

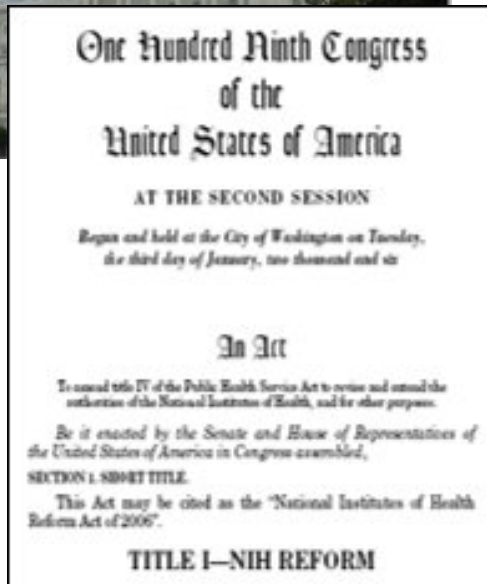
Complement-ARIE: Complement Animal Research In Experimentation

Margaret Ochocinska, PhD

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

2024 Scientific Advisory Committee on
Alternative Toxicological Methods

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

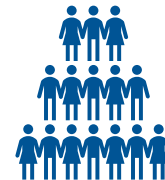
Making substantial investments in time-limited, goal-driven programs that significantly change the trajectory of biomedical research.



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.



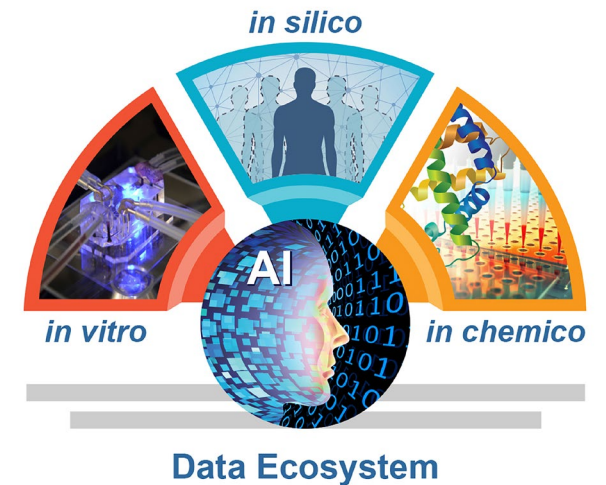
Leadership and staff from Institutes, Centers, and the Office of the Director work together to design funding opportunities and oversee the projects.

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



The Common Fund

Working Group Co-Chairs

Joni Rutter, NCATS
Rick Woychik, NIEHS

Common Fund Program Leaders

Margaret Ochocinska, OSC

Working Group Coordinators

Dan Tagle, NCATS
Dan Shaughnessy, NIEHS

Strategic Vision & SME

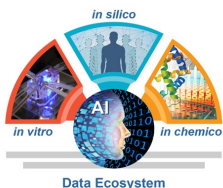
Nicole Kleinstreuer, NIEHS

Points of Contact

Katelyn Milora, OSC, SPEC
Tony Casco, OSC, OPS
Christy Kano, OSC, CDR
Chariz Johnstone, NCATS
Victoria Ledbetter, NIEHS

Scientific Review Contact

Jessica Smith, CSR



Working Group Members

Elaine Collier, NCATS
Passley Hargrove-Grimes, NCATS
Christine Happel, NCATS
Chariz Johnstone, NCATS
Dmitriy Krepiy, NCATS
Dobрила 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
Laura Long, OD
Yanli Wang, ODSS
Oleg Mirochnitchenko, ORIP
Sige Zou, ORIP
David Thomas, ORWH
Janine Clayton, ORWH

