Complement-ARIE: Complement Animal Research In Experimentation

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Program Leader
Re-engineering the Research Enterprise
Office of Strategic Coordination, NIH/OD

Federal Demonstration Partnership Meeting
May 23, 2024
NIH Recent Activities on NAMs

- Scientific Opportunities
- Report to Congress
- ACD Working Group on NAMs
- Complement-ARIE
The Promise of New Alternatives/Approaches Methods

Significant scientific advances such as complex in vitro systems, bioengineering, stem cells, precision medicine, EHR, AI/ML, and other computational methods

Biotherapeutics and other modalities driving the demand for increasingly sophisticated, human-based methods to study complex biological phenomena

Important for NIH to invest wisely in areas of greatest needs and priorities

NIH aims for a strategic approach to advance use and development of these potentially revolutionary technologies

Timely in view of FDA Modernization ACT 2.0
Report to Congress on NIH Investments on Alternative Methods

Mandate From Congress (March 2022)

1. NIH to appoint a working group to make recommendations for encouraging the use of non-animal models where appropriate (convened May 2022)

2. Report on effectively moving research away from methods that rely on poorly defined animal models to methods that rely on validated non-animal alternatives

3. Report filed with Congress (November 2022)
**Trans–NIH Working Group on New Alternative Methods**

### Co-Chairs
- **Lyric Jorgenson**
  - Acting Director, OSP
- **Danilo Tagle**
  - Director of Office of Special Initiatives, NCATS

### WG Members

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<tr>
<th>Agency</th>
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<td>NIAAA</td>
<td>Mark Egli</td>
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<td>NIAID</td>
<td>Mark Williams</td>
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<td>NIAMS</td>
<td>Richard Cibotti</td>
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<td>NIBIB</td>
<td>Grace Peng, Luisa Russell</td>
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<td>NICHD</td>
<td>Alan Hinnebusch</td>
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<td>NIDA</td>
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<td>NIDCD</td>
<td>Amy Poremba</td>
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<td>NIDDK</td>
<td>Brian Oliver</td>
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<td>NIEHS</td>
<td>Warren Casey</td>
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<td>OD/OSP</td>
<td>Neera Gopee</td>
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<td>OD/IMOD</td>
<td>Brittany Chao</td>
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<td>OD/OSP</td>
<td>Jess Creery</td>
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- Conduct NIH grant portfolio analyses (intramural and extramural) using novel alternative approaches to characterize value and limitations of current NIH investments
- Identify research opportunities away from methods that rely on poorly defined animal models to methods that rely on validated non-animal alternatives
NAMS WORKING GROUP CHARGE
CATALYZE THE DEVELOPMENT AND USE OF NAMs

- Advisory Committee to the Director (ACD) on NAMs convened December 2022

- Identify the types of alternative methods and assess their general strengths and weaknesses for studying human biology, circuits, systems, and disease states

- Characterize the types of research, condition, or disease for which NAMs are most applicable or beneficial

- Articulate high-priority areas for NIH investment in the use and development with human applicability to:
  - Advance progress into understanding specific biological processes or states
  - Augment the tools and capabilities for biomedical research to complement and/or potentially replace traditional models
Timeline of Activities
Gathering Data and Seeking Input

NAMs ACD WG announced

WG meetings and identification of opportunities and challenges

Seek Public Input through RFI

WG meets to determine recommendations and write report

Gathering Data and Seeking Input

NAMs ACD WG charged

Update to the ACD

Public Workshop

Present recommendations to NIH Director
WHAT WE HEARD
IMPORTANCE OF INTEGRATION

HIGH PRIORITY NEEDS

- Interoperable, Reliable Datasets
- Effective Technology Dissemination
- Coordinated Infrastructure
- Multidisciplinary Teams
- Comprehensive Training
- Socially Responsible Technologies
- Combinatorial NAMs
# RECOMMENDATIONS TO CATALYZE THE DEVELOPMENT AND USE OF NAMs

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<td>1</td>
<td>Prioritize the development and use of combinatorial NAMs</td>
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<td>Establish resources, infrastructure, and collaborations to promote the use of interoperable, reliable, and well curated/high quality datasets produced from research using NAMs</td>
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<td>3</td>
<td>Promote effective dissemination and interconnection of NAMs technologies</td>
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<td>4</td>
<td>Invest in comprehensive training programs to bolster continuous advances in NAMs development and use</td>
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<td>5</td>
<td>Facilitate multidisciplinary teams with expertise across technologies and the lifecycle of NAMs development and use</td>
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<td>6</td>
<td>Promote social responsibility in both the creation and deployment of NAMs across the research lifecycle</td>
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<td>7</td>
<td>Support and maintain coordinated infrastructure to catalyze effective and responsible NAMs development and use</td>
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OUR VISION

