DARPA-PS-25-03
Questions and Answers
Rapid Inhibitor Discovery and Development pipeLine (RIDDL)

Last Updated: 12/9/2024

Note: The subject Program Solicitation is not accepting abstract/pre-proposals. Full proposals are due on 12/20/24 – instructions can be found in Section 4.2 of DARPA-PS-25-03.

OT Guide

General Questions

1. **Is a DARPA representative available for a call to discuss our proposed approach?**
   In the interest of fairness to all proposers as Dr. Greene will not have availability to honor all requests, we will not be scheduling any program-related calls/meetings. Most answers to questions can be found in the Program Solicitation (PS), which describes the program and program requirements in detail. If you cannot find the answer to your question in the PS, please e-mail your question to RIDDL@darpa.mil. Please be aware that your question and its answer may be published on this Q&A, after the question has been revised (if necessary) to remove any proprietary details. If needed, please mark any portion of your question as proprietary to avoid unintentional publication.

2. **Are International Universities eligible to participate as collaborators in response to the BAA? What about non-US organizations?**
   As stated in Section 3.1.2 of DARPA-PS-25-03, "Non-U.S. organizations and/or individuals may participate to the extent that such participants comply with any necessary nondisclosure agreements, security regulations, export control laws, and other governing statutes applicable under the circumstances."

3. **Could you please provide a definition or explanation of what constitutes a "Prototype Project"?**
   OTs are contractual instruments other than standard procurement contracts, grants, or cooperative agreements. OT Prototype projects are distinguished from OT research projects in that a prototype project often requires the delivery of a product of the project (e.g., the prototype) to the government for testing and evaluation.
   Common Applications:
   - R&D activities to advance new technologies and processes and prototyping or models to evaluate feasibility or utility of a technology

- To address perceived obstacles to doing business with the government by non-traditional vendors to include intellectual property rights and compliance with cost accounting standards
- For flexibility to tailor agreements to reach non-traditional vendors with innovation research development and demonstration (RD&D) solutions
- For negotiable funding arrangements, payment milestones, and length of agreement to achieve research and prototype projects

A link to the OT Guide is provided above.

Submission Questions

4. **The program solicitation document mentions "Attachment F: Model OT for Prototype Agreement," as well as six additional attachments numbered 1 through 6. Could you please let me know where I can find these six attachments (such as the Task Description document, Report Requirements, etc.)?**
   The attachments can be found at the SAM.gov posting for the opportunity:

   https://sam.gov/opp/d04ec5d6949b435083f6f582300aca27/view

5. **Could you please clarify where the Technology Transfer plan should be in the proposal (specific attachment or separate file)? Additionally, is there a template or page limit for this section?**
   The Technology Transfer Plan should be included in the Volume 1 of the proposal, and the plan will count towards the total page limit. There is no set template or required format for the technology transfer plan. All elements required in the plan are described in the solicitation.

6. **What is meant by "Technical Papers" on page 1 of Attachment B?**
   Technical papers may include published journal articles as well pre-publication manuscripts.

7. **Who would be the appropriate authority at a university to sign the transmittal letter? PI? Head of Sponsored Programs? Vice President for Research? Does DARPA have a template or preferred format for the transmittal letter?**
   The VPR or another agent of the institution with contractual authority capable of binding the institution would be appropriate. Depending on the institution, this could be a contracting officer or specialist, the head of the Office of Sponsored Programs, or another member of the institution's administration. There is no template or preferred format.

8. **DARPA-PS-25-03 indicates that the contract opportunity application is due 12/20, however I cannot find it in grants.gov or an Opportunity Number to set-up a Workspace for submission. Has this been released?**
   DARPA intends to award Other Transactions or Prototype under the subject opportunity. As no assistance instruments (Grants or Cooperative Agreements) are expected, the Program

Solicitation will not be published to Grants.gov. Proposals must be submitted via DARPA's BAA Portal in response to DARPA-PS-25-03.

9. **What is a "non-traditional Defense contractor"?**
   A non-traditional defense contractor is defined as an entity that is not currently performing or has not performed in the last one-year period any contract for the Department of Defense that is subject to full Cost Accounting Standards (CAS) coverage. If the proposing team is not composed of the required entities listed above, the team will be required to provide at least 1/3 cost share from their own funds, unless a case can be made for a waiver. Waivers are not common and will require significant justification.

Program Structure Questions

10. **What's the earliest proposed start date?**
    Spring 2025.

11. **During our BSAFE application we were instructed that $10M was the maximum budget. Could you give us a reasonable target budget maximum for RIDDL?**
    This is a new, standalone solicitation. No assumptions should be made based on previous solicitations. As stated in the RIDDL program solicitation, DARPA has approximately $17M available in total for all performer awards and anticipates selecting multiple performers.

12. **The target of the new program seems to be rapid discovery, characterization and performance optimization. A focus of BSAFE was broad-spectrum, is it correct that spectrum is no longer a key target metric to optimize?**
    Please read the Program Solicitation carefully and ensure that submissions account for all metrics described in the text and tables. These metrics include – but are not limited to – potency, safety, and speed.

13. **Has the focus shifted to DNA-binders/cutters, and away Cas13 and other RNA-guided RNAses?**
    Solutions for DNA editors, including Cas9 and Cas12, are a program requirement. A solution that can also address Cas13 and other RNA-guided RNases would potentially be more competitive compared to a solution which only addressed DNA nucleases.

14. **Does the program aim for Acr proteins that specifically inhibit a particular type of Cas protein? Or is it more focused on Acr proteins that reduce off-target effects of Cas proteins, thereby increasing the specificity of the Cas editing system? Or perhaps both?**
    Specificity in this context is more closely aligned with inhibition of a specific nuclease without any off-target effects from the inhibitor molecule. In other words, an inhibitor molecule with only one effect.

15. **Regardless of meaning, may we use a non-percent metric (e.g., x-fold differences in IC50s)?**
    As stated in the PS, the example metrics are not intended to be prescriptive. Offerors may propose metrics that are best suited to their specific technical approach.

16. **Are the "intermediate metrics" mentioned on page 1 akin to 3–6-month milestones and deliverables? If not, please clarify.**
    Table 3 on page 10 provides required (minimum) and preferred (goal) metrics that function as a target product profile. The 3–6-month milestones and deliverables should be proposed to demonstrate increasing complexity and performance as progress toward achieving the final product.

Technical Questions

17. **What are the requirements for in vitro assays? For example, we plan to propose rapid validation of peptide-based inhibitors in IVTT mixes, followed by toxicity/off-target validation in bacterial and mammalian cells. Does the program expect specific metrics for cell lines (other than speed)?**
    If the proposed assay can meet metrics/milestones/capability demonstrations, the technical approach is open. The RIDDL program does not prescribe the technical approach that offerors should propose.