# Announcement of Requirements and Registration for the Complement-ARIE (Complement Animal Research in Experimentation) New Approach Methodologies (NAMs) Reduction to Practice (RTP) Challenge

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

OFFICE OF THE DIRECTOR

Authority: 15 U.S.C. 3719

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## DESCRIPTION

**Subject of the Challenge:**

Recent technological advances have set the stage for a renewed focus on human-based solutions called new approach methodologies (NAMs) that can complement, and in some cases replace, animal models in research and regulatory testing. These NAMs generally span advanced cell-tissue-organoid (*in vitro*), computational modeling (*in silico*), and cell-free biochemical analysis (*in chemico*) techniques, with each type of NAM offering different advantages. A combination and integration of multiple NAMs elements into a synergistic approach that augments gaps and/or deficiencies in individual NAMs approaches is a "combinatorial NAM" and could ultimately allow for improved predictions of human clinical response. Although many combinatorial NAMs are still early in development, not validated and standardized, nor available to the market broadly, combinatorial NAMs can potentially transform the way biomedical research, drug development, and clinical trials are conducted.

To accelerate development and validation of combinatorial NAMs for human-based scientific and regulatory purposes, the National Institutes of Health (NIH) Common Fund's Complement-Animal Research In Experimentation (Complement-ARIE) program in collaboration with the Food and Drug Administration (FDA) and Environmental Protection Agency (EPA), is launching the Reduction to Practice (RTP) Challenge. This challenge invites innovative

combinatorial NAMs solutions from multidisciplinary teams who can successfully demonstrate implementation of their human-based solution in a practical and usable form within a 3-year period. Solvers will have the chance to win up to $1,430,000 in cumulative cash prizes and have their solution provided validation and/or qualification support by the Complement-ARIE Validation and Qualification Network (VQN). This Challenge is open to the public. Participants and winners from the Complement-ARIE Ideation Challenge launched in November 2023 are also encouraged to apply.

The Reduction to Practice challenge will have three-phases: **1)** Proof of Concept and Feasibility Studies, **2)** Prototype Development and Milestone Achievements, and **3)** Prototype Delivery for Validation and Qualification.

In Phase 1, solvers will be asked to submit combinatorial NAM technology solutions and must include submission of preliminary data that is reproducible and demonstrates the integrated NAM technology can feasibly move to a prototype stage. Proposals must also outline a defined context of use (CoU) and product development strategy to demonstrate how a solution could complete Phase 2 milestones within the defined CoU. Up to 20 proposals that meet the requirements will be awarded $80,000 per winner. Only Phase 1 winners will be eligible for Phase 2. In Phase 2, solvers must complete **Milestone 1)** by constructing a prototype combinatorial NAM and successfully scaling the NAM platform according to fit-for-purpose needs. Solvers must also demonstrate clear progress in initial performance testing. Up to 10 winners will receive $150,000 per winner upon completion of Milestone 1. In **Milestone 2)** solvers must demonstrate progress toward internal validation and reproducibility of results generated by the NAM platform against reference standards or their equivalent, submit data that meets standards of the Complement-ARIE NAMs Data Hub and Coordination Center (NDHCC), and document how the NAM platform can be assessed by the VQN. These standards will be based on established principles (findable, accessible, interoperable, and reusable (FAIR), technological readiness levels, etc.) and will be more clearly defined by the NDHCC and VQN as the challenge progresses. Up to 7 winners will receive $200,000 per winner upon completion of Milestone 2. Only solvers that have completed Milestone 1 will be eligible to complete Milestone 2 and only Phase 2 winners who have successfully completed **both Milestones** will be

eligible to participate in Phase 3. For Phase 3, solvers must deliver a working NAM prototype with description and documentation that will facilitate validation and/or qualification. All Phase 3 submissions that meet the criteria will be awarded independent assessment by the VQN. Once assessment is completed, judges will award one grand prize winner $1,000,000, and 3 runners-up will be awarded $500,000 each.

Combinatorial NAMs prototype designs should be consistent with current best practices in the field. Deliverables could include, but are not limited to, modular, scalable, fit-for-purpose, flexible and/or versatile combinatorial NAMs prototype designs.

