

Complement-ARIE: Complement Animal Research In Experimentation

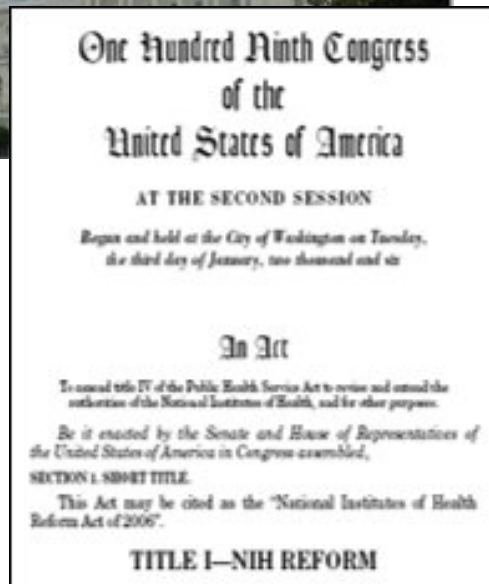
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Program Leader
Re-engineering the Research Enterprise
Office of Strategic Coordination, NIH/OD

2025 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

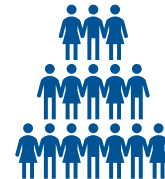
Making substantial investments in time-limited, goal-driven programs that significantly change the trajectory of biomedical research.



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.



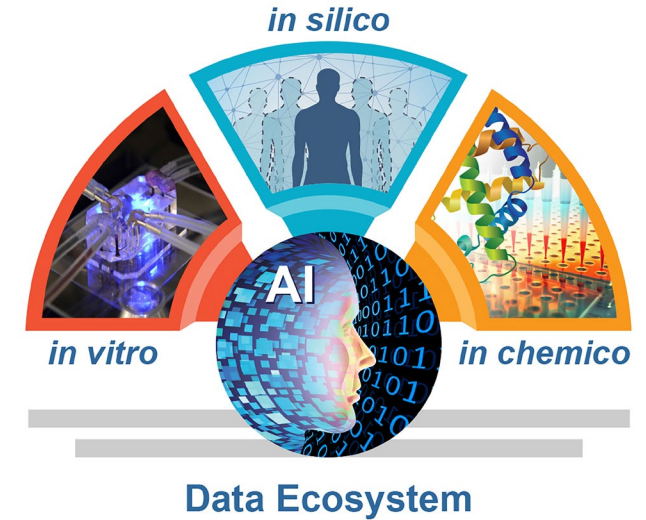
Leadership and staff from Institutes, Centers, and the Office of the Director work together to design funding opportunities and oversee the projects.

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 representative of the patient 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.**