Complement-ARIE Program Development Timeline

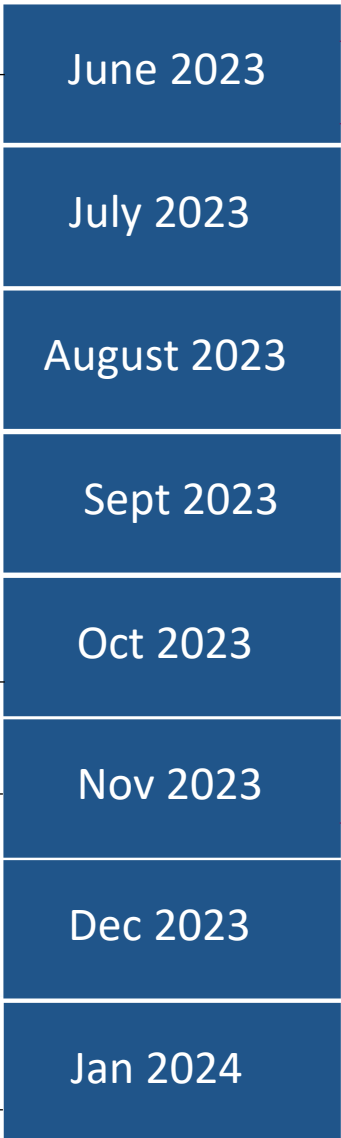
NIH Common Fund Complement-ARIE Working Group

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 8-9 ACD WG present preliminary findings

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

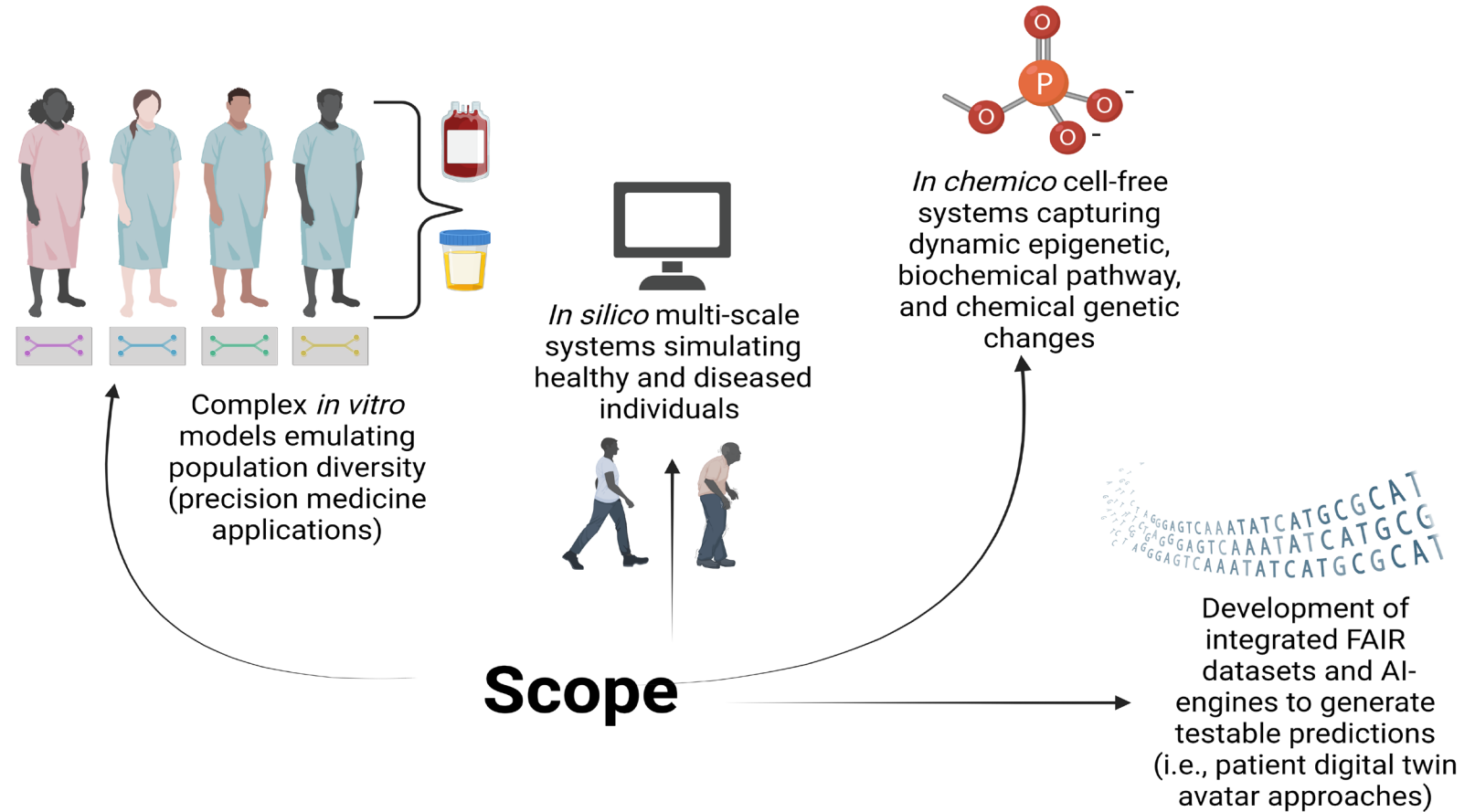
February 2, 2024
NIH Director accepts Recommendations