**Priority Areas**

These priorities represent areas of scientific and regulatory need as identified by the NIH Advisory Committee to the Director (ACD) Working Group on Catalyzing the Development and Use of Novel Alternative Methods to Advance Biomedical Research on NAMs, Complement-ARIE strategic planning activities, the EPA, and the FDA. Solvers are not limited to Priority Areas but are encouraged to consider them in their submission:

Chronicity (i.e. across the human lifespan) – characterizing long-term, systemic, and developmental health effects of environmental and drug exposures, including chronic disease.

Neurobiological Models – neurodegenerative and neurodevelopmental disease models, neuropsychiatry, ophthalmology, and/or modeling behavioral research.

Personalized Medicine – human-specific models to address biological therapeutics, including monoclonal antibodies, human proteins, oligonucleotides, gene editing, and cell therapies and incorporating population variability and sex as a biological variable.

Cross-Disease Pathogenesis – platforms that address developmental, metabolic, immune, inflammatory, reproductive, or nutritional health that span multiple diseases or are broadly generalizable across diseases including chronic disease.

Toxicology and Safety – Strategies that replace conventional animal toxicology or safety pharmacology studies, including assessment of potencies associated with systemic toxicity via either mechanism- or tissue-based assays assessed via proxy by simpler high-throughput models.

Human Health Protection – Strategies that inform special studies that are important for human health protection and include methods to assess development and reproductive toxicity (i.e. DART), neurotoxicity, endocrine disruption, immunotoxicity, and carcinogenicity

**Partners:**

The NIH Common Fund Complement-ARIE program is administered by the NIH Office of Strategic Coordination, the National Center for Advancing Translational Sciences (NCATS), and the National Institute of Environmental Health Sciences (NIEHS). This challenge involves non-financial collaboration with the Food and Drug Administration (FDA) and Environmental Protection Agency (EPA).

**Dates**:

Phase 1 Dates:

| | |
|---|---|
| 09/25/2025 | Phase 1 Launch |
| 10/14/2025 | (Registration Open) |
| 03/01/2026 | Phase 1 Submission Deadline |
| 07/01/2026 | Phase 1 Winners Announced |

Estimated Dates of Future Phases:

| | |
|---|---|
| ~July 2026 | Phase 2 Launched |
| ~March 2027 | Phase 2 Milestone 1 deadline |
| ~August 2027 | Phase 2 Milestone 2 deadline |
| ~August 2027 | Phase 2 Winners Announced |

| | |
|---|---|
| ~August 2027 | Phase 3 Launched |
| ~ August 2028 | Phase 3 Winners Announced |

**Statutory Authority to Conduct the Challenge:**

The NIH Common Fund is a component of the NIH budget which is managed by the Office of Strategic Coordination/Division of Program Coordination, Planning, and Strategic Coordination/Office of the NIH Director. Common Fund programs address emerging scientific opportunities and pressing challenges in biomedical research that no single NIH Institute or Center (IC) can address on its own and are of high priority for the NIH. [42 U.S.C. 282a(c)(1)]. The Complement-ARIE program is supported by the NIH Common Fund to catalyze the development, validation, and qualification of New Approach Methodologies (NAMs), and to accelerate human-based solutions that can complement, or in some cases replace, existing animal models.

The NIH Office of the Director is conducting this Challenge under the America Creating Opportunities to Meaningfully Promote Excellence in Technology, Education, and Science (COMPETES) Reauthorization Act of 2010, as amended [15 U.S.C. § 3719]. This Competition is consistent with and promotes the agency's mission by catalyzing the goal-driven development of innovative tools and technologies with the potential to enhance human health.

## PRIZES

**Amount of the Prize:** The cash prizes for this Challenge total $7,000,000 USD. Prizes will be awarded following the successful completion of each Phase of the Challenge in the following amounts:

Phase 1: Proof of Concept and Feasibility Studies

- $80,000 per winner, up to 20 winners across topic areas

Phase 2: Prototype Development and Milestone Achievements

- Phase 2 will include 2 milestones and achievement of each milestone will be awarded separately:
    - Milestone 1 Award: $150,000 per winning team, up to 10 winning teams across topic areas
    - Milestone 2 Award: $200,000 per winning team, up to 7 winning teams across topic areas

Phase 3: Prototype Delivery for Validation and Qualification

- Phase 3 will include 3 Runner-Up winners, each awarded $500,000 per winning team across topic areas, and 1 Grand Prize winner awarded $1,000,000.

