

Complement-ARIE: Complement Animal Research In Experimentation

Dan Shaughnessy

Co-Program Coordinator

NIEHS/DERT/ERTB

National Advisory Environmental Health
Council

Sept 12, 2024

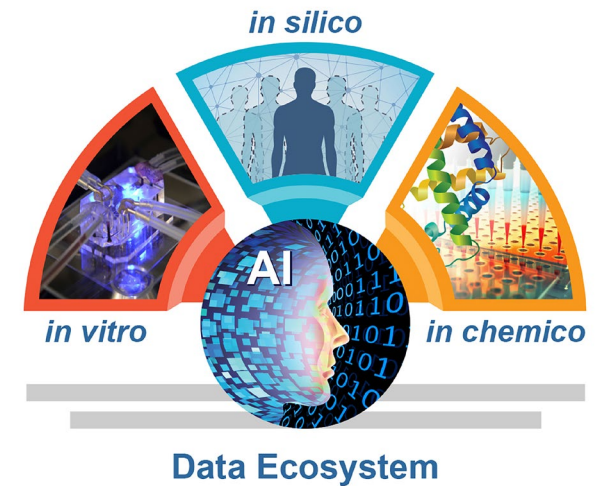


Statement of Purpose and Goals of Complement-ARIE

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



The Common Fund

Working Group Co-Chairs

Joni Rutter, NCATS

Rick Woychik, NIEHS

Common Fund Program Leaders

Margaret Ochocinska, OSC

Christy Kano, OSC

Program Coordinators

Dan Tagle, NCATS

Dan Shaughnessy, NIEHS

Strategic Vision & SME

Nicole Kleinstreuer, NIEHS

Common Fund Points of Contact

Katelynn Milora, OSC

Tony Casco, OSC

Scientific Review Contact

Jessica Smith, CSR

Working Group Members

Elaine Collier, NCATS

Passley Hargrove-Grimes, NCATS

Christine Happel, NCATS

Chariz Johnstone, NCATS

Dmitriy Krepkiy, NCATS

Dobriela Rudnicki, NCATS

Geetha Senthil, NCATS

Kris Sunderic, NCATS

Leah Tolosa-Croucher, NCATS

Elizabeth (Liz) Ginexi, NCCIH

Steven Becker, NCI

Elizabeth (Liz) Glaze, NCI

Ron Johnson, NCI

Erin Lavik, NCI

Altaf Mohammed, NCI

Asif Rizwan, NCI

Martha Flanders, NEI

Gus Matute-Bello, NHLBI

Regina Bures, NHLBI

Jue Chen, NHLBI

Dina Paltoo, NHLBI

Rahul Thakar, NHLBI

Nandini Arunkumar, NIA

Tiziana Cogliati, NIA

Chhanda Dutta, NIA

Zane Martin, NIA

Suzana Petanceska, NIA

Larry Refolo, NIA

Fei Wang, NIA

Mark Egli, NIAAA

Liliana Brown, NIAID

Jim Cherry, NIAID

Candace Kerr, NIAID

Shilpa Kulkarni, NIAID

Melody Mills, NIAID

Reed Shabman, NIAID

Uday Shankar, NIAID

Dave Yeung, NIAID

Aron Marquitz, NIAMS

Jermont Chen, NIBIB

Sai Majji, NICHD

Jagpreet Nanda, NICHD

Aaron Pawlyk, NICHD

Kathleen Borgmann, NIDA

Nancy Freeman, NIDCD

Preethi Chander, NIDCR

William Cefalu, NIDDK

Albert Hwa, NIDDK

Warren Casey, NIEHS

Chris Duncan, NIEHS

David Fargo, NIEHS

Jacqui Marzec, NIEHS

Kim McAllister, NIEHS

Ravi Ravichandran, NIEHS

Yael Mandelblat-Cerf, NIMH

Sarah Woller, NINDS

Julia Bachman, NINDS

Joseph Monaco, NINDS

Grace Hwang, NINDS

Vamsi Kodali, NLM

Lauren Topper, NLM

Jessica Creery, OD

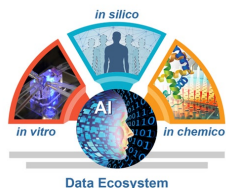
Matthew Arnegard, OD

Yanli Wang, ODSS

Sige Zou, ORIP

Oleg, Mirochnitchenko, ORIP

Janine Clayton, ORWH



Data Ecosystem

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**)

