Welcome

Informational Webinar for RFA-RM-24-010: Complement-ARIE New Approach Methodologies (NAMs) Technology Development Centers (UM1 Clinical Trial Optional)

National Institutes of Health
Office of Strategic Coordination–The Common Fund

Informational Webinar for RFA-RM-24-010

NOFO Description and Application Information

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New Approach Methodologies

- New Approach Methodologies (NAMs) can be defined as any in vitro, in chemico, or in silico method, that when used alone, or in concert with others, enables improved disease models, including toxicology as well as complex human-relevant models, and as a result, complement animal models in biomedical research.
- NAMs offer unique strengths that, when utilized strategically or in combination, can complement animal models in ways that enable researchers to answer previously difficult or unanswerable questions, especially in areas where in vivo models are lacking or have consistently underperformed.
- The recent passage into law of the FDA Modernization Act 2.0 enables drug registration without the absolute requirement for the use of animals in safety toxicology assessment where alternative risk assessment tools are available.

NIH Common Fund's Complement Animal Research In Experimentation (Complement-ARIE) program

Complement-ARIE Program

The overarching goal of the Complement-ARIE program is to catalyze the development, standardization, validation, and use of human-based NAMs that will transform the way basic, translational, and clinical sciences are done. Specific program goals include:

- Develop better models and understand human health and disease outcomes representative of the impacted patient populations.
- Develop NAMs that provide insight into specific biological processes or disease states.
- Validate mature NAMs to support standardization and clinical use.
- Complement traditional models and make biomedical research more efficient and effective.

Complement-ARIE will address current challenges in NAMs which include, validation and testing in complex systems, and the ability to generate preclinical data needed for first-in-human trials; characterize long-term, systemic and developmental health effects of environmental and drug exposures, and develop systems that better model the physiology and disease pathology of human diseases or conditions for which current experimental models are lacking (e.g. neuroscience and behavior research).

Complement-ARIE Program

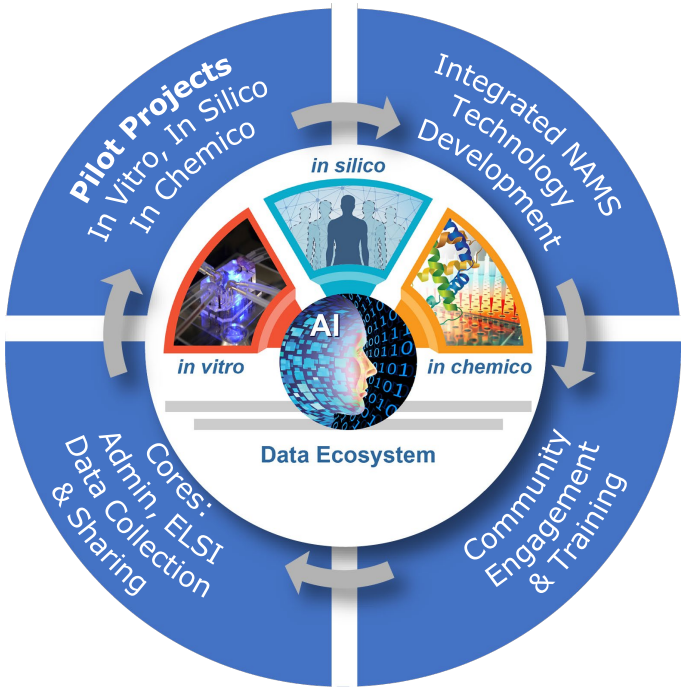
To achieve its goals, Complement-ARIE consists of the following key components and centers.

- **Comprehensive NAMs Technology Development Centers (TDCs)** – stimulate the development of NAMs to address areas of greatest need, with emphasis on increased biological complexity and throughput, innovative combinatorial approaches, and data sharing.
- **NAMs Data Hub and Coordinating Center (NDHCC)** – create integrated data structures, including standards for model credibility, improve FAIRness of NAMs-relevant data, and create a searchable NAMs repository. (RFA-RM-24-013)
- **Validation and Qualification Network (VQN)** – establish common data elements and standardized reporting, apply validation/qualification frameworks, accelerate deployment and regulatory implementation of NAMs.

