DARPARA2601
Protean
Frequently Asked Questions (FAQs)

Last Updated: 3/9/2026
Updates **bolded/highlighted/underlined** below

GENERAL INFORMATION

1. **Q:** My research is not geared specifically to meet the Protean program goals. Is there an alternate solicitation that I can respond to?
   A: Yes. DARPA/BTO has an office-wide solicitation (HR001126S0003) for this purpose. Responses are being collected through September 30, 2026.

2. **Q:** Is Dr. Feasel available for a call or meeting to discuss our approach?
   A: Due to scheduling limitations, and in the interest of fairness to all proposers, Dr. Feasel will not be taking program related calls and meetings. The best way to receive feedback on an approach is through the submission of a proposal abstract prior to the deadline specified in the Research Announcement (RA). The RA describes the program, including metrics, in detail. Specific questions may be submitted by email to ProteanTherapeutics@darpa.mil. Proposers should be aware that submitted questions and answers may be published on an FAQ page, with revisions to remove proprietary information.

3. **Q:** Will Protean Proposers Day materials (attendee questions, meeting transcription, and slide decks) be shared?
   A: Yes. Attendee questions will be part of the program FAQ document that is accessible to everyone, and slide decks will be posted to the program page on DARPA's website. Teaming profiles and lightning talks will be sent out to all meeting registrants. Transcripts will not be shared.

4. **Q:** Can FFRDCs, UARS, and Government entities participate in the program as performers?
   A: DARPA encourages technical solutions from all responsible sources capable of satisfying the government's needs. To ensure fair competition across the ecosystem, DARPA prohibits contractors/performers from concurrently providing Systems Engineering Technical Assistance (SETA), Advisory and Assistance Services (A&AS), or similar support services and being a technical performer, unless the DARPA Deputy Director grants a written waiver. DARPA extends this prohibition to University-Affiliated Research Centers (UARCs) and FFRDCs including National Labs, who because of their specialized expertise and areas of competencies, are able to accomplish integral tasks that cannot be met by Government or contractor resources.

Therefore, these entities are highly discouraged from proposing against this solicitation as awards to UARCs or FFRDCs will only be made by exception. UARCs and FFRDCs interested in this solicitation, either as a prime or a subcontractor, should contact the Agency Point of Contact (POC) listed in the Overview section prior to the proposal (or abstract) due date to discuss potential participation as part of the government team or eligibility as a technical performer.

SUBMISSIONS/TEAMING

5. **Q:** Is teaming required? Is there a limit on team size? Is there a recommended team size? Can DARPA facilitate teaming if a proposer cannot address all aspects of the program on their own?
   A: Specific content, communications, networking, and team formation are the sole responsibility of the proposer team. Teaming profiles and lightning talks were distributed to Proposers Day registrants and are available upon request via email to ProteanTherapeutics@darpa.mil. If you would like more information about working with DARPA, please go to the DARPA Connect webpage at www.DARPAConnect.us.

6. **Q:** Is an individual or organization able to submit more than one abstract in collaboration with different teams?
   A: Yes. Teams can be primes or subcontractors on multiple proposals. If chosen for multiple awards, a clear path will need to be established to ensure no conflicts are present between the efforts. Proposers who are 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 tasks.

7. **Q**: Is there a preference for institutional type and/or scientific background of a PI that plans to propose to?
   A: There is no preference for institutional type or background of a proposal's PI. The PI and key personnel should, however, have appropriate technical expertise to support the work proposed (as supported by previous publications, patents, companies, or other evidence of productivity).

8. **Q:** Will templates and attachments for Gate 2 of the Protean Proposal process be made available anywhere online?
   A: Instructions and templates for different award types (including the reference to attachment 6 in the RA) will be provided to proposers in feedback letters following review of Gate 1 proposals.

9. **Q:** Should proposers identify proprietary information in their proposal?
   A: Yes. Proposers are responsible for clearly identifying proprietary information with labels such as "Proprietary" or "Company Proprietary" (See page 12 of the Protean RA).

10. **Q:** Do proposers need to register in SAM.gov to submit to the Protean RA?
    A: You will not need to register in SAM.gov to submit, but should be registered there to be considered for award (See Section 4.4 of the RA for more information).

11. **Q:** Will there be any competitive disadvantage for proposing PIs who are non-U.S. citizens?
    A: All proposed senior/ key personnel will be subject to DARPA's Fundamental Research Risk-Based Security Review Process to identify the possible vectors of undue foreign influence. If proposing personnel are eligible as DARPA performers, there will be no competitive disadvantage. Performers must be able to comply with Protean's CUI Guide.