NIH ACD Working Group on Catalyzing the Development and Use of NAMs to Advance Biomedical Research

June 2023

June 8-9 ACD WG present preliminary findings

July 2023

August 2023

Sept 2023

Oct 2023

Nov 2023

Dec 2023

Jan 2024

June – November:

ACD WG Stakeholder Engagement

Expert Workshop on “Catalyzing Development and Use of Novel Alternative Methods – August 21-22 (videocast)

RFI published:

<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-23-140.html>

Closed September 5

December 14

ACD WG present final report w/recommendations

February 2, 2024
NIH Director accept



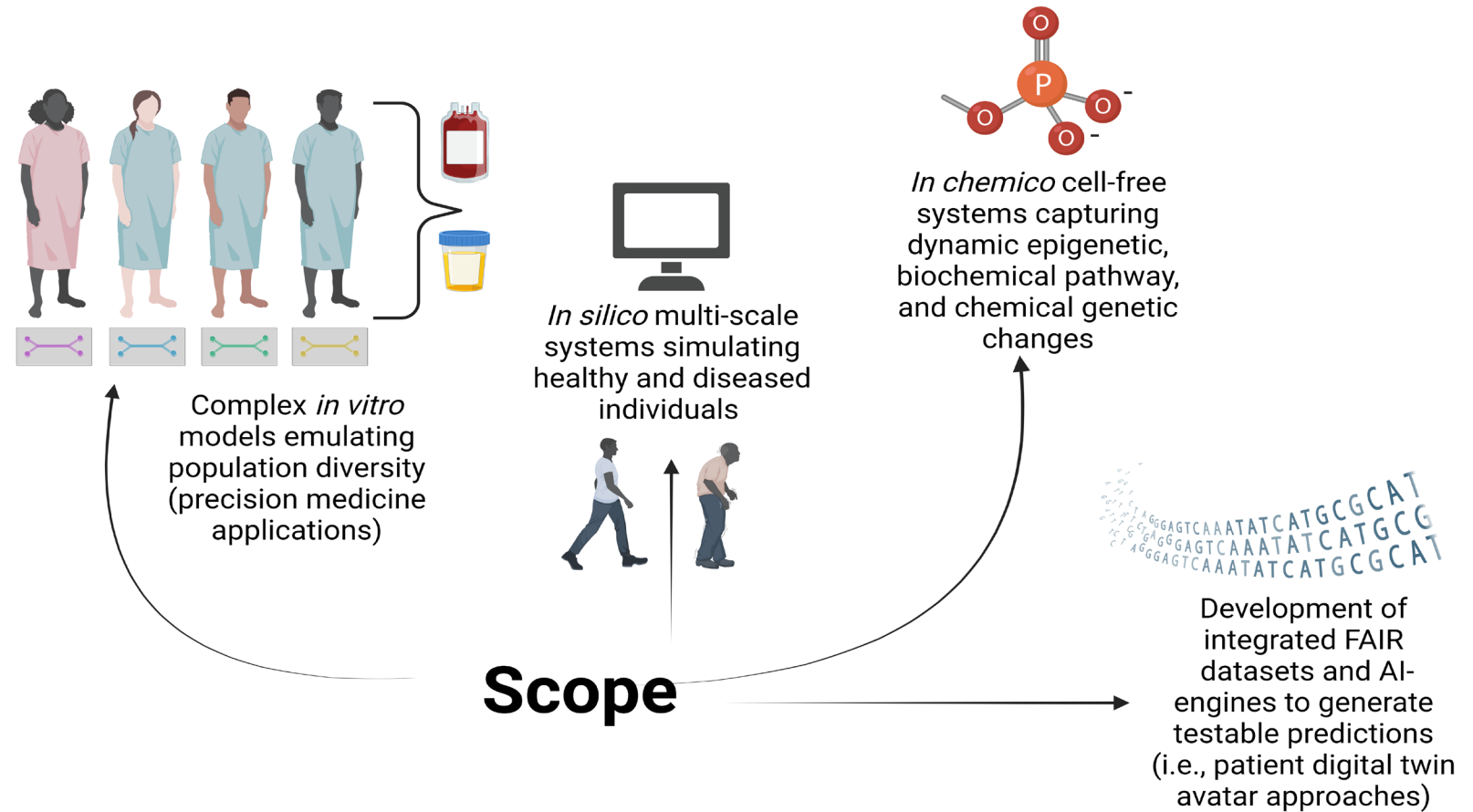
NIH National Center for Advancing Translational Sciences