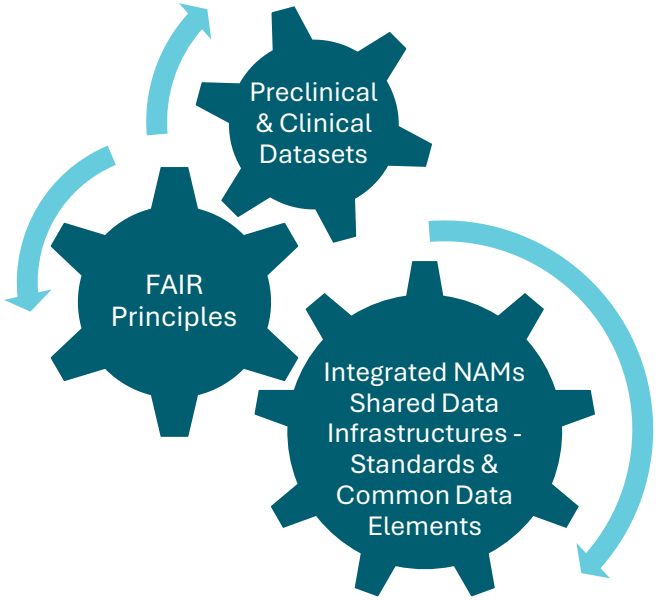
Within each of the three key program components, training and outreach activities are required to facilitate dissemination, capacity building, and adoption of NAMs. Complement-ARIE will participate in strategic engagement with key partners from other federal agencies including regulatory bodies, industry, non-profits, and other NGOs to advance emerging opportunities in the development and use of NAMs in basic, translational, and clinical research.

Summary: Complement-ARIE Consortium

NAMs Tech Dev Centers (TDCs)

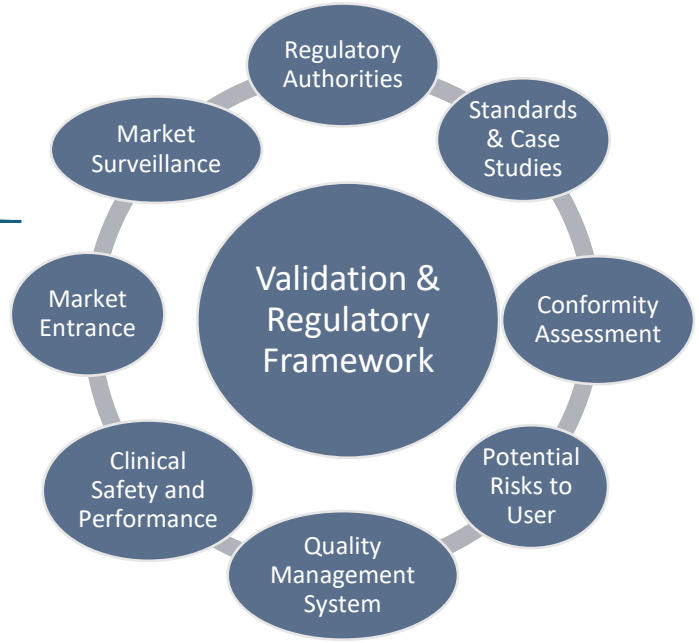


NAMs Data Hub and Coordinating Center (NDHCC)

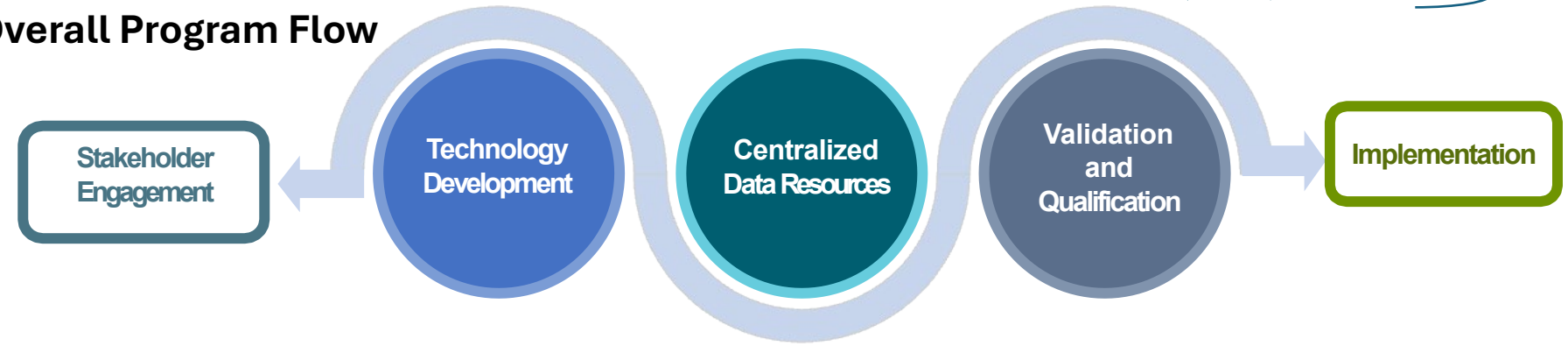


Validation and Qualification Network (VQN)

