HR001118S0037
Frequently Asked Questions

Last Updated: 6/20/2018

General

1. **Is a DARPA representative available for a call to discuss our proposed approach?**
   The best way to receive feedback on an approach is through the submission of a proposal abstract by July 12, 2018, 4:00 PM EST. Most answers to questions can be found in the BAA, which describes the program and program requirements in detail. If you cannot find the answer to your question in the BAA, please e-mail your question to PREPARE@darpa.mil. Please be aware that your question and its answer may be published on this FAQ, after the question has been revised (if necessary) to remove any proprietary details.

2. **Will the Proposers Day slides be posted online?**
   Briefing materials that were presented by DARPA at the PREPARE Proposers Day will be made available on the BTO section of the DARPA Opportunities webpage: http://www.darpa.mil/work-with-us/opportunities.

3. **Are Federal Laboratories and International Universities eligible to participate as collaborators in response to the BAA?**
   Yes. Per the BAA, "All responsible sources capable of satisfying the Government's needs may submit a proposal that shall be considered by DARPA." Federally Funded Research and Development Centers must adhere to the guidelines listed in Section 3.1.1 of the BAA, found on page 26. Information about Non-U.S. Organizations can be found in the following Section (3.1.2).

4. **Do I need to submit an abstract? What is the advantage of submitting an abstract? Does my abstract need to match the full proposal submitted?**
   Abstracts are strongly encouraged, but not required, to submit a full proposal. DARPA will provide written and/or verbal feedback for each abstract submitted. DARPA will provide feedback regarding technical approach and will highlight components for proposers where additional information or clarification should be provided in the full proposal to meet the requirements of the BAA and vision of the program. Feedback will also be provided to encourage or discourage submission of a full proposal to the PREPARE solicitation based on the proposal's alignment with the program vision and technical innovation.

5. **When is the expected award date?**
   Spring 2019.

6. **How many awards are expected under PREPARE, and what is the total budget available for the PREPARE program?**
   The BAA states the following: "Multiple awards are anticipated. The amount of resources made available under this BAA will depend on the quality of the proposals received and the availability of funds."

Teaming

7. **Is there a limit on team size? Is there a recommended team size? Can DARPA assist with team formation?**
   No. It is the responsibility of proposers to assemble a team that can effectively address all technical and programmatic requirements of the program. DARPA will not provide any recommendations on team size, makeup, etc.

8. **Does DARPA expect us to have a project coordinator or manager?**
   Yes. Each team is expected to include one project coordinator or manager to ensure effective communication and task management amongst team members and with DARPA.

9. **Is it preferable if teams are co-located?**
   There is no preference for co-located teams, however, multi-PI and multi-institute teams should indicate how they plan to manage efforts that are distributed.

10. **Do teams need to be finalized prior to submitting an abstract?**
    No. However, proposers must finalize teams prior to submitting the full proposal.

11. **Can a team member be an employee at a government organization (CDC, NIH, etc)?**
    Yes. There is no restriction on including team members from government agencies as subcontractors. However, if a proposal includes a government agency as the prime contractor, the agency must provide authority to compete with industry in its BAA proposal submission or must submit its proposal directly to the DARPA Program Manager in lieu of submitting the proposal directly to the BAA.

12. **Can multiple groups work on the same technical area?**
    Yes. However, each group in a single technical area should provide unique expertise and capabilities to ensure successful completion of milestones. More than one team member may work within a technical area, or across multiple technical areas.

13. **Can a performer team be on multiple proposals/awards?**
    Yes. Teams can be subcontractors on multiple proposals. If chosen for multiple awards, a clear path will be established for ensuring no conflicts are present between the efforts. Proposers who are subcontractors on multiple teams should be cognizant of the distribution of the level of effort across multiple awards and will be required to ensure that DARPA is only charged once for any potential duplicate efforts.

Programmatic

14. **How should a proposer determine an appropriate budget?**
    Cost realism is an important evaluation criterion for proposers to address. Proposers must provide a realistic estimate of the costs (e.g. staff, resources, equipment) necessary to successfully complete milestones and deliverables.

15. **Is in-kind support from PI teams acceptable?**
    Yes. This type of support (e.g., HHMI PI salary) is acceptable, but must be defined and justified in the proposal.

16. **Is there a limit to how much a subcontractor can receive in funds?**
    No. All budgets should be realistic and represent costs associated with the tasks assigned to each subcontractor.

17. **Will the program accept grant proposals?**
    No. DARPA does not intend to award grants under the PREPARE program. PREPARE awards may include cooperative agreements, procurement contracts, or other transactions.

18. **Do I have to stick to the program structure/timeline outlined in the BAA? How rigid is the schedule?**
    Yes, key technical areas, milestones and timelines as outlined in the BAA should be maintained in the proposed efforts.

19. **Is progression from Phase I to Phase II purely milestone based, or is it also constrained by budget?**
    Progression from Phase I to Phase II is dependent on multiple factors, including technical progress demonstrated by teams and the available budget for the program.

