SOM Center

- Established by the National Cancer Act of 1971 and focuses on human cancer and other diseases.
- In 1975 the FNLCR was designated as a Federally Funded Research and Development Center (FFRDC).
- Frederick National Laboratory is **the only FFRDC dedicated solely to biomedical research.**

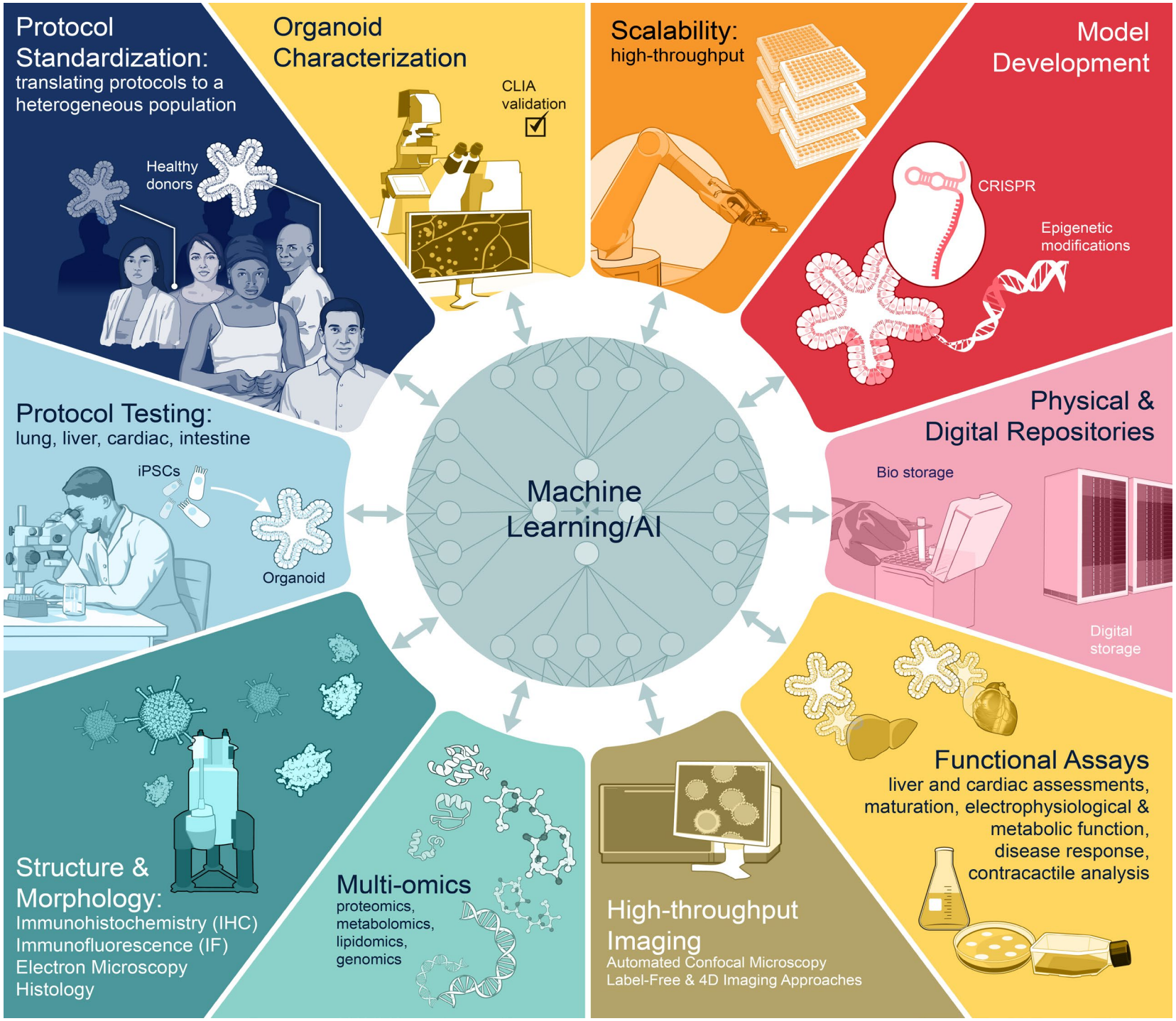
Frederick National Laboratory



Launching a New Era in Translational Biology

Hub & Spoke Resource!

Neutral hub for scientific standardization



NIH Funding Announcements to Align with NIH Initiative to Prioritize Human-based Research

- **Change:** All new Notices of Funding Opportunity (NOFOs) that relate to animal models must now also support human-focused approaches such as clinical trials, real world data, or new approach methods (NAMs).
  - Applicants may continue to propose research exclusively involving human participants, laboratory animals, alternative approaches, or a combination of different models.
  - NIH will continue to support grants that use animal models if they are scientifically appropriate, justifiable, and have appropriate animal welfare oversight.
- **Intent:** Ensure that investigators consider the models most appropriate for understanding human states of health and disease and are not constrained by the NOFO.
- **Example:** A NOFO previously titled "Improved Mouse Models of *X*" will be titled "Improved Models of *X*" and include language on NAMs.

Thank You!

Clarifying Questions?