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

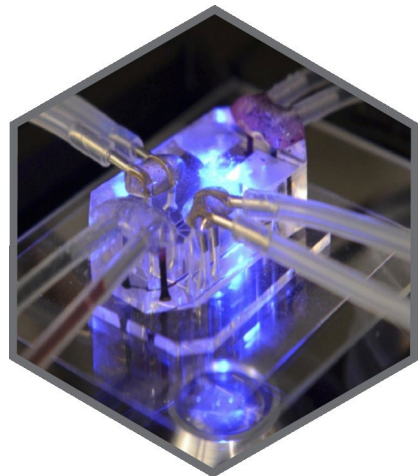
Digital Twin Models

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

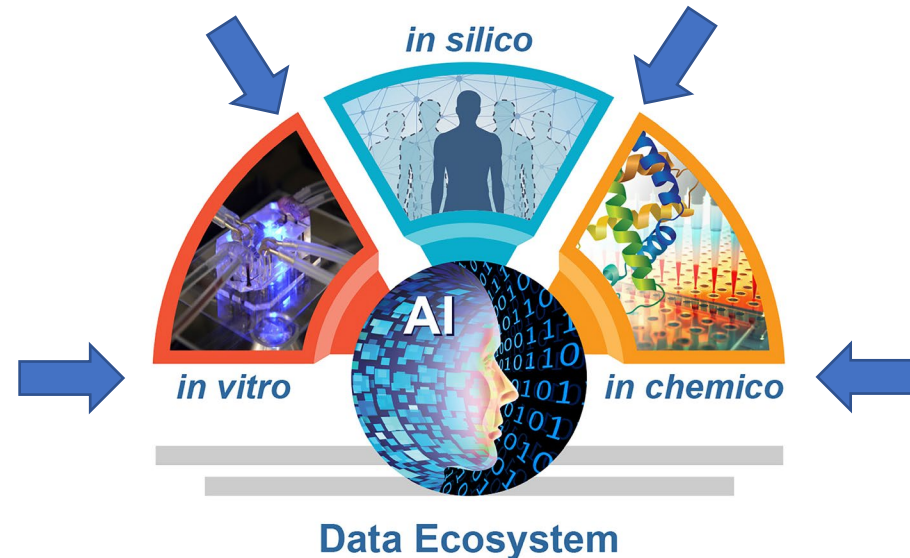


In Silico Models

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

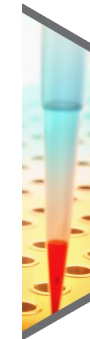


Complex In vitro
MPS and 3D cell culture
for multiple treatment
and disease conditions



In Chemico Screening

Tox21 high-throughput studies, biochemical assays for skin irritation, ocular toxicity



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



Complement-ARIE Landscape Analysis

The NIH Common Fund **Complement Animal Research In Experimentation (Complement-ARIE) program** released a comprehensive landscape analysis on the field of New Approach Methodologies (NAMs)

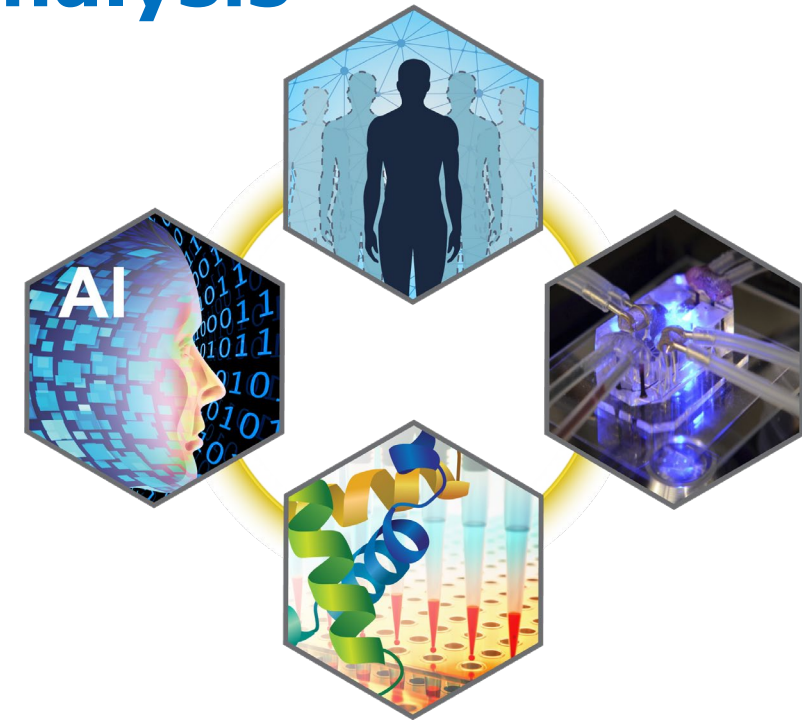
This analysis was conducted as part of strategic planning to inform the Complement-ARIE program.