Complement-ARIE Program: Major Work Products

Program Goals:

NAMs that incorporates the following features:

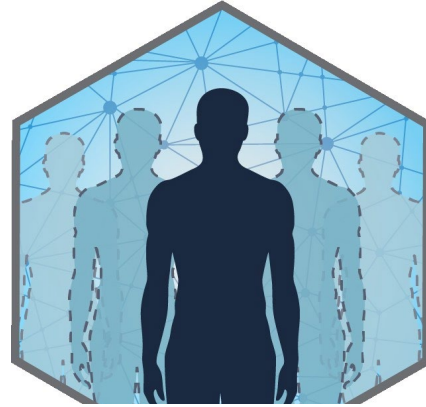
- Complex *in vitro* models emulating population diversity
- *In silico* multi-scale systems simulating healthy/diseased individuals
- *In chemico* cell-free systems capturing dynamic changes
- **Combinatorial NAMs** and integrated **FAIR datasets** and **AI-engines** for all NAMs



Build on NAMs activities across NIH

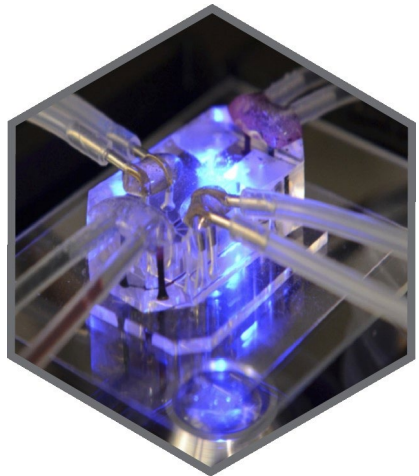
Digital Twin Models

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

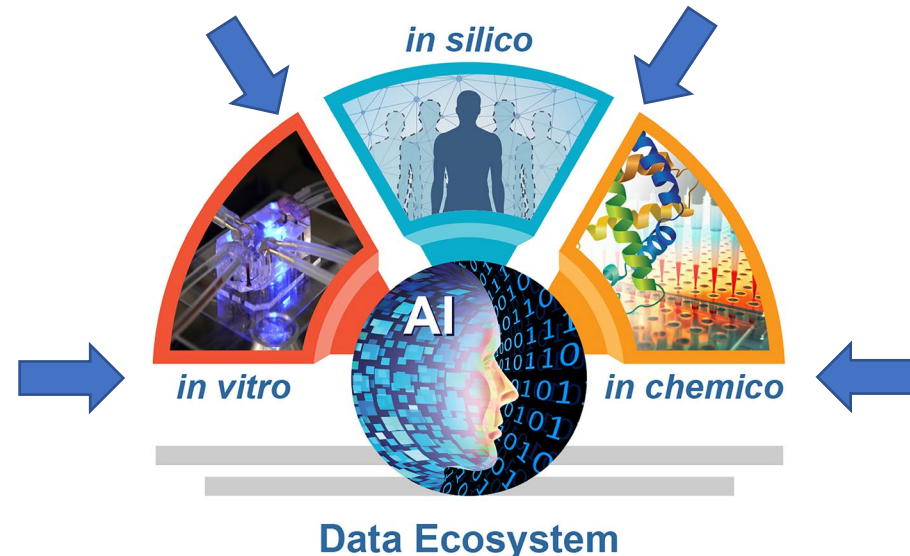
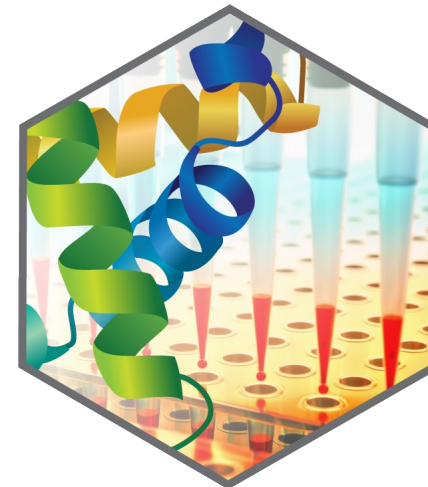


Complex In Vitro Systems