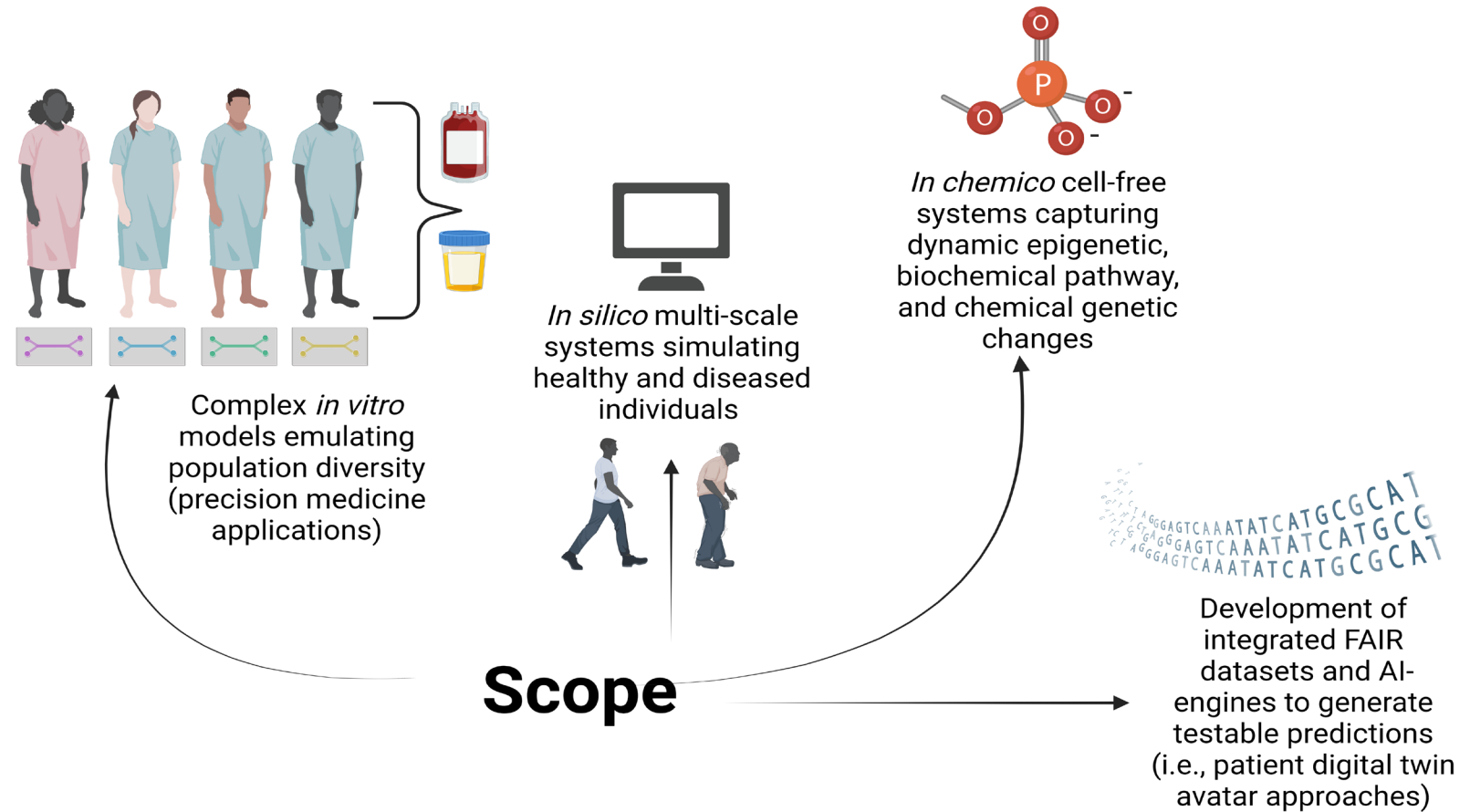
Link to Complement-ARIE website

Complement-ARIE Program: Major Work Products

Program Goals:

NAMs that incorporates the following features:

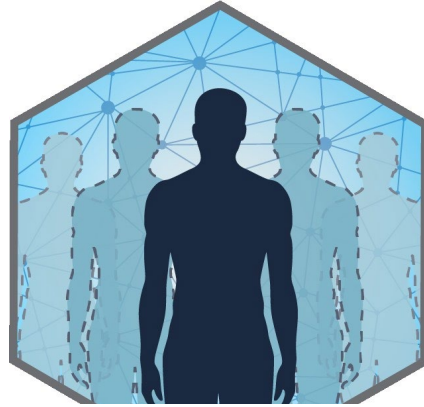
- Complex *in vitro* models emulating population variability
- *In silico* multi-scale systems simulating healthy/diseased individuals
- *In chemico* cell-free systems capturing dynamic changes
- **Combinatorial NAMs** and integrated **FAIR datasets** and **AI-engines** for all NAMs