The analysis describes existing efforts, and highlights gaps, challenges, and opportunities in the following areas of NAMs:

- **In vitro** models
- **In silico** models
- **In chemico** cell-free models
- **FAIRness of data needed to train, interpret, and use NAMs** (FAIR = findable, accessible, interoperable, reusable)

View the landscape analysis: go.nih.gov/complement-arie_landscape

Join the Complement-ARIE listserv: go.nih.gov/ComplementARIE_listserv



Link to Complement-ARIE comprehensive landscape analysis on NAMs

Complement-ARIE Concept Prize Competition

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)

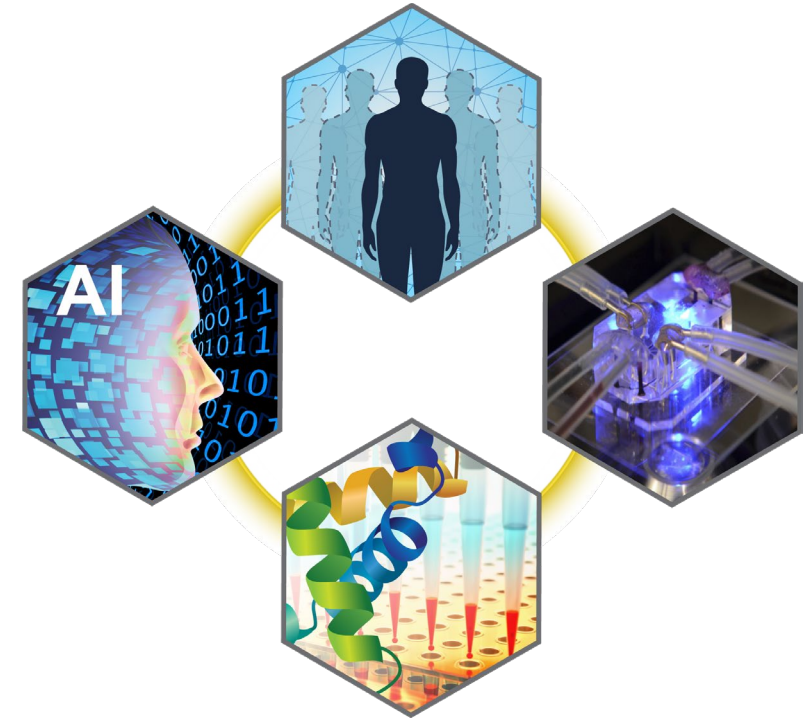
The Common Fund issued the Complement-ARIE Challenge Prize Competition to solicit entries for new methods and approaches in NAMs. Winning solutions provided NIH with information about where innovation can be incorporated into NAMs and what types of new NAMs may benefit from further investment.

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>

Join the Complement-ARIE listserv: go.nih.gov/ComplementARIE_listserv



Link to Complement-ARIE Challenge
winner announcement

Complement-ARIE Prize Competition Winner Highlights

• **[Click Chemistry Magic for Drug Screening](#)**. Novel chemistry NAM for high throughput drug screening, tissue engineering, and precision medicine.