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



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:
 - Ideation Challenge Prize: <https://go.nih.gov/Complement-ARIEPrizeWinners>
 - Landscape Analysis: <https://commonfund.nih.gov/complementarie/strategicplanning/landscape-analysis>



Complement-ARIE Challenge 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)

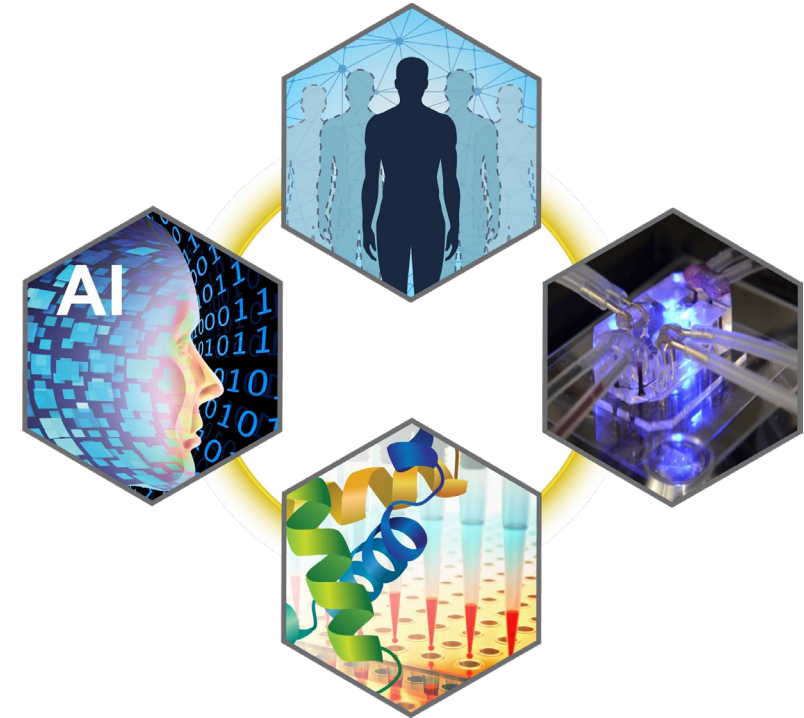
The Common Fund issued the Complement-ARIE Challenge Prize Competition to solicit entries for new methods and approaches in NAMs. Winning solutions provided NIH with information about where innovation can be incorporated into NAMs and what types of new NAMs may benefit from further investment.