**Table 1: Complement-ARIE Reduction-to-Practice (RTP) Challenge Phases**

| **Phase** | **Description** | **Total Prize Money** | **Prize Money/ Award; Number of Awards** |
|---|---|---|---|
| Phase 1 | **Proof of Concept and Feasibility Studies** | $1,600,000 | $80K/award;<br>up to 20 winners |
| Phase 2 | **Prototype Development and Milestone Achievements** | | |
| | Milestone 1 | $1,500,000 | $150K/award;<br>up to 10 winners |
| | Milestone 2 | $1,400,000 | $200K/award;<br>up to 7 winners |
| Phase 3 | **Prototype Delivery for Validation and Qualification** | | |
| | Runner-Up Winners (3) | $1,500,000 | $500K/award;<br>up to 3 winners |
| | Grand Prize Winner (1) | $1,000,000 | $1,000,000;<br>1 winner |

Any prize funds unawarded at the completion of earlier phases of this Challenge may be allocated to future phase(s) of the Challenge. Any such allocation of and decisions to award the

unspent prize funds in future phases, including modification of prize categories, prize amounts and/or prize number, is entirely at the discretion of NIH.

**Award Approving Official**:

The Award Approving Official will be the Director of the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), or as otherwise delegated, within the NIH Office of the Director.

**Payment of the Prize**:

Prizes awarded under this Challenge will be paid by electronic funds transfer and may be subject to federal income taxes. HHS/NIH will comply with the Internal Revenue Service withholding and reporting requirements, where applicable.

Entities participating in this Challenge are encouraged, but not required, to request and obtain a free Unique Entity ID (UEI), if they have not already done so, via SAM.gov as this will expedite prize payment. Additional information can be found at https://sam.gov/content/entity-registration

If participating as a Team, in the event of winning a cash prize, the Team Leader shall be paid the prize in full and is solely responsible for allocating any prize amount among the members of the Team. If participating as an Entity, in the event of winning a cash prize, the prize will be paid directly to the Entity, not the Entity Point of Contact. NIH will not arbitrate, intervene, advise on, or resolve any matters between team members.

**NIH reserves the right, in its sole discretion, to (a) cancel, suspend, or modify the Challenge, or any part of it, for any reason, and/or (b) not award any prizes if no submissions are deemed worthy.**

## RULES

**Eligibility Rules:**

To be eligible to win a prize under this Challenge, a Participant (whether participating as a Team or Entity) —

a. Shall have registered to participate in the Challenge under the rules promulgated by the National Institutes of Health (NIH) as published in this announcement;

b. Shall have complied with all the requirements set forth in this announcement;

c. In the case of an Entity, shall be incorporated in and maintain a primary place of business in the United States. In the case of a Team, the Team Leader shall be a citizen or permanent resident of the United States. However, non-U.S. citizens and non-permanent residents can participate as a member of a Team or Entity that otherwise satisfies the eligibility criteria. Non-U.S. citizens and non-permanent residents are not eligible to win a monetary prize (in whole or in part). Their participation as part of a winning Team or Entity, if applicable, may be recognized when the results are announced.

d. Shall not be a federal entity or federal employee acting within the scope of their employment;

e. Shall not be an employee of the Department of Health and Human Services (HHS, or any other component of HHS) acting in their personal capacity;

f. Who is employed by a federal agency or entity other than HHS (or any component of HHS), should consult with an agency ethics official to determine whether the federal ethics rules will limit or prohibit the acceptance of a prize under this Challenge;

g. Shall not be a judge of the Challenge, or any other party involved with the design, production, execution, or distribution of the Challenge or the immediate family of such a party (i.e., spouse, parent, step-parent, child, or step-child).

h. Shall be 18 years of age or older at the time of submission.

**Participation Rules:**

(1) Federal grantees and recipients of cooperative agreements or other transaction (OT) awards are eligible to participate in the Challenge, but may not use Federal funds from a grant award,

cooperative agreement, or OT award to develop their Challenge submission or to fund efforts in support of their Challenge submission unless use of such funds is consistent with the purpose, terms, and conditions of the grant award, cooperative agreement, or OT award. Each Participant (whether a Team or Entity) intending to use Federal grant, cooperative agreement, or OT award funds must register for and participate in the Challenge as an Entity on behalf of the awardee institution, organization, or entity. If a Participant uses Federal grant, cooperative agreement, or OT award funds to win the Challenge, the prize must be treated as program income for purposes of the original grant, cooperative agreement, or OT award in accordance with applicable Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards [2 CFR § 200].