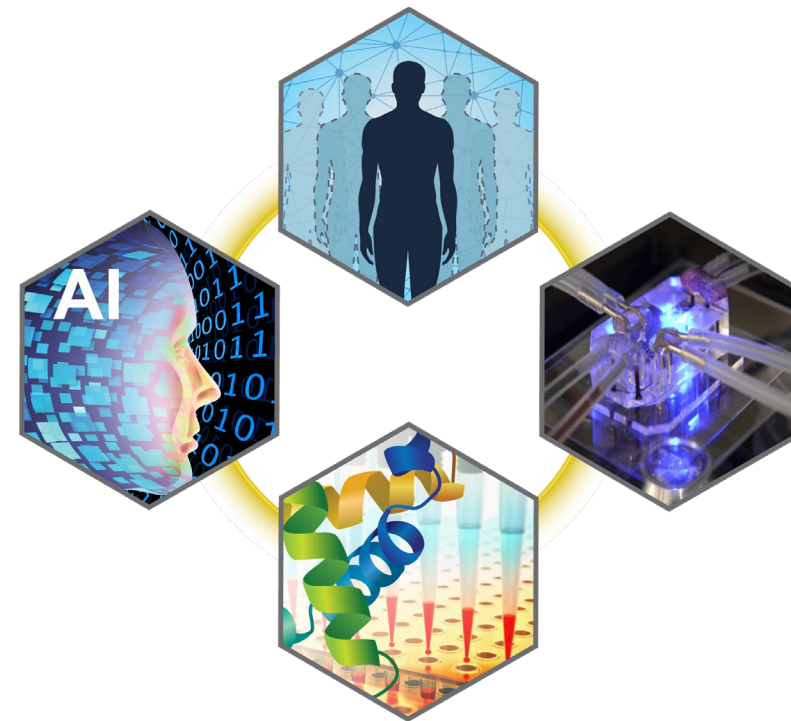
Team: [Delaware Click Chemistry](#)

• **[DevTox - Developmental Toxicity Predictor](#)**. Comprehensive approach for developmental toxicity prediction to enhance maternal drug safety.

Team: [Predictive, LLC](#)

• **[Pulse of the Future: AI-human MEHC](#)**. Integrated solutions to analyze multi-scale engineered heart constructs (MEHC) and model human cardiovascular health and disease

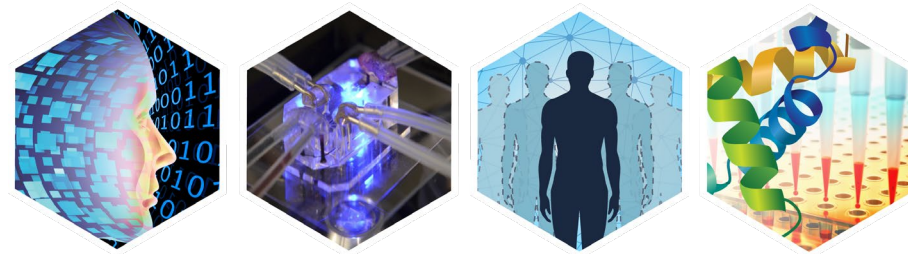
Team: [Pulse of the Future: AI-human MEHC](#)



Link to Complement-ARIE Challenge
winner announcement

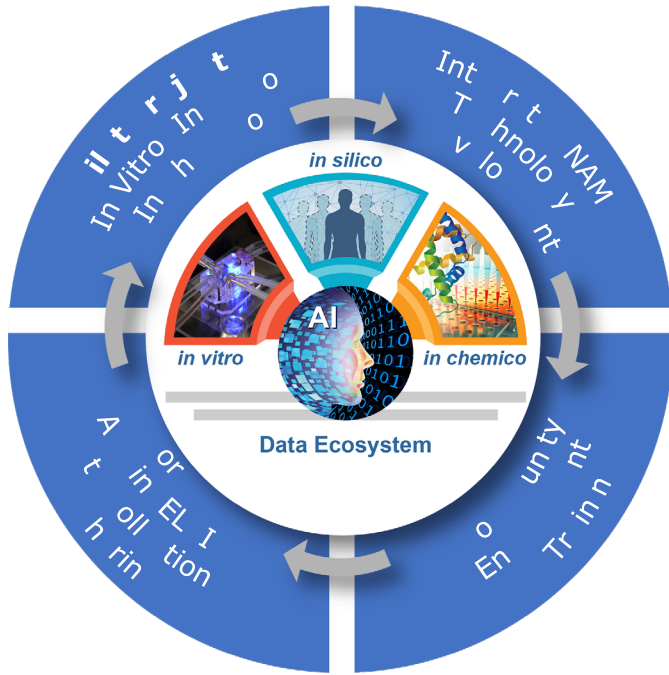
Complement-ARIE: Program Components

- **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.