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>

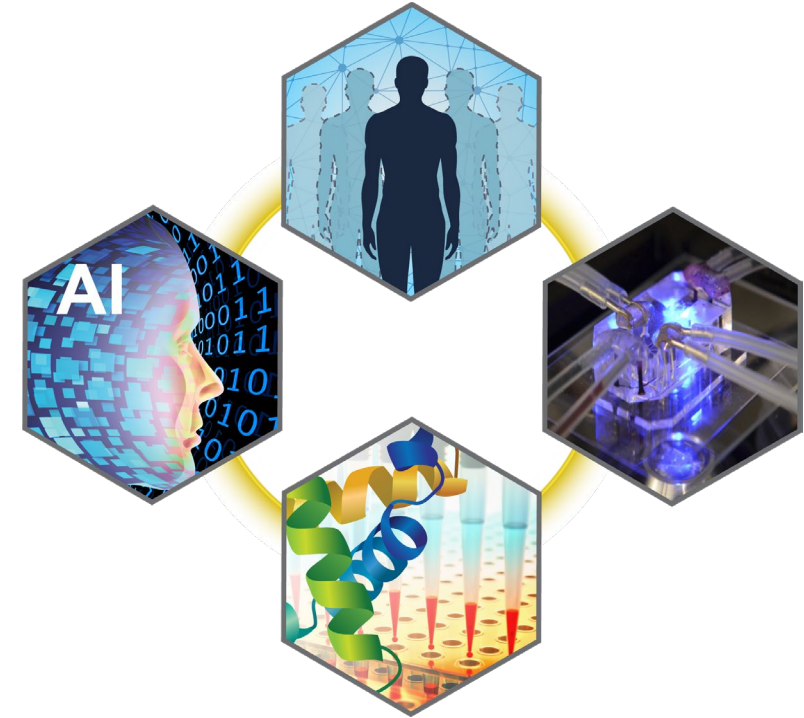
Join the Complement-ARIE listserv: go.nih.gov/ComplementARIE_listserv



Link to Complement-ARIE Challenge
winner announcement

Complement-ARIE Challenge Prize Competition Winner Highlights

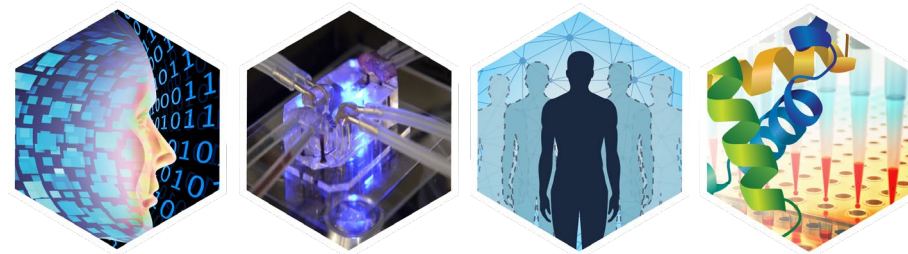
- [Click Chemistry Magic for Drug Screening](#). Novel chemistry NAM for high throughput drug screening, tissue engineering, and precision medicine.
Team: [Delaware Click Chemistry](#)
- [DevTox - Developmental Toxicity Predictor](#). Comprehensive approach for developmental toxicity prediction to enhance 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

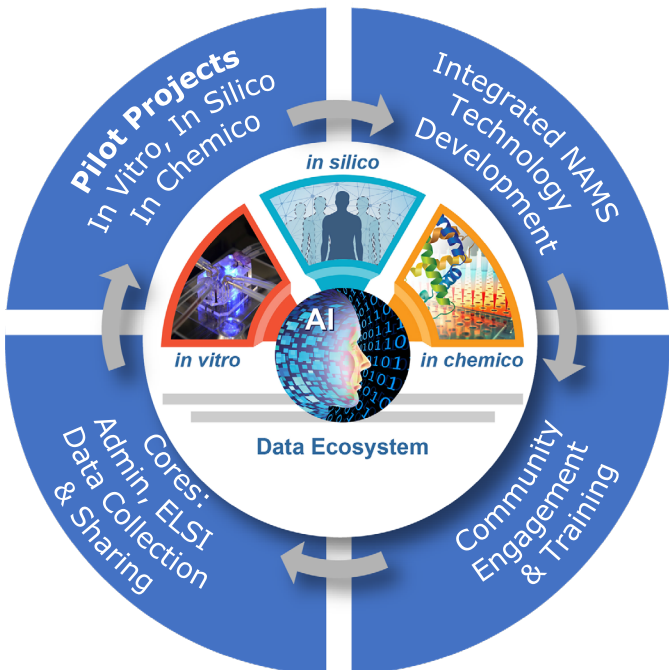
Complement-ARIE: Program Components

- **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.