20. **Is data sharing required? Is data sharing an allowable budget item?**
    Yes. BAA Section 1.5 states, "the PREPARE program will require that information be shared with DARPA and US Government stakeholders." However, data sharing between teams funded under the PREPARE program is not required. Data sharing is an allowable budget item.

21. **Since this is a four-year program, will there be more opportunities to apply for funding throughout the program's lifecycle?**
    No, this will be the only open call for proposals for the PREPARE program.

22. **Can gene target identification continue beyond the initial deadlines, such as Month 13 or Phase I?**
    Yes. Proposers are welcome to identify new targets that could improve threat protection (either single or multiplexed targets). However, the balance should shift from discovery to pre-clinical translation as the program progresses.

Controlled Unclassified Information (CUI)

23. **What is Controlled Unclassified Information (CUI)?**
    CUI is information that requires safeguarding or dissemination controls pursuant to and consistent with applicable laws, regulations, and government-wide policies, but it is not classified under Executive Order 13526 or the Atomic Energy Act, as amended. For more information, see https://www.darpa.mil/work-with-us/additional-baa

24. **If data generated during the program are considered CUI, can it still be published?**
    As stated in the BAA, "All performers (prime contractor and subcontractor) desiring public release of project information that may contain CUI as defined above must submit a request for public release from DARPA/PRC in accordance with their contractual requirements." Thus, prior to submission of a study to a scientific journal, teams will submit manuscripts to DARPA for review. If a manuscript contains

CUI (e.g., gene names of concern), DARPA will work with the team to omit specific instances of CUI prior to publication.

Technical

25. **Do I need to apply to all 3 TAs?**
    Yes.

26. **What happens if research in one of the TAs fails while the others are successful?**
    Proposers should provide risk mitigation strategies to ensure that progress towards the end of the program is not halted by technical issues in a portion of the overall effort.

27. **Are cell therapies that involve *ex vivo* genome modulation prior to *in vivo* administration allowed?**
    Yes. *Ex vivo* genome modulation may be explored as an intermediate step for research and discovery purposes, however, proposers must still meet and/or exceed the metrics outlined in the BAA for developing a highly-effective PGM-MCM that targets relevant cells and tissues *in vivo*. Proposers should also consider how *ex vivo* therapies will be both generalizable to demonstrate its platform capability and also readily manufacturable and scalable in a cost effective manner for future production.

28. **Do I need to perform both activation and repression screens?**
    There is no requirement for what type of screen is performed. Proposers are encouraged to utilize any techniques and technologies that will yield high quality, reliable data that can be quickly leveraged to achieve program goals. However, proposers should understand the dynamic range of expression for protective genes to enable maximal PGM-MCM efficacy may include both up or down regulation of genes. Knock-down screens have been well documented for decades and approaches that only consider knock-out or knock-down of gene activity will not explore the full range of possible solutions.

29. **Does DARPA provide preliminary data?**
    No.

30. **I have previously identified interesting gene targets for a select threat, do I still need to perform genome-wide agnostic screens?**
    Yes. Proposers are highly encouraged to leverage previous datasets and past research experience (either published or not) relevant to the threat proposed. However, proposers with significant preliminary data are expected to use screens during the program to identify additional targets or combinations of targets to yield maximum threat protection.

31. **To what extent can organ-on-a-chip technologies replace or supplement animal model studies?**
    Organoid or “on-a-chip” technologies are within the scope of the program and can be useful systems to test PGM-MCMs. However, given that these technologies cannot yet comprehensively replicate a whole organism, they should not replace animal model studies. Proposers must determine which systems are the most appropriate to meet all requirements of the program and expectations set by the FDA for product development.

32. **Would the transient introduction of a DNA construct that codes for the expression of a human gene be considered responsive to the BAA?**
    No. Transient introduction of DNA constructs to express human genes (gene therapy) are not within the scope of this program as it does not modulate the expression of endogenous human genes. However, these tools may be used in support of PGM development, such as gene dosing controls, etc.

33. **Is it sufficient to address a subset of pathologies associated with a threat rather than all pathologies?**
    The PREPARE program seeks novel, disruptive PGM-MCMs against four primary threats. Pathologies and sub-pathologies for any given threat may be explored as part of the effort, and a full characterization of all pathologies and the impact of PGM-MCMs on alleviating those pathologies should be explored. It is understandable that a given PGM-MCM may not alleviate all pathologies, however, proposers are encouraged to include ambitious goals for threat protection.

34. **Can I propose more than one modulator or delivery modality?**
    Yes. Proposers are welcome to propose multiple parallel technologies as it is not known *a priori* which will be the best suited for a given threat. However, proposers should down-select the best performing technologies that progresses through the program.

35. **Are AAVs (Adeno-associated viruses) acceptable for TA3?**
    While AAVs are not prohibited in TA3, proposers must demonstrate technological innovation for PGM delivery beyond the state of the art. Utilizing current or previously-developed AAV technology is not sufficient to meet TA3 requirements. However, current AAV technologies are suitable benchmarks for comparison purposes to newly developed PGM-MCMs.