(2) Federal contractors may not use federal funds from a contract to develop their Challenge submissions or to fund efforts in support of their Challenge submissions.

(3) By participating in this Challenge, each Participant (whether a Team or Entity) agrees to assume any and all risks and waive claims against the federal government and its related entities, except in the case of willful misconduct, for any injury, death, damage, or loss of property, revenue, or profits, whether direct, indirect, or consequential, arising from participation in this Challenge, whether the injury, death, damage, or loss arises through negligence or otherwise.

(4) Based on the subject matter of the Challenge, the type of work that it will possibly require, as well as an analysis of the likelihood of any claims for death, bodily injury, property damage, or loss potentially resulting from Challenge participation, no Participant (whether a Team or Entity) participating in the Challenge is required to obtain liability insurance, or demonstrate financial responsibility, or agree to indemnify the federal government against third party claims for damages arising from or related to Challenge activities in order to participate in this Challenge.

(5) A Participant (whether a Team or Entity) shall not be deemed ineligible because the Participant used federal facilities or consulted with federal employees during the Challenge if the facilities and employees are made available to all Participants participating in the Challenge on an equitable basis.

(6) By participating in this Challenge, each Participant (whether a Team or Entity) warrants that they are sole author or owner of, or has the right to use, any copyrightable works that the submission comprises, that the works are wholly original with the Participant (or is an improved version of an existing work that the Participant has sufficient rights to use and improve), and that the submission does not infringe any copyright or any other rights of any third party of which the Participant is aware.

(7) As a condition for winning a cash prize in this Challenge, each Participant (whether participating as a Team or Entity) grants to the NIH an irrevocable, paid-up, royalty-free nonexclusive worldwide license to reproduce, publish, post, link to, share, and display publicly the Team/Entity Name, Title, Executive Summary, and Plain Language Summary components of the submission on the web or elsewhere. Each Participant will retain all other intellectual property rights in their submissions, as applicable. To participate in the Challenge, each Participant must warrant that there are no legal obstacles to providing the above-referenced nonexclusive licenses of the Participant's rights to the federal government. To receive an award, Participants will *not* be required to transfer their intellectual property rights to NIH, but Participants must grant to the federal government the *nonexclusive licenses* recited herein.

(8) Each Participant (whether a Team or Entity) agrees to follow all applicable federal, state, and local laws, regulations, and policies.

(9) Each Participant (whether a Team or Entity) participating in this Challenge must comply with all terms and conditions of these rules, and participation in this Challenge constitutes each such Participant's full and unconditional agreement to abide by these rules. Winning is contingent upon fulfilling all requirements herein.

(10) As a condition for winning a cash prize in this Challenge, each Participant (whether a Team or Entity) that has been selected as a winner must complete and submit all requested winner verification and payment documents to NIH within 7 business days of formal notification. Failure to return all required verification documents by the date specified in the notification may be a basis for disqualification of a cash prize winning submission.

(11) As a condition for winning a cash prize in this Challenge, each Participant (whether participating as a Team or an Entity) irrevocably grants to NIH the right to the use of their name, affiliation, city and state, and likeness or image for the purposes of publicity releases and any other promotion of this Challenge.

(12) As a condition for winning a cash prize in this Challenge, each Participant (whether a Team or Entity) that has been selected as a winner must complete and submit all requested winner verification and payment documents to NIH within 7 business days of formal notification. Failure to return all required verification documents by the date specified in the notification may be a basis for disqualification of a cash prize winning submission.

## JUDGING CRITERIA

### Basis Upon Which a Winner Will be Selected

Submissions will first undergo a preliminary evaluation to review solver eligibility to compete in this Challenge as well as submission completeness and applicability of scope. Complete and applicable submissions from eligible participants will then be evaluated by a panel composed of scientific and technological experts using the Judging Criteria listed in the Phase 1 Criteria Table. A Judging Panel composed of federal employees will review these evaluations and select the winners, pending final decisions by the Award Approving Official. Participants' evaluation or judging results will not be made available to Participants or the public. Participants will be notified of the final determinations by email and winners will be publicly announced.