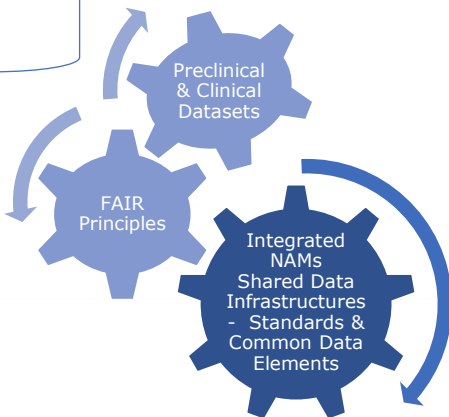
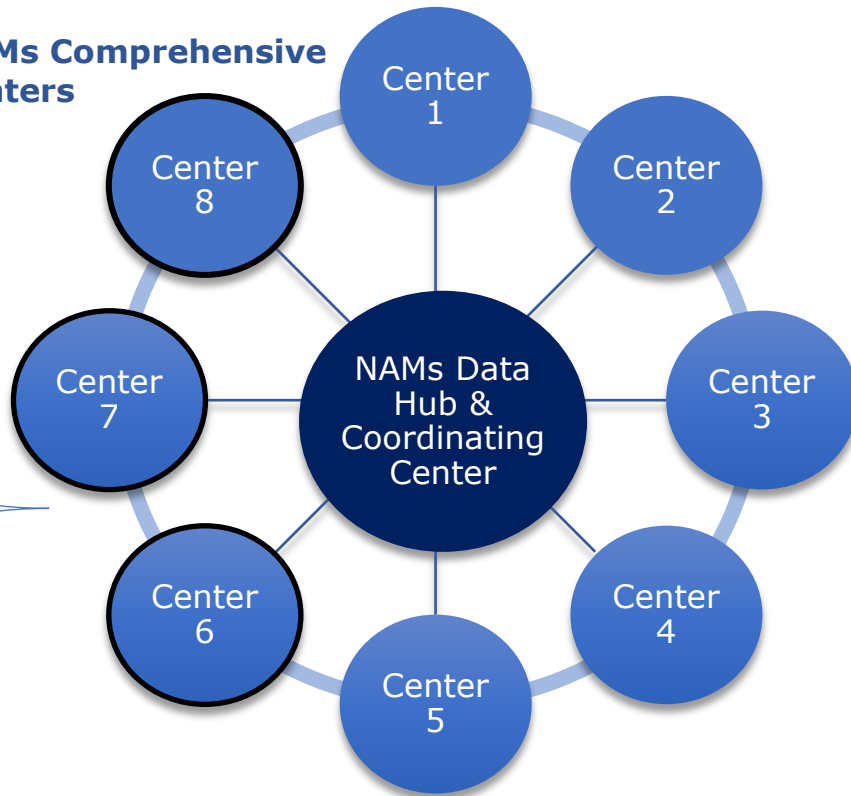
Complement-ARIE Consortium

NAMs Center Activities



NAMs Data Hub & Coordinating Center (NDHCC)

NAMs Comprehensive Centers



Validation & Qualification Network for NAMs Adoption and Implementation

- ICCVAM/Other Agencies
- Regulatory Partners
- Industry Partners
- International
- Non-Profits
- Others