36. **Is phage delivery within scope for TA3?**
    Novel approaches to TA3 are within scope so long as they meet the requirements outlined in the BAA.

37. **Is there a preferred route of administration for a PGM-MCM?**
    No. There is no preferred route or method of administration. However, proposers may consider the end use case for PGM-MCM administration and the potential for widespread, rapid use (e.g., pandemic flu).

38. **What role does data analytics and informatics play in the project? By phase?**
    Analytics and informatics play critical roles throughout the program.

39. **Does a 2x, 10x, 100x improvement in the state of the art include improvements in manufacturability, shelf-life, etc.?**
    It can. However, the primary goal of the program is to develop novel, innovative PGM-MCMs that provide greater protection against influenza, opioids, organophosphates, and gamma irradiation. Improvements in manufacturability, shelf-life, etc., while crucial for the development of any MCM, should supplement the primary aims of the program, and will not exclusively satisfy the 2x, 10x, and 100x requirement.

40. **Can I propose to address more than one of the four threats?**
    Yes. Proposers are welcome to address more than one threat, particularly if they demonstrate the generalizability of the PGM-MCM platform. However, each threat proposed must be investigated with equal rigor and will be measured against ambitious metrics and milestones.

41. **Can I propose a threat that is not included in the BAA?**
    Proposers must choose at least one threat (influenza, opioid overdose, organophosphate poisoning, gamma irradiation) as the primary threat that is tested. However, secondary threats can be included to demonstrate generalizability or multiplexability of the PGM-MCM platform. Proposers must provide justification for the DoD-relevance of secondary threats.

42. **Are non-opioid approaches to pain management suitable to propose?**
    Yes. The program expects proposers to address either (a) chronic or acute pain in a non-opioid manner or (b) reversal of opioid overdose. However, ways to mitigate opioid *addiction* specifically will not be considered.

43. **Mammalian systems upregulate expression of more genes in the transcriptome below 0.1 Gy, while this has not been found above 1.0 Gy. Therefore, chronic low-dose radiation may be a fundamentally different modulator than acute higher-dose radiation. Can these two exposure types be treated as two separate threats?**
    DARPA is interested in understanding the performance of PGM-MCMs at various doses of threats that may result in any number of pathologies. Experimental complexity is expected to increase with each Capability Demonstration, and may include additional doses of a given threat.

44. **Do I need special permits for working with certain opioids or organophosphates?**
    Yes, special permits are required to perform work with certain opiates and OPs. It is the responsibility of the proposers to ensure they have the proper permits, expertise, and facilities to conduct the work that is proposed.

45. **Are bacterial or parasitic pathogens within scope of biological threats?**
    Influenza is the primary biological threat to be explored under the PREPARE program, however in order to achieve goals to demonstrate that PGM-MCMs are generalizable, at the end of Phase I, other biological threats may be explored in a limited manner.

Transition, FDA IND/EUA, ELSI

46. **Will intellectual property freedom to operate be reviewed for this program?**
    Yes. However, proposers should determine if intellectual property restrictions of their projects will prevent a viable transition strategy (BAA Section 1.5) for the technologies developed under the program. Proposers are encouraged to address any IP challenges as part of their transition and commercialization plan.

47. **Given FDA requirements for demonstration of human relevance where *in vivo* animal model tests are used to validate efficacy, what "metrics for success" will DARPA accept for validating study results for the *in vivo* studies? How closely must results for the program's Phase I and II studies replicate those which will be necessary for eventual licensure? It would seem that DARPA standards would need unification with FDA standards to meet the ambitious timelines, but it is not entirely clear that FDA standards currently exist for programmable gene modulator (or similar genome editing products).**
    It is the goal of the program to submit an IND application for the PREPARE technologies. Therefore, there should be significant overlap between the PREPARE program metrics and FDA requirements.

However, given that FDA standards for these technologies has not been finalized, it is expected during the program that proposers routinely engage with FDA to discuss what standards would be appropriate.

48. **Is it required that academic labs partner with industry for meeting the final IND submission goal?**
    While industry partnerships are not required, IND submission does require a sponsor or applicant, and proposers should identify an appropriate party to serve in this role.

49. **With IND submission being the ultimate objective, GLP toxicology and cGMP manufacturing is expected to be completed before the end of the program. How does that fit with the timing of Capability Demonstration 3 and the end of the program?**
    Compliance with GLP regulations is expected for IND submission, it is DARPA's understanding that cGMP manufacturing is not required at the time of submission. It is the responsibility of the proposer to determine how to best comply with GLP regulations, and to review FDA guidance, and engage regularly with regulators to ensure compliance with IND submission requirements.

50. **In responding to the BAA, are proposers directed to respond to DURC (Dual Use Research of Concern) or is that included in ELSI?**
    Yes, proposers should address any DURC concerns they anticipate along with ELSI considerations.