Additional Answers to Q&A Webinar Questions

Date of Q&A Webinar - December 10th, 2025

Link to recording - https://www.herox.com/Complement-ARIE-RTP/update/7884

Link to FAQs - https://www.herox.com/Complement-ARIE-RTP/faq

Please see below for answers to additional questions submitted via the Q&A Webinar on December 10th, 2025.

1. For non-profits: Is this only for small businesses or can larger companies apply?
    a. U.S. based nonprofits are eligible to submit. There is no limit on the size of the organization provided the organization registers to participate in the Challenge under the rules as published in the Challenge Announcement and complied with all the requirements set forth therein.

2. What is the relationship of this challenge to TDC and VQN mechanisms, is it allowed to apply to both?
    a. Recipients of TDC or VQN awards will be eligible to compete if they follow the limitations on use of federal funds to develop their solutions (refer to answer for Q3) and if they are proposing a solution that is sufficiently different from what is already funded through the TDC or VQN.

3. How is the award typically allocated?
    a. This is not a grant. This is a Challenge competition where prize money is awarded after winners are selected for each phase. Use of prize money from any Phase is unrestricted.

4. I have my own project and want my own team and just want to know if other teams would like to collaborate. Do you help with team collaborations?
    a. HeroX provides the capability to search for other teams but it is incumbent on the solvers to connect and collaborate.

5. Can I change my team into an entity?
    a. You can edit your submission up until the deadline and change your name to an entity name. It is important to note that 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.

6. Can more than one US based Entity submit a joint proposal?
    a. Yes, but NIH will only pay a prize to one Entity if the submission is selected for a prize. A joint submission can be submitted, providing you submit one submission on behalf of an Entity.

7. Can multiple proposals with the same/similar COU but different teams be selected as winners for phase 1?
    a. Yes.

8. Can NIH give examples of contexts of use tied to priority areas?
    a. A wide range of contexts-of-use are possible and highly dependent on the NAM. Some examples could be drug-induced liver injury or other toxicity-related contexts.

9. How is "scale-up" defined for Phase 2, Milestone 1?
    a. Detailed requirements for Phase 2 and Phase 3 (including "scale-up" specifics and evaluation criteria) will be announced later on the challenge website as those stages approach.

10. If there are several publications and the users of a product, can we say that this product is validated?
    a. Publications and evidence of use are important supporting indicators, but on their own they do not automatically mean a product is "validated." In this challenge, validation is understood in the context of a defined use and

involves demonstrating that the method or platform consistently produces reliable, interpretable results appropriate to that use. Teams should describe what validation means for their specific context of use and provide documented evidence that their processes/methods produce expected results. This could include publications, prior use, and performance data.

11. Should a proposal focus on one context of use or propose multiple contexts of use?
    a. While the Challenge does not limit solvers to a single context-of-use, it can be generally advantageous to have a single, well-defined context of use as projects move toward validation efforts.

12. How will validation account for variability in primary human cells?
    a. This will be assessed case-by-case as projects move through the competition, with added expertise/support expected via the broader partner network (including the validation/qualification ecosystem) as the program matures.

13. Can you comment on CoU and regulatory requirements for the submission?
    a. These are defined in the Background and Glossary

       Context of use (CoU) - Clearly articulated description delineating the manner and purpose of use for a particular method or approach. Having a more specific CoU greatly aids the validation and/or qualification process.

       Qualification - Within a stated context of use, qualification is a conclusion that the results of an assessment using a model or assay can be relied upon to have a specific interpretation and application in product development and regulatory decision making. Qualification must identify the boundaries of the available data that adequately justify the use of the tool. The qualification process evaluates the fitness of the model for a specific context of use (CoU), with characterization of the challenge agent(s) and exposure, primary and secondary endpoints, triggers for intervention, and key disease values to be replicated for quality assurance and control.

14. How much preliminary data is expected (like R01 or more like R21)

a. This challenge encourages preliminary data submission. There is no expectation for the amount of preliminary data submitted, as long as it fits within the 10-page limit of the “Project Description and Data” (excluding References).

15. How will scale-up be assessed?
    a. This is dependent on the particular NAMs and CoU and can be justified in the submission. Detailed requirements for Phase 2 and Phase 3 (including “scale-up” specifics and evaluation criteria) will be announced later on the challenge website as those stages approach.

16. Are ex vivo models allowed (e.g., lung slices)?
    a. Yes, ex vivo models (e.g., human-based lung slices) are allowed. Ex vivo tissues must be sourced from humans.

17. Who is the “end user” for these NAMs?
    a. End users are stakeholders involved in the validation/qualification ecosystem (including public/private entities), depending on the context of use (e.g., regulatory and biomedical research stakeholders).

18. Could a combination of organoids and organ on chip qualify as a combinatorial NAM?
    a. Likely yes. This would be an example of two distinct NAM technologies within a modality.

19. When do you anticipate setting milestone acceptance criteria for Phase 2?
    a. More information on phase 2 requirements will be provided at the start of Phase 2, for Phase 2 teams.

20. Do proposed NAMs need to match or outperform animal testing, or is reducing reliance on animal testing sufficient?
    a. Neither is a strict requirement. The intent is to advance human-based NAMs that support broader adoption/implementation and help reduce reliance on animal studies; demonstrating practical impact is advantageous.

21. Must teams include all three NAM categories (in vitro, in silico, in chem), or can they propose fewer?

    a. Teams are not required to include all three categories. Combinatorial NAMs must span at least two categories, or are clearly different within category, to help address gaps/deficiencies of any single approach.

22. Is an in silico component required—and how complex must it be?
    a. There is no requirement that proposals include an in silico model; it is up to solvers to define their combinatorial NAM approach.

23. For iPSC-derived NAMs, is it important to use multiple donor sources?
    a. This depends on the model/context of use; there is no requirement to use multiple donor sources. The emphasis is on reproducibility and what is most reasonable to support the stated context of use.

24. In the combinations - are the two individual NAMS involved already validated on their own? Can any of the NAMs already be validated?
    a. There is no prohibition on NAM components being validated in combination, and the overall combinatorial NAM should not yet be validated. The aim of this challenge is to accelerate validation of near-ready combinatorial NAMs. For example, a combinatorial NAM with validated components may require further development to be ready for overall validation that this Challenge would support.

25. Are proposal evaluation criteria equally weighted?
    a. The weights for the evaluation criteria are in the challenge guidelines on the challenge website.

26. Is toxicity a priority area? How does toxicity vs. efficacy rank?
    a. Toxicity and Safety is a priority area. Please see its description on the challenge website.

27. For other NAM initiatives, ocular/opthalmology focused approaches have not prioritized while areas like lung or toxicity have been. Are ocular approaches considered a priority here?
    a. Priority areas are: Chronicity, Neurobiological Models, Personalized Medicine, Cross-Disease Pathogenesis, Toxicology and Safety, Human Health Protection, and/or a solver defined area of equivalent scientific need. Please see the challenge website for more details.

28. Not a question, but for example Context of Uses, teams could look at existing Drug Development Tool (DDT) within the Innovative Science and Technology

Approaches for New Drugs (ISTAND) Pilot program applications on the FDA website link here.

a. Please feel free to add this to the forum!