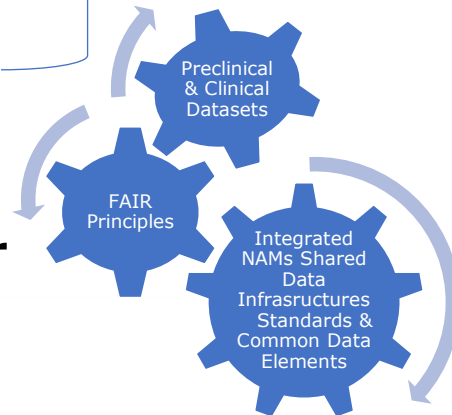


Complement-ARIE Consortium

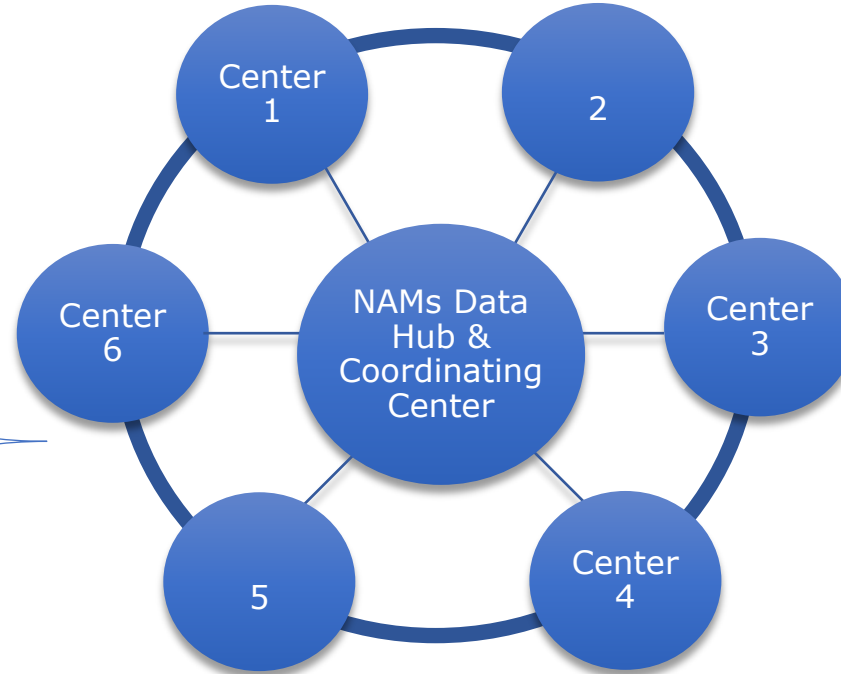
NAMs Center Activities



NAMs Data Hub & Coordinating Center (NDHCC)



NAMs Comprehensive Technology Development Centers



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

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

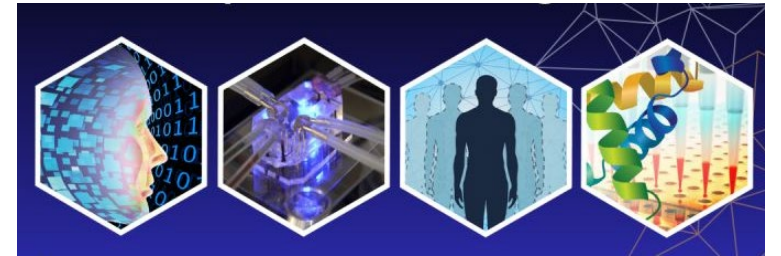


Potential NIH-FNIH Public-Private Partnership

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



Complement-ARIE NAMs Technology Development Center Notice of Intent to Publish a Funding Opportunity

The NIH Common Fund Complement Animal Research In Experimentation (Complement-ARIE) Program **has released a Notice of Intent to Publish a Funding Opportunity.**