Build on NAMs activities across NIH

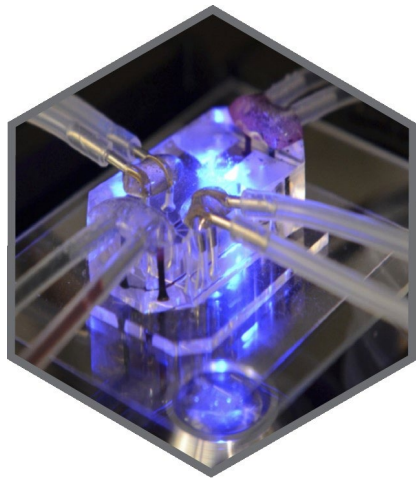
Digital Twin Models

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

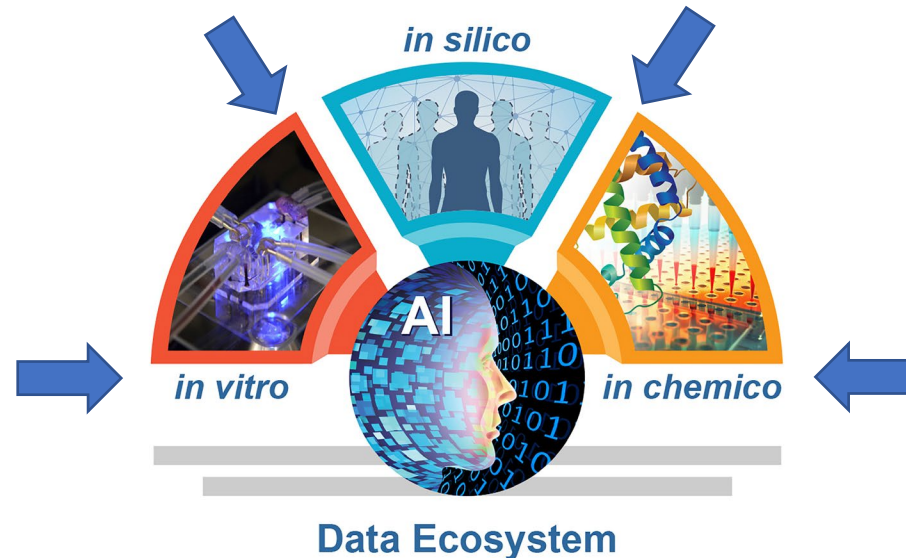


In Silico Models

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



Complex In
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for multiple t
and disease c



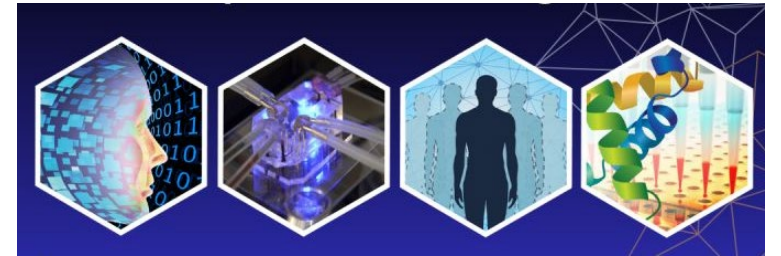
In Chemico Screening

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



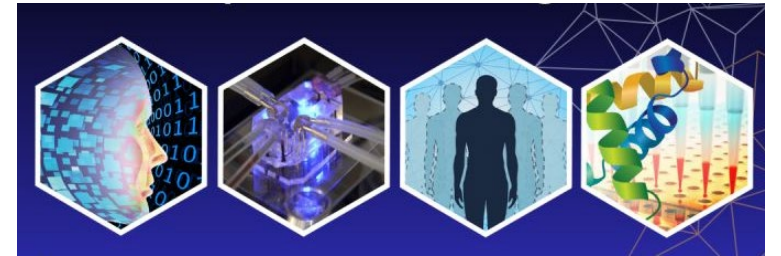
Complement Animal Research in Experimentation (Complement-ARIE)

- NIH-wide, involving 23 NIH Institutes, Centers, and Offices
- Focus: development, standardization, validation and use of **human-based NAMs** to transform basic, translational, and clinical sciences
- To Date:
 - Strategic planning: listening sessions, interagency retreat, landscape analysis
 - Prize Competition: \$1M total awarded to 20 teams
 - Launch of **Validation and Qualification Network** – PPP with FNIH, design phase underway with > 50 public, industry, and non-profit partners to date
- Additional Components to launch in FY26:
 - **Technology Development Centers**
 - **NAMs Data Hub & Coordinating Center**



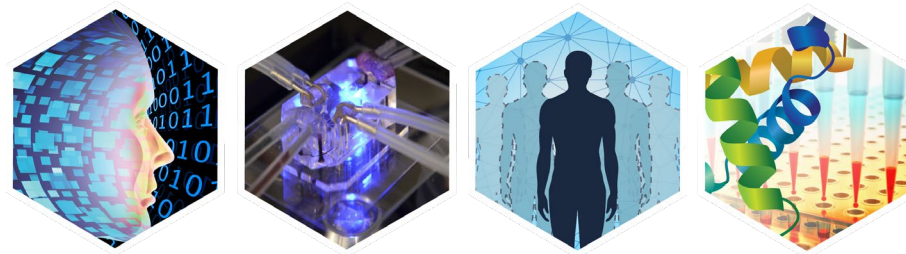
NIH-FDA Coordinated Efforts to Advance Goals of Complement-ARIE

- 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.