An integrated ecosystem to catalyze scientific discovery
Complement-ARIE
Complement Animal Research In Experimentation
A New NIH Common Fund Program
Common Fund Historical Perspective

2004: NIH Roadmap is launched

December 9, 2006: Congress unanimously reauthorizes the NIH

Establishes the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) within Office of the Director and the NIH Common Fund to provide a dedicated source of funding to enable *trans*-NIH research.
The Common Fund Moves the NIH Mission Forward – Faster

Supporting bold scientific programs that catalyze discovery across all biomedical and behavioral research

Advances areas of biomedical and behavioral research important to the missions of multiple NIH Institutes and Centers

Spurs subsequent biomedical advances that otherwise would not be possible without an initial strategic investment
Features of Common Fund Programs and How They Catalyze Biomedical Discovery

Making substantial investments in time-limited, goal-driven programs that significantly change the trajectory of biomedical research.

- Accelerate emerging science
- Remove research roadblocks
- Enhance the research workforce
- Support high-risk, high-reward science
Common Fund Science and Management are Collaborative

Scientists from diverse disciplines provide input as we plan new programs.

Researchers participate in interdisciplinary consortia to tackle shared goals.

Leadership and staff from Institutes, Centers, and the Office of the Director work together to design funding opportunities and oversee the projects.
Statement of Purpose and Goals of Complement-ARIE

**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 across diverse populations**.
2. Develop NAMs that **provide insight into specific biological processes** or disease states.
3. Validate mature NAMs to **support regulatory use** and standardization.
4. Complement traditional models and **make biomedical research more efficient and effective**.
Complement-ARIE Working Group

**Working Group Members**
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**Strategic Vision & SME**
Nicole Kleinstreuer, NIEHS

**Common Fund Points of Contact**
Katelynn Milora, OSC  
Tony Casco, OSC

**Scientific Review Contact**
Jessica Smith, CSR
**Complement-ARIE Program Development Timeline**

**NIH Common Fund**
**Complement-ARIE Working Group**

**June**: NIH Common Fund selects concept proposal and convened Complement-ARIE WG

**June–October**: Program Planning/Development
- **Deep landscape analysis**
  - data infrastructure needs
  - current use of NAMs
- **Listening sessions (roundtables)**
  - engage investigators and
  - current challenges in NAM development
- **Inter-agency workshop**
  - Shared interests with other stakeholders in the NAM space (Oct. 19-20)
- **Ideation/Design Prize**
  - engage community
  - identify opportunities in NAM development, validation, and adoption

**Nov - Jan**: Concept refinement and approvals for continued development and implementation
- ICD presentation (Dec 21, 2023)
- Council of Councils (January 25, 2024)

**June 2023**
- June 8-9 ACD WG present preliminary findings

**July 2023**
- June – November: ACD WG Stakeholder Engagement
- Expert Workshop on “Catalyzing Development and Use of Novel Alternative Methods – August 21-22 (videocast)
  - Closed September 5

**August 2023**

**Sept 2023**

**Oct 2023**

**Nov 2023**

**Dec 2023**

**Jan 2024**
- December 14 ACD WG present final report w/recommendations
- February 2, 2024 NIH Director accepts Recommendations

**NIH ACD Working Group on Catalyzing the Development and Use of NAMs to Advance Biomedical Research**
Complement-ARIE Program: Major Work Products

Program Goals:

NAMs that incorporates the following features:

- Complex *in vitro* models emulating population diversity
- *In silico* multi-scale systems simulating healthy/diseased individuals
- *In chemico* cell-free systems capturing dynamic changes
- Combinatorial NAMs and integrated FAIR datasets and AI- engines for all NAMs
Build on NAMs activities across NIH

**Digital Twin Models**
Digital Twins for treatment of cancers and neuropsychiatric diseases, host-gut microbiome studies

**In Silico Models**
In silico and ML/AI models for neurodegenerative disease, wound healing, learning/behavior, SARS-CoV-2 propagation, many other diseases

**Complex In Vitro Systems**
MPS and 3D organoid models for multiple tissues, organs and disease conditions

**In Chemico Screening**
Tox21 high-throughput studies, biochemical assays for skin irritation, ocular toxicity

**Data Ecosystem**
Strategic planning activities: Stakeholder outreach

- 3 listening sessions were held with major stakeholders (Academia, Industry, NGO, Government, International)

- Federal Inter-agency retreat Oct 19-20, NIH/Natcher
  - NIH, FDA, EPA, NSF, ARPA-H, BARDA, VA, DARPA, NIST, NASA, CPSC, ICCVAM

- Scientific Needs: Innovate and Transform
  - Chronicity
  - Neuroscience
  - Personalized health
  - Cross-disease pathogenesis
  - Population diversity

- Operational Needs: Integrate, Coordinate, and Collaborate
  - Shared data infrastructure
  - Standardized frameworks
  - Validation
  - Training

- Other strategic planning activities informing concept development:
  - Landscape Analysis, Ideation Challenge Prize
The NIH is conducting planning activities to inform a Common Fund research program to **Complement Animal Research In Experimentation (Complement-ARIE)** by catalyzing the development, standardization, validation, and use of New Approach Methodologies (NAMs).