### Phase 1: Proof of Concept and Feasibility Studies

Phase 1 submissions require a clear description of intended use for the proposed combinatorial NAM solution. Submissions also require a well-described research and development plan that demonstrates feasibility of achieving Phase 2 milestones and completing the entire RTP Challenge within its 3-year timeframe. The following table contains the full review criteria for Phase 1:

**Phase 1 Criteria**

| Criterion | Description | Relative Weight |
|---|---|---|
| Significance/ Impact | What added value is the proposed combinatorial NAM providing that is more significant than each individual NAM approach alone?<br><br>How well does the combinatorial NAM address a critical area of need and resolve potential roadblock(s) to its development and validation?<br><br>To what extent does the solution advance the use of NAMs in a priority area or its equivalent?<br><br>How will the proposed combinatorial NAM align with the principles of replacing, reducing, and refining the use of animals in research and testing? | 15 points |
| Innovation | How is the proposed design innovative, creative, and novel compared to existing approaches/methodologies?<br><br>How is the proposed approach expected to be better than the current state-of-the-art approaches? | 10 points |
| Team | To what extent does the team composition represent interdisciplinary expertise and an environment that is appropriate for advancing the proposed solution?<br><br>Has the team engaged end-user, industry, regulatory, and/or patient communities that would benefit from this technological development?<br><br>Does the team have the appropriate expertise and resources to accomplish the proposed solution? | 15 points |
| Feasibility and | Does the technical readiness of the proposed combinatorial NAM demonstrate that the technology could progress to validation within the duration of the challenge? | 25 points |

| | | |
|---|---|---|
| Preliminary Data | Generally, how likely is the proposed combinatorial NAM to be successfully deployed at the conclusion of the Challenge to proceed to validation/qualification?<br><br>To what degree does the data presented reproducibly demonstrate potential for success in solving the Challenge?<br><br>How likely will the use of the proposed combinatorial NAM predict outcomes in humans? Is the verification/validation strategy sound?<br><br>How compatible and feasible is the proposed technological approach with the stated context of use? | |
| Approach | How well does the milestone plan outline construction, testing, data submission for the purpose of validation and delivery of the NAMs?<br><br>How well do the NAM approaches integrate to create a more powerful predictive tool for human translatability?<br><br>Does the proposed scientific method/approach ensure that the research design, methods, analysis, interpretation, and reporting are rigorous and reproducible?<br><br>Is the recording and sharing of data and information about research procedures sufficiently described and available so that other scientists can repeat the study accurately and validate the original findings?<br><br>To what degree did the NAMs design incorporate best practices from the field and are consistent with applicable regulatory requirements/guidance?<br><br>Are strategies for addressing challenges that may arise during solution development adequately considered?<br><br>Does the proposed solution detail the utility of the developed methods including expected outcomes? | 35 points |

| | | |
|---|---|---|
| | Does the proposal include adequate metrics along with the timeline to demonstrate the progress towards the milestones stated in the challenge?<br><br>Does the proposal include appropriate details on the technical development and capabilities of the solution?<br><br>Did the proposal provide adequate considerations on potential strategies for validation and testing of the technological solution?<br><br>Did the proposal include adequate details on how the design and technical specifications of the proposed technology solution support the context of use?<br><br>To what degree is the proposed approach likely to succeed in the proposed context of use? | |
| | **Total** | **100** |

The Judging Criteria for Phase 2 milestone 1, Phase 2 milestone 2, and Phase 3 will be announced at the time of launching those future phases and will be informed by the range of maturity levels of Phase 1 submissions, among other factors.

Judging Criteria for Phases 2 and 3 are expected to weigh the demonstrated performance of combinatorial NAMS more heavily than its theoretical potential, with consideration of the appropriate experimental models used to infer potential performance. Capability to execute is expected to remain a factor for judging in subsequent Phases. Specific details related to desired endpoints, the level of maturity of technologies, testing, commercialization, and other requirements will be further developed. The Judging Criteria for Phase 3 are expected to include evaluation of the required, desired, and possible attributes as described in Phase 3 Deliverables. The Phase 3 Judging Criteria will evaluate Participant-provided information about the solution and the results of the independent validation testing studies. If Phase 3 deliverables are met, prototypes and associated datasets will be shared with the Complement-ARIE VQN for independent testing and evaluation. At the conclusion of this validation and testing stage, it is

anticipated that the VQN will create reports evaluating the NAMs platforms' performance based on a set framework, criteria, and other metrics established by the VQN. These reports will be reviewed and evaluated by a panel of judges, who will then select the grand prize winner and runners-up, subject to final decision by the Award Approving Official.