12. **Q:** Will there be any advantage to having the proposal support multiple FAs rather than just focusing on one of the three?
    A: No. The technical strength of each FA will be evaluated independently and addressing more than one FAs provides no explicit advantage.

13. **Q:** Is there a video format preference (or a list of acceptable formats)?
    A: Please see the following for acceptable formats (https://www.videolan.org/vlc/features.html).

BUDGET/COST

14. **Q:** Is there a maximum value or budget cap on for a proposal's total value or annual direct costs?
    A: While there is not an explicit value maximum for what funds proposer can request, the cost associated with every proposal will be evaluated for alignment and realism with the work proposed (see pg. 12 of the Protean RA).

15. **Q:** Does in vivo work performed by the proposing team qualify for funding?
    A: Yes, in vivo work can qualify for funding as long as the associated tasking can be justified in relation to Protean program milestones and metrics.

16. **Q:** Does DARPA funding allow certain reagents/materials to be procured internationally?
    A: Yes, DARPA allows for international procurement of reagents except in specific cases.

17. **Q:** Should ROM costing be limited to Phase 1 and portions of Phase 2 excluding the animal studies being performed at a government laboratory? Could a proposer submit costs to use a known partner who is capable of performing CWA animal efficacy studies?
    A: Costing from the proposer should not include funding for the government team. Respective government partners will be determined by DARPA at the appropriate time if an award is made.

PROGRAM STRUCTURE

18. **Q:** Is the availability of preliminary data a detriment to a proposal? How can proposers balance the inclusion of preliminary data without appearing to focus solely on incremental improvements rather than disruptive advancements?
    A: Preliminary data is not a detriment to a proposal. All proposals, whether they include preliminary data or not, must justify why their solution represents an innovative and disruptive advancement rather than incremental improvements. Incremental improvements to existing medical countermeasures are explicitly excluded, as stated on pg. 5 of the research announcement. Proposals that do not involve significant or fundamental advances on state-of-the-art approaches may be considered non-conforming.

19. **Q:** Do preliminary data have to be from the exact target or set of targets proposed for study under Protean?
    A: Not necessarily, but proposers must present a compelling case for the relevance of the data, and how they align to the goals of the Protean RA.

20. **Q:** Before Gate 1, is there an opportunity to discuss high level proposal alignment with the Protean program manager?
    A: No. The first opportunity to discuss proposals with the Protean program manager will occur after Gate 1 via proposal feedback calls. The details of these calls will be provided when selection letters are sent out to proposers in April, 2026.

21. **Q:** What is DARPA's position on intellectual property ownership of new chemical entities and/or derivative chemical entities based on prior hits?
    A: Intellectual property considerations are discussed in the research announcement on pg. 14, section 4.2. Proposals "should appropriately identify any potential restrictions on the Government's use of any Intellectual Property contemplated under the award instrument in question. This includes both Noncommercial Items and Commercial Items."

22. **Q:** Would a threat-agnostic antiviral treatment fall under the umbrella of this program?
    A: No, anti-viral treatments are not applicable to the Program. Proposals must address at least one of the Focus Areas "based on threat class of interest: 1) nerve agents, 2) synthetic opioids, 3) and ion channel toxins." [pg. 5].

23. **Q:** Would a countermeasure targeting a newly discovered intrinsic cellular pro-survival pathway, which protects critical tissues, be of interest in the Protean program?
    A: The proposal must demonstrate how its approach will meet all program metrics listed on pg. 8 in Table 2.3.1 RA Metrics and Milestones. For example, the proposed approach must meet metrics such as the 12-month milestone: "Demonstrate a >10-fold decrease in threat simulant binding affinity for its protein target, while ensuring endogenous ligand/substrate binding is minimally impacted." If the

proposed approach satisfies these metrics, it could be considered for the Protean program.

24. **Q:** Would an *in vivo* efficacy assessment be acceptable within Phase 1?
A: Provided that the Metrics and Milestones in Table 2.3.1 of the RA are satisfied, an accelerated efficacy assessment in an animal model could be acceptable within the Phase 1 timeline.

TECHNICAL

25. **Q:** Is AI/ML use critical in the response?
A: There is no requirement for the use of AI/ML.