The Common Fund issued the Complement-ARIE Challenge Prize Competition to solicit entries for new methods and approaches in NAMs. Winning solutions provided NIH with information about where innovation can be incorporated into NAMs and what types of new NAMs may benefit from further investment.

Twenty Complement-ARIE Challenge prize winners will share the total prize purse of $1,000,000, with each winning team receiving $50,000 for their innovative solutions.

View the winners on the NIH Common Fund website: [https://go.nih.gov/Complement-ARIEPrizeWinners](https://go.nih.gov/Complement-ARIEPrizeWinners)

Join the Complement-ARIE listserv: [go.nih.gov/ComplementARIE_listserv](go.nih.gov/ComplementARIE_listserv)
Complement-ARIE: Program Structure

• **Technology Development Centers** – stimulate the development of NAMs to fill in areas of greatest need, with emphasis on increased biological complexity and throughput, innovative combinatorial approaches, and data sharing.

• **NAMs Data Hub & Coordinating Center (NDHCC)** – create integrated data structures, including standards for model credibility, improve FAIRness (Findability, Accessibility, Interoperability, and Reusability) of NAM-relevant data, create searchable NAMs repository.

• **Validation and Qualification Network (VQN) for NAMs Adoption and Implementation** – establish common data elements and standardized reporting, apply validation/qualification frameworks, accelerate deployment and regulatory implementation of NAMs.

• **Community Engagement and Training** – promote the development of an inclusive, diverse biomedical research workforce with the skills to build/use new NAMs, community engagement, societal and ethical considerations.

• **Strategic Engagement** – set aside ~2-5% of program funds to dynamically engage with emerging opportunities.
Complement-ARIE Consortium

NAMs Center Activities

- Integrated NAMs Shared Data Infrastructures - Standards & Common Data Elements
- FAIR Principles
- Preclinical & Clinical Datasets

NAMs Comprehensive Technology Development Centers

Center 1
Center 2
Center 3
Center 4
Center 5
Center 6

NAMs Data Hub & Coordinating Center

Validation and Qualification Network (VQN) for NAMs Adoption and Implementation

- ICCVAM/Federal Partners
- Regulatory Partners
- Industry Partners
  - International
  - Non-Profits
  - Others

- Regulatory Authorities
- Standards & Case Studies
- Conformity Assessment
- Market Surveillance
- Market Entrance
- Clinical Safety and Performance
- Quality Management System
- Potential Risks to User

NAMs Comprehensive Technology Development Centers

Center 1
Center 2
Center 3
Center 4
Center 5
Center 6

NAMs Data Hub & Coordinating Center

Validation & Qualification Framework

Potency Validation

- Regulatory Authorities
- Standards & Case Studies
- Conformity Assessment
- Market Surveillance
- Market Entrance
- Clinical Safety and Performance
- Quality Management System
- Potential Risks to User

Preclinical & Clinical Datasets

Integrated NAMs Shared Data Infrastructures - Standards & Common Data Elements

FAIR Principles

NAMs Data Hub & Coordinating Center (NDHCC)
Potential NIH-FNIH Public-Private Partnership

Validation network for regulatory implementation

Work with comprehensive centers and NDHCC to establish common data elements and standardized reporting, apply validation/qualification frameworks, accelerate deployment and regulatory implementation of NAMs

- Exploring an NIH-FNIH PPP to bring industry, NGOs, non-profits, etc into the network leveraging existing FNIH PPP infrastructure
- Pre-competitive data sharing and potentially supporting validation activities across labs and locations for specific use cases for implementation
- Support community outreach and training
- Provide a fluid funnel for potential solutions which may be developed through the comprehensive centers
- Include additional Federal partners
- Synergize and coordinate with other global activities on NAMs
The diagram illustrates the key components of the Complement-ARIE program including technology development, centralized data resources, Validation and Qualification, along with key training and dissemination activities to provide a fluid conduit from stakeholder engagement to implementation.
Complement-ARIE: Innovate, Integrate, Coordinate, and Transform

- **Innovate** understanding of human health and disease pathways across diverse populations
- **Integrate** innovative NAMs (*in vitro, in chemico, and in silico*) with AI and FAIR data ecosystems
- **Coordinate** with ICs, agencies, and public-private partnerships
- **Transform** the way we do basic, translational, and clinical sciences by leveraging the full scientific toolbox
Questions/Discussion

To learn more about Complement-ARIE Program, visit:
https://commonfund.nih.gov/complementarie