**Phase 2 Criteria: Prototype Development and Milestone Achievements**

Phase 2 will include 2 milestones and achievement of each milestone will be awarded separately:

***Milestone 1 Prize***

- Deliverable 1: Quantifiable progress toward meeting the initial performance and testing requirements of the NAMs platform in a specific context-of-use
- Deliverable 2: Successful construction and scaling of the NAMs platform according to fit-for-purpose industry guidance

***Milestone 2 Prize***

- Deliverable 1: Quantifiable progress toward internal validation of the NAMs platform using reference standards/compounds/agents and demonstrated within-laboratory reproducibility of results
- Deliverable 2: Documented use of the platform in addressing areas of need, and meeting the data standards in coordination with the NAMs Data Hub and Coordination Center (NDHCC) for the particular NAMs platform
- Deliverable 3: Deposition of data and resources for purposes of efficient validation and/or qualification by the VQN
- Deliverable 4: Documented interactions with the VQN for a possible use case

**Phase 3 Criteria: Prototype Delivery for Validation and Qualification**

Phase 3 deliverables:

- Deliverable 1: Detailed description and requisite documentation (and materials if applicable) for the successful transfer of the comprehensive NAMs platform to the VQN for independent validation and testing.
- Deliverable 2: Detailed description of how the prototype performs in one or more workflows specified by the solver. This document should include thorough operating instructions for executing the workflow using the platform.

## HOW TO ENTER

**Phase 1 Registration and Submission Process:** The official challenge announcement for the Complement-ARIE (Complement Animal Research In Experimentation) NAMs Reduction-to-Practice Challenge can be found on Challenge.gov at https://www.challenge.gov/?challenge=NAM-RTP. The Challenge registration and submission process is administered by HeroX, a challenge platform and management provider under contract with the NASA Center of Excellence for Collaborative Innovation on behalf of NIH. All interested Participants must register on the official challenge portal by going to www.herox.com/Complement-ARIE-RTP by the registration deadline on 03/01/2026. Upon registering, participants will be required to identify whether they are registering as either of the following: as an independent Team (i.e., registering as a group of individuals competing together but not on behalf of an established organization, institution, or corporation) or as an Entity (i.e., registering as a group of individuals competing together on behalf of a legally established organization, institution, or corporation). Participants will need to provide the name, affiliation, and contact information of all individuals competing in this Challenge as part of a Team or on behalf of an Entity. All Participants will also be required to acknowledge whether federal funding will be used in the development of the Challenge submission (see Participation Rule 1). All Participants must certify they have read, understand, and agree to abide by the official eligibility rules, participation rules, and requirements for the Challenge as stated in this announcement.

**Phase 1 Submission Requirements:** Each participant must submit the Challenge Registration Form to define who is participating in the Challenge and provide contact information for the Participant, and then upload the Proposal Submission on the Challenge website.

For your submission to be eligible for judging, you must:

- Be eligible to compete as part of a Team or Entity (see Eligibility Rules).
    - For Teams: Each participating Team is required to identify a Team Leader who will register and submit on behalf of the Team members. The Team Leader is responsible for all communications with the Challenge sponsors and, in the event of winning a cash prize, will be paid the prize in full. To be eligible to receive a

cash prize, the Team Leader must be a citizen or permanent resident of the United States. In the event that a dispute regarding the identity of the Team Leader who actually submitted the entry cannot be resolved to NIH's satisfaction, the affected submission will be deemed ineligible.

- For Entities: Each participating Entity is required to identify a Point of Contact who will register and submit on behalf of the Entity. The Point of Contact is responsible for all communications with the Challenge sponsors. In the event of winning a cash prize, the prize will be paid directly to the Entity, not to the Point of Contact. To be eligible to receive a cash prize, the Entity must be incorporated in and maintain a primary place of business in the United States. As stated in the Participation Rules, Participants intending to use Federal grant, cooperative agreement, or other transaction (OT) award funds must register for and participate in the Challenge as an Entity on behalf of the awardee institution or organization. In the event that a dispute regarding the identity of the Point of Contact who actually submitted the entry cannot be resolved to NIH's satisfaction, the affected submission will be deemed ineligible.