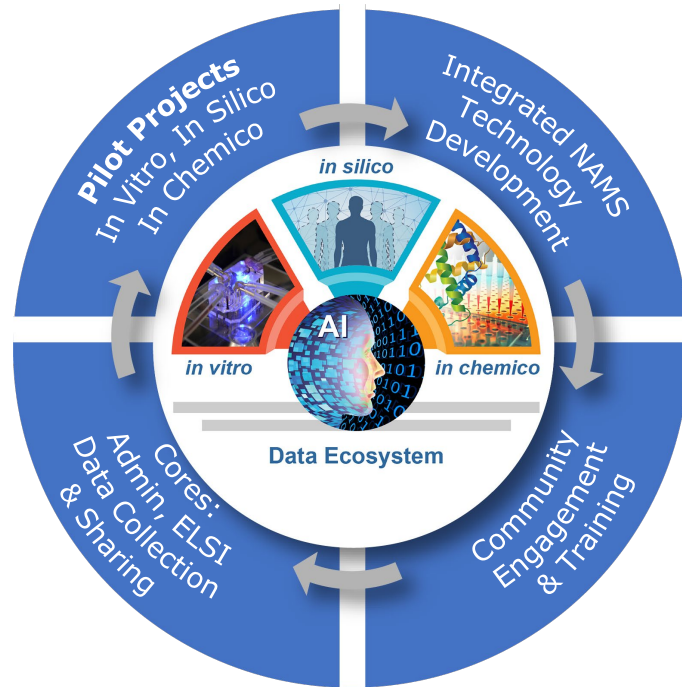
Complement-ARIE: Program Components

- **Technology Development Centers (TDC)**– 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 a biomedical research workforce with the skills to build/use new NAMs, community engagement, societal and ethical considerations.*

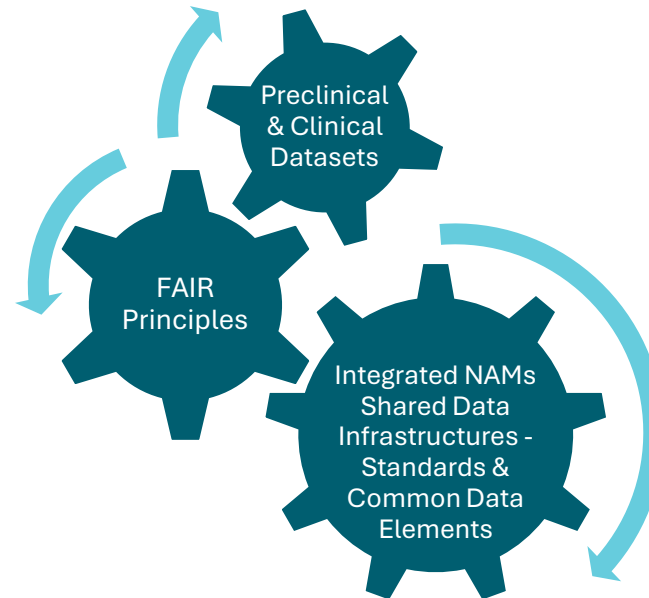


The Complement-ARIE Consortium

NAMs Tech Dev Centers (TDCs)



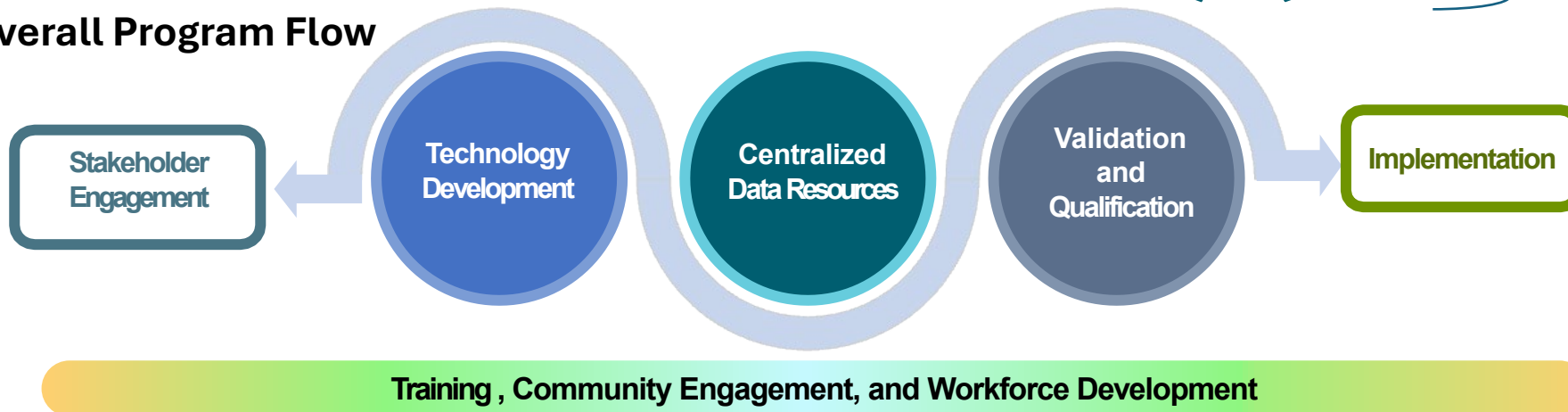
NAMs Data Hub and Coordinating Center (NDHCC)