26. **Q:** Will the animal study design be determined by the performer or DARPA through their sponsored laboratory?
A: Animal study and *in vivo* experimental design will be determined by the government team.

27. **Q:** What rodent models will the T&E partner be working with? Are the models humanized for any of the proposal targets?
A: Model selection has not been finalized with T&E partners and will be refined in conjunction with program performers throughout phases 1 and 2.

28. **Q:** When planning the efficacy studies in Phase 2, will the Government sponsored laboratory be able to use and administer an agent dose up to 1000-10000x LD50? This would likely represent many milligrams of agent per animal and could exceed dosing volume maximum limits with animal studies.
A: The government team will test countermeasures against large agent doses to evaluate toxicity. The specifics depend on the potency of the agent, as well as route of administration, and the animal model being employed; the ultimate goal is to render agents nontoxic by protecting over 10,000x LD50s.

29. **Q:** Are there any limitations to proposing a multi-pronged approach targeting both primary and two key downstream proteins?
A: There are no limitations to proposing a multi-pronged approach, provided the approaches align with the Protean program goal (pg. 4) and adhere to the inclusion and exclusion criteria specified in the research announcement on pg. 4-5.

30. **Q:** What is the difference, if any, between allosteric and "non-orthosteric"?
A: Non-orthosteric sites on a protein include allosteric sites, cryptic binding sites, or other non-competitive interactions with orthosteric ligands.

31. **Q:** How long is the allosteric regulator expected to modulate protein activity for protection?
A: Per the Month 30 Metric on pg 8 of the RA: the half-life of the intervention must be greater than or equal to half-life of the threat agent compound or target-threat

adduct. However, molecules developed under the program should also have favorable drug-like properties, with longer prophylaxis being preferable. Proposing teams should discuss and justify drug property considerations within their submission.

32. **Q:** Is DARPA strictly interested in countermeasures that inactivate broad classes of targeted toxins, or are countermeasures that promote survival of exposed personnel also of interest? Are countermeasure adjuvants of interest?
A: Supportive care and countermeasure adjuvants are excluded based on the RA exclusion criteria 4 and 5 (pg. 5). However, a proposal could include an adjuvant as part of a novel strategy to meet the research announcement metrics, provided the inclusion and exclusion criteria on pg. 4-5 are also satisfied.

33. **Q:** According to the slides presented on Proposer's Day, the project aims for the medical countermeasure to bind target proteins/enzymes and block toxins when they are present, while remaining inactive without toxins. Does the medical countermeasure need to detach from the target protein after blocking or neutralizing the toxin, or can it remain bound?
A: Proposals need only follow the guidelines outlined in the research announcement; the slides presented on Proposer's Day were examples only. If the proposed medical countermeasure can maintain "binding and downstream activity associated with endogenous ligand(s)" [pg. 7] while attached to the target protein, this approach could be proposed.

34. **Q:** Are performers expected to both procure and test at least three toxin or toxin-like compounds as part of the Phase 1 expected deliverables? If so, are performers expected to either create specialized protocols or team with a group that has specialized protocols in place to test the compounds?
A: Yes, "Performers are expected to either work on a surrogate of a known chemical threat (e.g., organophosphate-based pesticides vs. sarin, or VX) or directly on a chemical warfare agent itself, if containment strategies and handling restrictions can be appropriately addressed by the proposing institution" [pg. 7]. Proposals should justify the selection of each chosen surrogate or simulant. If the selected surrogate or simulants require special handling, justification should be provided for the team's ability to safely and legally work with them.

35. **Q:** From a preclinical safety demonstration perspective, what Metrics are expected during Phase 2 of this program to identify unintended consequences or off-target effects of allosteric modulation?
A: Proposers should consider molecule safety in their submissions, and the Protean RA contains metrics for lack of acute toxicity at 24 Months, as well as pharmacokinetic and pharmacodynamic studies.

36. **Q:** How many surrogates or simulants should be tested by the performer to support the argument for class efficacy proof of concept?

A: Per the 16 Month metric in table 2.3.1. of the RA: >3 threat surrogates/ simulants must be tested as evidence for in-class efficacy.

37. **Q:** Would you consider submissions that propose to develop binders or degraders (e.g., multi-valent binders, enzymes, absorbers, etc.) for a threat and its analogs as responsive to the Protean RA?
A: Strategies designed to absorb or degrade a specific chemical threat are specifically excluded from consideration under Protean per exclusion criterion 2, page 5 of the RA.