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.**

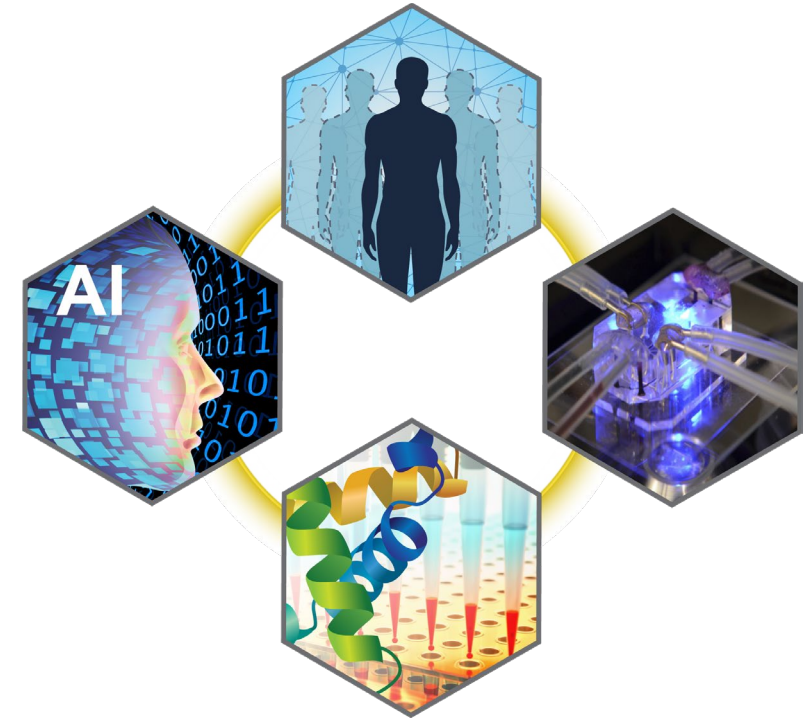
The goal of the Comprehensive NAMs Technology Development Centers is to stimulate the development of combinatorial NAMs to support the areas of greatest need.

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

View the Complement-ARIE NOITP: <https://go.nih.gov/iuuNC9v>

Explore the Complement-ARIE FAQs: <https://commonfund.nih.gov/complementarie/faqs>

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

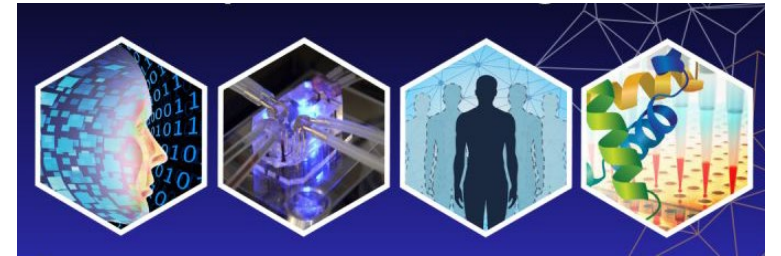


Link to Complement-ARIE Notice of Intent
to Publish a Funding Opportunity

Exploring Potential Public-Private Partnerships

Validation and Qualification Network (VQN) for the Adoption and Implementation of New Approach Methodologies (NAMs)

- Exploring Public-Private Partnerships 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 Validation Network: Three-Phased Approach

1

DESIGN (Year 1)

- Plan, develop network with Industry, NGOs, CROs and fed partners
- Determine scope of validation efforts
- Develop governance/criteria selection of use cases
- Refine goals for network
- ICCVAM subgroup to advise on validation steps
- Workshops with stakeholders

2

IMPLEMENTATION Phase I (Year 2-5)