- The Team Leader or Point of Contact must register on the Challenge website.
- Complete and submit the Registration Form.
- Upload your responsive Proposal and supporting documents in PDF format through the designated Challenge webpage. All submissions must be written in English and cannot be handwritten.
- Submissions must not include the HHS' logo or official seal or the logo of NIH or any of its components and must not claim federal government endorsement.
- Each Team may only propose 1 solution. An Entity may submit multiple entries provided there isn't substantial overlap in team members, the team leaders are not the same, and each entry has a distinct and separate focus.

**Phase 1 Proposal Submission**

Solvers will be required to fill in an Eligibility Review Form answer multiple questions to determine the eligibility of the Team/Entity submitting, as well as confirmation that the Team/Entity meets and accepts all rules to participate in the challenge.

Submissions to Phase 1 must follow the structure outlined below and adhere to the stated page limits. Do not include any proprietary or confidential information in the Title, Executive Summary, and Plain Language sections as they may be publicly shared if the participant is selected to win a prize across any phase of this Challenge (see Participation Rule 7)

- Cover page (**1 page**)
    - Submission Title
    - Team/Entity Name
    - Logo (optional)
    - Team/Entity location (State, Country)
- Executive Summary (**1 page**): Provide a concise summary of your proposed solution, emphasizing its significance, innovation, human-relevance, and feasibility. Note that the winners' Executive Summary section will be shared publicly.
- Plain Language Summary (**0.5 page**): Provide a summary of your submission that can be easily understood by a general audience. Describe your technical proposal in a manner that ensures the main ideas and impacts are clear and accessible to those without specialized knowledge or technical background in the field. This summary will be made public for winners and used for broader dissemination to inform the public about the contributions and significance of your work.
- Team Composition & Expertise (**1 page**): Provide details about the individuals competing together on behalf of your Team/Entity, emphasizing interdisciplinary expertise. Indicate if Team/Entity members are members of the academic, industry, government, non-government organizations, advocacy communities, or a combination.
- Project Description and Data (**10 pages, including all figures, tables, and data, but excluding references.)**
    - Select the priority areas your proposed solution addresses, or define an equivalent scientific need addressed by your solution.

    - Explain how the components of your combinatorial NAMs integrate to fill in technological gaps and describe the potential impact of your NAM should it become a validated solution.
    - Highlight the novelty and innovation of your proposed solution.
    - Describe the technical specifications of the NAM in detail and discuss challenges that may arise in its development. Discuss how well the proposed combinatorial NAM will predict outcomes in humans and your prospective verification/validation strategy.
    - Describe planned activities, milestones, and technical readiness on a timeline that demonstrates Phase 2 capability and will enable the solution to successfully complete the full RTP challenge in a 3-year period.
    - Provide any data to support the feasibility and readiness of your combinatorial NAM in successfully completing the RTP challenge.
    - Provide a clear explanation, scientific rationale, and evidence base for your proposed solution.
- **Supporting Documents (10-page max addendum)**
    - Include references and letters of support for the project from proposed facilities, collaborators, and/or your organization or company. References do not count towards the 10-page limit.

All submission content must be provided in English. Submissions must not include the HHS logo or official seal or the logo of NIH or any of its components and must not claim federal government endorsement.

**Phase 2 (Milestone 1 & 2) and Phase 3 Submission Requirements**

The submission requirements for Phase 2 (Milestones 1 & 2) will be provided to winners of Phase 1 prior to the initiation of Phase 2. The submission requirements for Phase 3 will be provided to the final winners of Phase 2 prior to the initiation of Phase 3.

## ADDITIONAL INFORMATION

**Supplementary Information**: Additional Background on the Challenge Announcement and related Glossary are provided as an attachment.

**For Further Information Contact:**

Inquiries will be directed to: solve@herox.com

**Award Approving Official:**

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|---|---|
| Nicole C. Kleinstreuer, Ph.D. | Date |
| Acting Deputy Director for Program Coordination, | |
| Planning, and Strategic Initiatives, National Institutes of Health | |