Validation and Qualification Network (VQN) Foundation of NIH



Overall Program Flow



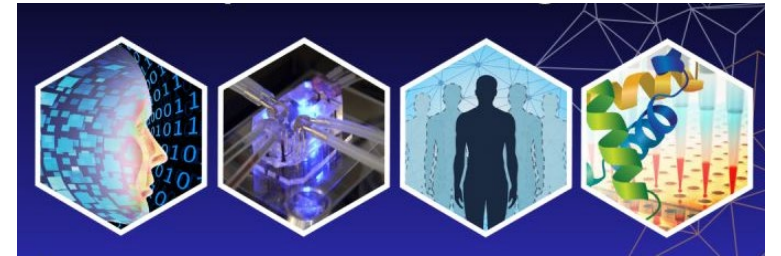
- Regulatory Partners
- Industry Partners
- ICCVAM/Other Agencies
- International Partners
- Non-Profits
- Other end users

Validation and Qualification Network (VQN)

The Complement-ARIE Program has partnered with the Foundation for the National Institutes of Health (FNIH) to establish the **Validation and Qualification Network (VQN)**.

VQN goals:

- Accelerate the implementation and adoption of NAMs in research and regulatory contexts by **ensuring NAMs are robust, reliable, and reproducible**
- Demonstrate **biological relevance and establish confidence in NAMs** to ensure each NAM is “fit for purpose”
- Multi-pronged approach:
 - Establish common data elements and standardized reporting
 - Ensure NAMs have well-described protocols
 - Design and fund transferability studies
 - Conduct quality assessment



NIH/FNIH Public-Private Partnership



Exploring partnerships to bring together NIH, other federal agencies, industry, NGOs, non-profits, etc.



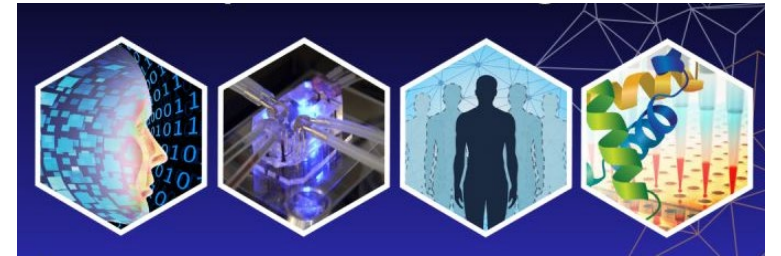
Pre-competitive data sharing and funding validation activities for integrated NAMs platforms across labs for specific use cases



Synergize and coordinate with Complement-ARIE network and other national and international activities on NAMs

What makes the VQN unique

- **Novel combinatorial NAMs** for regulatory and pre-regulatory use (biomedical research, safety/hazard screening, drug discovery, and drug development)
- **Cost sharing with NIH** to support significantly expanded efforts for validation and/or qualification studies
- Pre-competitive space for establishing **consensus validation/qualification frameworks** and supporting the required studies and data packages for validation and qualification of robust, reproducible methods that will broadly benefit the scientific community and pharmaceutical/chemical/other industries
- Build upon and accelerate existing efforts and ultimately provide more **cost effective, human relevant/translational and rapid** approaches to bring products to market



VQN Timeline: A Phased Approach

1

DESIGN (FY25)