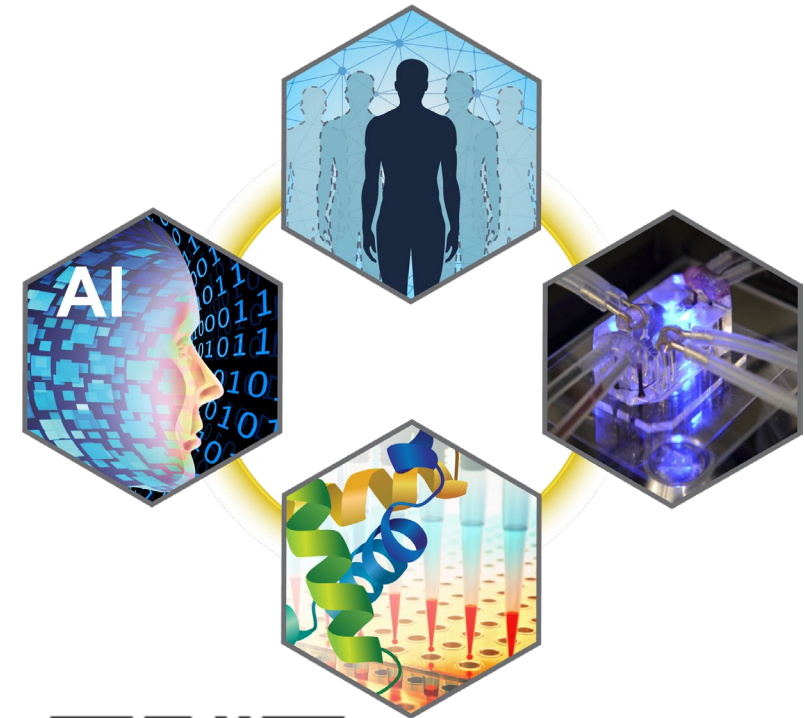
The purpose of this Notice is to alert the research community of a pending funding opportunity to **support Complement-ARIE NAMs Technology Development Centers.**

The goal of the Comprehensive NAMs Technology Development Centers is to stimulate the development of combinatorial NAMs to support the areas of greatest need.

The estimated release date of the NOFO is: **October 18, 2024.**

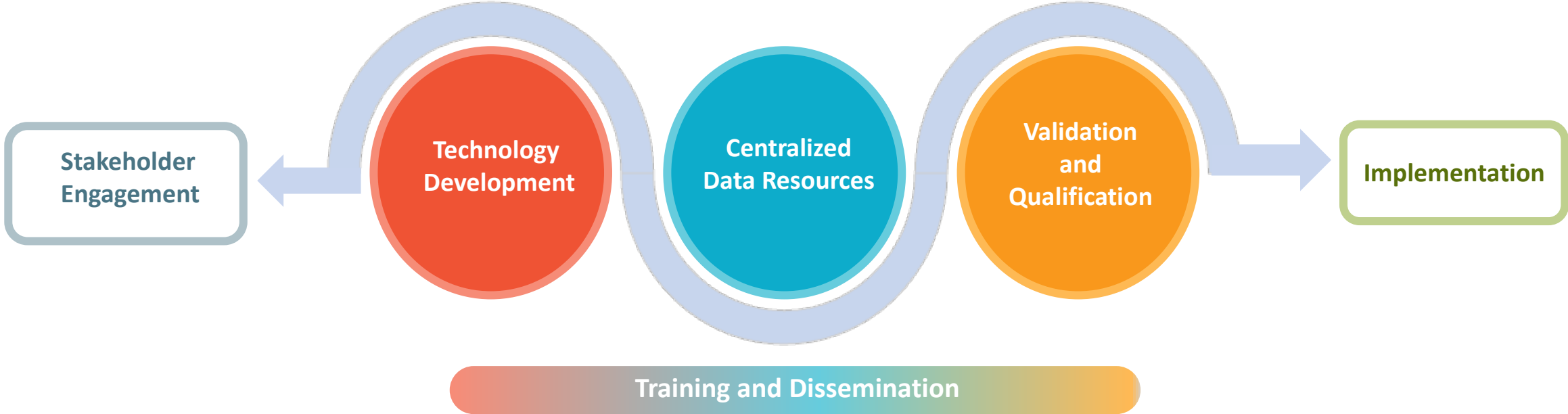
View the Complement-ARIE NOITP: <https://go.nih.gov/iiuNC9v>

Join the Complement-ARIE listserv: go.nih.gov/ComplementARIE_listserv



Link to Complement-ARIE Notice of Intent to Publish a Funding Opportunity

Complement-ARIE: Program Flow Diagram



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.**

Questions / Discussion

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



National Institutes of Health

Office of Strategic Coordination – The Common Fund