DARPA-PS-25-08
Red Blood Cell Factory (RBC-Factory)
Questions and Answers (Q&A)
as of 1/24/2025

Updates HIGHLIGHTED below.

Note: As a reminder, RBC-Factory is an UNCLASSIFIED fundamental research program. There is a security Classification Guide available to guide proposers away from areas likely to produce classified data or information. Please email RBC-Factory@darpa.mil to request the SCG.

Note: Amendment 1 to DARPA-PS-25-08 was published to SAM.gov on 1/16/2025 and can be found at the URL below:

https://sam.gov/opp/3e752c2630ad4ce38fc296c47c39b264/view

GENERAL INFORMATION

1. **Q: Will the Industry Day slides be posted online?**
   A: Yes; information relayed during the Industry Day will be made available on the RBC-Factory Program Page: https://www.darpa.mil/research/programs/rbc-factory

2. **Q: My research is not geared specifically to meet the RBC-Factory program goals. Is there an alternate solicitation that I can respond to?**
   A: Yes. DARPA/BTO has an office-wide solicitation, HR001124S0034, for this purpose. (https://sam.gov/opp/5fff3c4c76c341a4a6b1d2010211c793/view

3. **Q: What is the expected team makeup?**
   A: Please see Section 4.1 of DARPA-PS-25-08.

CONTRACTING/COST

4. **Q: How much funding is allocated per award/phase?**
   A: DARPA has approximately $18.1M total for performer awards and anticipates making multiple awards.

5. **Q: How are conflicts of interest (or their appearance) that are not at the organization level handled, and what is required of the proposers?**
   A: No action/notification of an anticipated COI with DARPA personnel is required. DARPA's internal COI process handles COI.

6. **Q: Could in-kind contribution be considered cost sharing?**
   A: No. An in-kind contribution is typically a non-monetary contribution and is not considered a cost-share.

ABSTRACTS/PROPOSALS

7. **Q: Is more than 1 abstract submission from the same (Prime) proposer allowed? Is a subcontractor /vendor allowed to be included in more than 1 abstract submitted by a prime proposer?**
   A: Yes. If an organization submits multiple abstracts as a Prime, each submission should describe a distinct technical approach. If multiple proposals are selected with overlapping team members, negotiations will need to deconflict SOWs and describe what safeguards are in place to ensure that time is not double billed and that the selected organizations have the personnel and bandwidth to support multiple efforts.

8. **Q: Is the abstract executive summary required to discuss proposer technology?**
   A: The executive summary should demonstrate the proposer's understanding of the purpose and goals of the RBC-Factory program in their own words.

9. **Q: Is there a preference for the estimated cost to be a table or narrative?**
   A: No – either is fine.

10. **Q: Will you please clarify the abstract submission process? Should we email a completed abstract packet to RBC-Factory@darpa.mil?**
    A: As stated in Section 4.1 of DARPA-PS-25-08: "Submit Proposal Abstracts to RBC-FACTORY@darpa.mil." Abstracts Due Date and Time: January 28, 2025, 12:00 PM Eastern Time

PROGRAM STRUCTURE

11. **Q: What is the timeline for ELSI milestones and deliverables? What deliverables are anticipated?**
    A: The proposer provides interim milestones to demonstrate progress toward the final deliverable. Please see the M&D table for some milestone requirements; ELSI discussions with DARPA are expected at months 13 and 15, then formal reports are due at months 19 and end of the PoP. Deliverables may include any materials used to prepare for impact discussions, and briefing materials as needed. The outcomes of the meetings are expected to be included in the final reports. Reports should outline the ELSI issues the performer and the ELSI discussions have identified and discuss how these risks might manifest and how they might be mitigated.

12. **Q: Is in-person attendance expected/required for group meetings? What is the expected frequency?**
    A: ELSI meetings are likely to be virtual except at formal scientific review meetings, which will likely be in person.

TECHNICAL - GENERAL

13. **Q: What is the intended and planned transferability of the RBC product to the warfighter's biology? Clinical introduction? Introduced in the combat field? "Grown" inside the host? How are the Accessorized RBC best intended to be introduced/deployed?**

A: DARPA is agnostic to the CONOPS/Future Application. We're interested in any possible solution that is going to meet the goals/metrics of the RBC-Factory program.

14. **Q: Is there an assumed or preferred red blood cell input (purified cells, whole blood, etc.), formulation (buffered, suspended, whole blood), or source (manufactured RBC, donor blood, blood fraction, etc.?**
    A: No, DARPA is agnostic to the input composition at the point of insertion into the 'device' and modification of the cells. Any input RBCs must be 1) physiologically equivalent to RBCs found in the circulation of a normal healthy adult, 2) mature (enucleated), and not genetically modified to alter form or function. Please keep in mind that RBC-Factory is focused on characterizing the ability to insert materials into RBCs.

15. **In reviewing the physical and chemical properties of cargos to be investigated in the RBC program (Table 1, p.6), we would like to confirm whether the mass-to-charge ratio (m/z) is expressed in units of Da/e instead of kg/Coulomb.**
    A: Da/e (Daltons per electron).