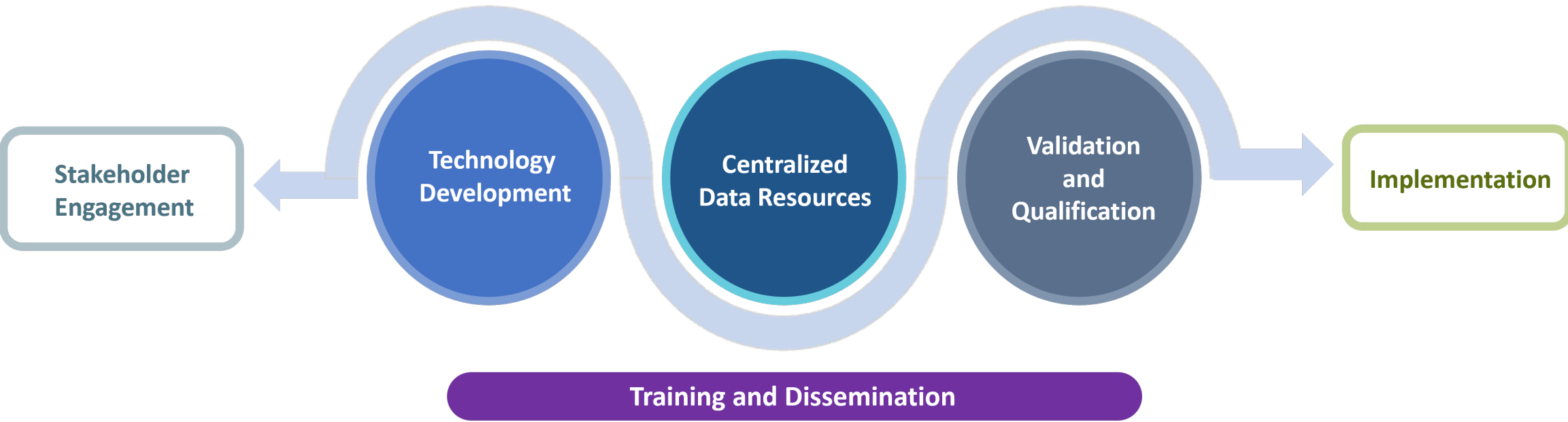
- Implement validation efforts with partners
- Select Use cases (across NAMs categories)
- Fund at least 8 Use Case Validation studies
- Bi-annual reporting
- PPP interactions with Data Hub and training components
- Develop long term sustainability plans

3

IMPLEMENTATION PHASE II (Year 6-10)

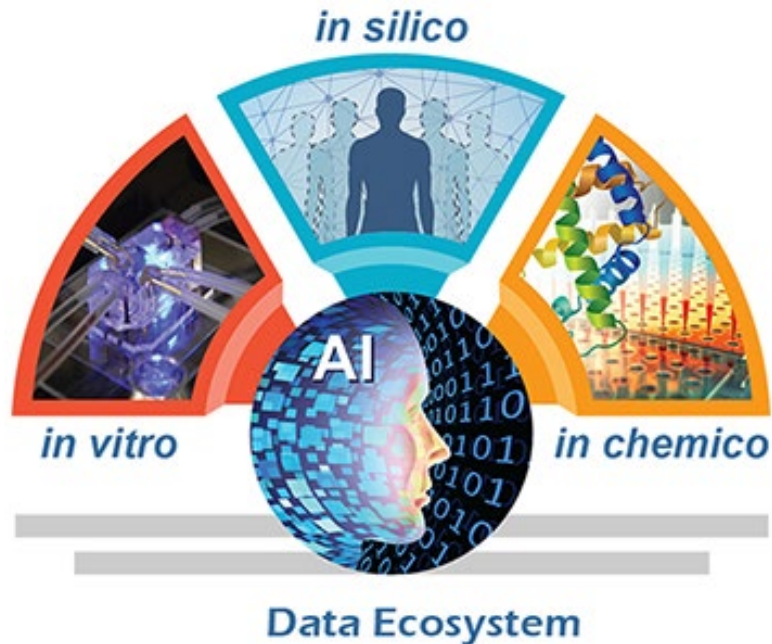
- Apply reporting standards to new NAMS dev in Tech Dev Centers
- Tech Dev investigators to interact with regulators, industry, CROs in dev of NAMs (general advice)
- Nominate mature NAMS from Tech Dev Centers for Validation Network
- Training opportunities with PPP partner groups

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.**

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>



National Institutes of Health

Office of Strategic Coordination – The Common Fund