Foundation of NIH



Overall Program Flow



Training , Community Engagement, and Workforce Development

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

Complement-ARIE New Approach Methodologies (NAMs) Technology Development Centers (UM1 Clinical Trial Optional)

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U mechanism – Cooperative agreement

Substantial NIH staff involvement

UM1 Research Project with Complex Structure Cooperative Agreement

To support cooperative agreements involving large-scale research activities with complicated structures that cannot be appropriately categorized into an available single component activity code, e.g. clinical networks, research programs or consortium. The components represent a variety of supporting functions and are not independent of each component. Substantial federal programmatic staff involvement is intended to assist investigators during performance of the research activities, as defined in the terms and conditions of the award.

Complement-ARIE NAMs Technology Development Centers

Purpose

The purpose of this Notice of Funding Opportunity (NOFO) is to establish Comprehensive NAMs Technology Development Centers to support NIH Common Fund's Complement Animal Research In Experimentation (Complement-ARIE) program. The Complement-ARIE program will accelerate the development, standardization, validation, and use of human-based New Approach Methodologies (NAMs). Complement-ARIE will significantly advance understanding of human health and disease by providing a range of mature and/or validated and standardized biomedical research models.

The Comprehensive NAMs Technology Development Centers will stimulate the development of combinatorial NAMs to support scientific areas of need, with emphasis on increased biological complexity and throughput, innovative combinatorial approaches, and data sharing according to FAIR principles. Developing these NAMs will require multi-disciplinary expertise in disease research, personalized medicine, screening therapeutics for safety and efficacy, and regulatory science.

Complement-ARIE NAMs Technology Development Centers

The Comprehensive NAMs Technology Development Centers will integrate research and training components dedicated to the development of combinatorial NAMs, with an emphasis on increased biological complexity and focused on applicability to high priority scientific areas identified below. Each TDC should be focused on a scientific area of need that can benefit from the development and application of NAMs. This program will develop a range of mature combinatorial NAMs, for a breadth of applications, from drugs, medical devices, diagnostics, and biologics, to chemical exposure and toxicology assessment tools.

NAMs should incorporate lifespan, population diversity (within the context of the disease/condition), sex as a biological variable, and other human variables as relevant models for the scientific area of focus.

Complement-ARIE NAMs TDCs Research Scope

High priority scientific areas of focus for NAMs were identified through a number of strategic planning activities including the Advisory Committee to the Director on catalyzing the development and use of NAMs to Advance Biomedical Research and their recommendations, the Complement-ARIE Challenge, and NIH Common Fund strategic planning activities, and a NAMs landscape analysis.

High priority scientific needs identified include, but are not limited to:

- **Chronicity** (i.e. across the lifespan - characterizing long-term, systemic, and developmental health effects of environmental and drug exposures)
- **Neuroscience** (e.g. neurodegenerative disease models, neuropsychiatry, ophthalmology, behavioral research)
- **Personalized Health** (e.g. human-specific models to address the rapid growth in biological therapeutics, including monoclonal antibodies, human proteins, oligonucleotides, gene editing, and cell therapies, and incorporating population diversity and sex as a biological variable)
- **Cross-disease Pathogenesis** (e.g. developmental, metabolic, immune, reproductive health)

ACD recommendations

Complement-ARIE New Approach Methodologies (NAMs) Technology Development Centers (UM1 Clinical Trial Optional)

Important Dates

Posted Date – December 10, 2024

Letter of Intent Due – January 24, 2025

Open Date – January 28, 2025

Application Due Dates			Review and Award Cycles		
New	Renewal / Resubmission / Revision (as allowed)	AIDS - New/Renewal/Resubmission/Revision, as allowed	Scientific Merit Review	Advisory Council Review	Earliest Start Date
February 28, 2025	Not Applicable	Not Applicable	July 2025	October 2025	December 2025

Complement-ARIE NAMs TDC Application Structure

- Element A: Center Overview
- Element B: Strategic Management
  - Module B1: Center Management
  - Module B2: Consortium Liaison
- Element C: Integrated NAMs Technology Development
  - Module C1: Major NAMs Technology Development
  - Module C2: Technology Pilot Projects
- Element D: Center Core Facilities
  - Module D1: Administration
  - Module D2: Data Collection and Bioinformatics
  - Module D3: Resources
- Element E: Technical Characterization
- Element F: Training & Outreach
  - Module F1: Ethical, Legal and Social Implications (ELSI)
  - Module F2: Workforce Development and Training
  - Module F3: Community and Stakeholder Engagement

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Page Limitations

Specific Aims. Briefly summarize the aims for the entire application, including all Elements and Modules. 1 page