16. **Further clarifications on the experimental cargo expectations:**

    Q: Is it required to select a disease model, specific therapeutic, or use-case?
    A: RBC-Factory is posing a biophysical question: what are the physical, chemical, and mechanical limits of RBCs as a carrier molecule based on the characteristics of the cargo inserted. Cargo selections should be justified by how they fulfill the metrics. It does not seek specific cargos for specific use cases or applications. It is not required that cargo be selected with any application (disease or other) in mind. The cargo selection is intended to survey the described parameter space.
    Q: Is pursuing novel cargoes within scope?
    A: Cargo discovery is out of scope as a sole aim. Incidental discovery of potential cargoes is not prohibited.
    Q: Can we propose cargoes that might have DoD specific end applications?
    A: These cargoes are not universally proscribed but are not recommended. RBC-F is an unclassified fundamental research program and proposals that will generate classified data are out of scope. Please request and closely review the Security Classification Guide to understand the prohibited cargo(s).
    Q: Is there any requirement for cargo reuse, release, etc.?
    A: No- the only requirement is the cargo be stably inserted into the RBC for the life of that RBC or the duration laid out in the metrics. RBC Factory is not a drug delivery program.
    Q: Does a single cargo have to fulfil all parameters laid out in Table 1?
    A: No, it is expected that multiple cargo selections will be required to explore the parameter space defined in Table 1. The guidance is to select cargoes that will allow proposers to probe the boundaries of cargo loading into RBCs. Whatever cargos are selected, there should be a rationale supporting the selections.

17. **Q: What about other RBC-related attributes like hemostasis, storage toxicity and those involving other cells?**
    A: In this program, the metrics require that the modified RBC be safe to mix with whole blood/unmodified RBC. For example, the performers should characterize this response generally and assess that the introduction of mRBCs vs. native RBCs have no significant difference in inflammatory markers. Your proposal should outline experiments demonstrating equivalency on these indices between mRBCs and unmodified native RBC. Proposers may describe additional metrics that are aligned with the overall goal of gathering preliminary safety data related to mRBCs.

18. **Q: What timeframe for the [RBC modification] effect is acceptable or expected?**
    A: The final device should be capable of meeting the metrics in the program solicitation listed in table 2, goal 4.

19. **Q: What fraction of the RBCs in the total blood volume for the in vivo evaluation must be modified? Are there limitations or performance targets for minimum cell concentration or volume throughput, in addition to the stated goals for cell throughput?**
    A: DARPA is agnostic to these parameters so long as the metric for throughput is achieved (see Table 2).

20. **Q: There is a mention of small animal models with no humans, what about large animal models (i.e., pig)?**
    A: Large animal models are not prohibited but should be fully justified to support the program goals and metrics. These models are in scope if the prospective data sets will help inform questions about prospective safety profiles of mRBCs.

21. **Q: The metrics do not include oxygen transport by RBC – are proposers permitted to augment the metrics?**
    A: Additional metrics proposed by the performer are welcome, but not required. Proposals may include additional metrics to generate insight specific to their proposed approaches. Additional metrics should support the overall goal of the program and be justified accordingly. DARPA reserves the right to review and approve any additional metrics. Final metrics are to be determined at time of award negotiation and are subject to DARPA approval.

22. **Q: Does the survey of the parameter space include failure points, or is the program interested in the optimization of specific components?**
    A: A comprehensive and efficient survey of the cargo parameter space is critical to the program. This includes creating knowledge where certain combinations of RBC modification techniques and/or cargos fail based on the characteristics of the cargo. Conversely, optimizing processes for specific cargo is not in the spirit of the RBC-Factory program.

23. **Q: Are there preferred timepoints for in vivo assessment, e.g. number of days after injection? What is the required dose for animal safety evaluation, e.g., what fraction of the RBCs in the animal's total blood volume, or minimum number of treated RBCs to be infused? Is there a specific method requested for quantifying "Circulation Time" in Table 2, regarding in vivo evaluation?**
    A: Please review the published amendment to program Goal #3, there is no longer an in vivo component required.

24. **Q: For the 60-day assessment of cargo persistence in vitro, are there specified process, storage, or handling conditions?**
    A: Please review the published amendment to Table 2 (requirement changes from 60days to 40 days); comparison of unmodified RBC in any storage format compared to modified RBC in that same format is required.

25. **Q: How much blood volume (and/or number of RBCs) is envisioned to be processed in future full-scale applications? It is understood that this not part of this specific program, but helpful for understanding future scaling needs.**
    A: For the current program, we have no requirements for absolute scaling beyond the processing/throughput metric.

TECHNICAL - INDEPENDENT VERIFICATION AND VALIDATION (IV&V)

26. **Q: For IV&V are performers expected to provide a device to the US Gov't team for IV&V experiments?**
    A: Yes – see Section 1.5.4 of DARPA-PS-25-08 for additional details.

27. **Q: Please clarify which in vivo metrics are to be evaluated by the performer vs which are evaluated by the IV&V entity, or are the two identical?**
    A: Please see the published amendment regarding the changes to the in vivo modeling metrics. Performers should plan to provide their own data showing satisfactory completion of the metrics. Then, separately, the performers work with prospective IV&V partners to allow IV&V teams to reproduce the results.