- Plan, develop network with Industry, NGOs, CROs and fed partners
- Determine scope of validation efforts
- Develop governance/criteria selection of use cases
- Workshops with stakeholders

2

IMPLEMENTATION Phase I (FY26-30)

- Implement validation efforts with partners
- Select and fund 4-8 Use Case Validation studies
- Bi-annual reporting
- Coordinate with other Complement-ARIE components

3

IMPLEMENTATION PHASE II (FY31-35)

- Nominate mature NAMs from Complement-ARIE for Validation Network
- Apply reporting standards to new NAMs from Complement-ARIE
- Foster interactions between researchers and regulators/industry
- Training opportunities with partner orgs

Launching the VQN

1

DESIGN (FY25)

- Plan, develop network with Industry, NGOs, CROs and fed partners
- Determine scope of validation efforts
- Develop governance/criteria selection of use cases
- Workshops with stakeholders

We are here

- Developing PPP framework
- Launched **April 2025**
- The FNIH webpage for the Design Phase is **LIVE!**
- NIH Design Phase contribution **\$300,000 in FY25**
- Private Sector Design Phase contribution **~\$200,000 in FY25**
- NIH anticipates to contribute **~\$3-4M/year** during implementation (pending availability of funds)
- **Private Sector funds and in-kind support will be solicited for the remaining resources** needed to conduct the NAMs projects selected

List of Currently Participating Organizations

Public-Sector Partners

- Advanced Research Project Agency-Health
- Biomedical Advanced Research and Development Authority
- Consumer Product Safety Commission
- Department of Defense Congressionally Directed Medical Research Program
- Defense Threat Reduction Agency
- Environmental Protection Agency
- European Commission (Europe)
- Food and Drug Administration
- Interagency Coordinating Committee on the Validation of Alternative Methods
- National Aeronautics and Space Administration
- National Centre for the Replacement, Refinement, and Reduction of Animals in Research
- National Institutes of Health
- National Institute of Health Sciences (Japan)
- National Institute of Standards and Technology
- National Science Foundation
- Pharmaceuticals and Medical Devices Agency (Japan)
- US Department of Agriculture
- Veterans Administration

Private-Sector Partners (Industry and Nonprofit)

- Alternatives Research and Development Foundation
- American Chemistry Council
- Americans for Medical Progress
- Ananda Devices Inc.
- Animal Welfare Institute
- Asymmetrex
- Charles River Laboratories
- CN Bio
- Critical Path Institute
- Draper
- Eyescreen, Inc.
- GlaxoSmithKline
- Health and Environmental Sciences Institute
- Hesperos
- Humane World for Animals
- Humane World for Animals International
- Humble Alliance L3C
- Institute for Invitro Sciences
- International Foundation for Ethical Research
- The Jackson Laboratory
- JRF Global
- Labcorp
- Novo Nordisk
- Physicians Committee for Responsible Medicine
- Precision Quantomics
- Radahaim
- Sanofi
- Spanios
- SRI international
- The 3Rs Collaborative
- Toxys
- UCB
- Unilever
- Vivodyne

Complement-ARIE VQN Submission Request

The VQN is a component of the Complement-ARIE program that will accelerate regulatory approval and deployment of NAMs for biomedical research.

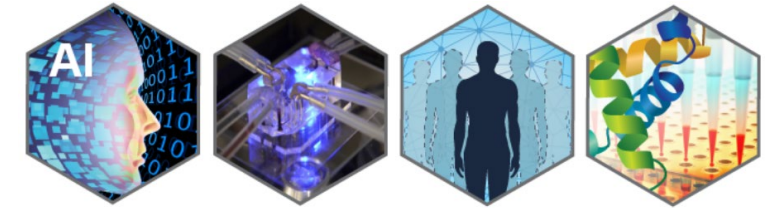
FNIH is **issuing a submission request for well-developed New Approach Methodologies (NAMs) projects** for initial assessment by the Complement-ARIE VQN as part of its design phase.

The scientific community is encouraged to submit in vitro, in silico, in chemico, or combinatorial NAM research models.

- Submissions are due: **August 31, 2025, 8PM ET** for the first cycle of review.
- Rolling reviews will be completed every one-two months through **Dec 31, 2025**

To learn more about the VQN partnership with FNIH, visit: <https://bit.ly/4hY1DcA>

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



Link to NAMs submission request

Questions/Discussion

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

Reach out to us: complement-arie@od.nih.gov

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