Research Strategy. The Research Strategy must consist of the following sections with the indicated page limits:

- Element A. Overview; one required, 5 pages
- Element B. Strategic Management; one required, 3 pages
- Element C. Integrated NAM Technology Development; one required, 10 pages
- Element D. Center Core Facilities; one required, 10 pages
- Element E. Technical Characterization; one required, 6 pages
- Element F. Training & Outreach; one required, 5 pages

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Other Attachments

Milestone Plan

The applicant is required to provide detailed information and timelines for completing all proposed activities according to the specific aims. Applicants must include specific yearly milestones that will need to be met in order to accomplish the work set out in a five-year period. Milestones that reflect progress in each specific aim should be easily measurable and realistic. Project milestones that quantitatively measures progress towards each of the proposed specific aims are required. A timeline to achieve the proposed milestones, in the form of a Gantt chart, is also required.

Plan for Enhancing Diverse Perspectives (PEDP)

•The PEDP may be no more than 2 pages in length and should include:

- Actionable strategies using defined approaches for the inclusion of diverse perspectives in the project;
- Description of how the PEDP will advance the scientific and technical merit of the proposed project;
- Anticipated timeline of proposed PEDP activities;
- Evaluation methods for assessing the progress and success of PEDP activities.

Milestones

- Milestones and a Gantt chart are required.
- All projects will be milestone-driven with clear go/no-go criteria that are quantifiable.
- Milestones are deliverables with quantifiable success metrics for each specific aim of the project and include annual and/or intermediate quantitative criteria with key success metrics specifically defined.
- Each Complement-ARIE award is expected to have yearly milestones for the overall and for each individual component.
- Milestone timeline in the form of a Gantt Chart
- The Program Official and the applicant will negotiate and agree on a final set of milestones, the final approved milestones will be specified in the Notice of Award.

RFA-RM-24-010 Cooperative Agreement Terms and Conditions of Award

- Review the Section VI. Award Administration Information - Cooperative Agreement Terms and Conditions
- NIH staff have substantial programmatic involvement that is above and beyond the normal stewardship role in awards
- In accepting the award, the recipient agrees that any activities under the award are subject to all provisions currently in effect or implemented during the period of the award, other Department regulations and policies in effect at the time of the award, and applicable statutory provisions.

RFA-RM-24-010 Cooperative Agreement Terms and Conditions of Award

Terms and Conditions

- Negotiate and agree on a final set of milestones, the final negotiated and approved milestones will be specified in the Notice of Award.
- Meet yearly milestones as defined by investigators and NIH program officials and referenced in the Notice of Award.
- Participate and present findings at the semi-annual Complement-ARIE Consortium meetings convened by the Complement-ARIE Data Hub and Coordinating Center.
- Participate in recurring monthly meetings to discuss progress, obstacles and any other Complement-ARIE related issues and/or activities.
- Recipients agree to governance, through voting and decision making, of the Complement-ARIE consortium.

RFA-RM-24-010 Contact Information

Pre-application consultation with NIH Program staff is encouraged.

Scientific/Research Contact(s)
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Application Review Information

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Review Process

- Reviews will take place ~July 2025
- Applications deemed unresponsive will be administratively withdrawn
- Applications will be reviewed by a **Special Emphasis Panel (SEP)** organized by the **NIH Center for Scientific Review (CSR)**
  - Panel will include only temporary members
  - Panel will only review applications submitted to RFA-RM-24-010
  - Meeting rosters posted online 30 days prior to the review meeting
- **Summary Statements** provided 30 days after review meeting, provide a summary of key discussion points, comments and scores of assigned reviewers
  - All applications will receive a written critique
  - Only those applications deemed to have the highest scientific and technical merit will be Discussed and assigned an Overall Impact score

Review Criteria: how applications are scored

- **Overall Impact Score (1-9)**
  - Likelihood for the project to exert a sustained, powerful influence on the research field(s) involved
  - In consideration of the five score criteria and additional review criteria
- **Five Scored Criteria (also on 1-9 scale):**
  - *Significance*
  - Investigator
  - Innovation
  - *Approach*
  - Environment
- **Additional Review Criteria:** Protection for Human Subjects, Vertebrate Animals, Biohazards

Specific Considerations for RFA-RM-24-010:

- For further review information, refer to Section V of the funding announcement "**Application Review Information**". *Read the Review Criteria carefully.*
- Pay special attention and address "**Specific to this NOFO**" review questions under each criterion, especially Significance and Approach

Questions/Discussion

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

For FAQs visit:
https://commonfund.nih.gov/complementarie/faqs

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

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Adjourned

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