DARPA-PS-25-12
BioElectronics to Sense and Treat (BEST)
Frequently Asked Questions

Version 4
30 April 2025
Updates are highlighted and underlined below

General Information

1. **Has the Program Solicitation been published? Where is it posted?**
   Answer (A): Yes, it was published on 25 February 2025, and can be found at this the URL below:
   https://sam.gov/opp/e2f29ccf8e0347449b275667f4c465e5/view

2. **Will the Industry Day slides be posted online?**
   A: Yes, information provided during the Industry Day has been made available on the BEST program page:
   https://www.darpa.mil/research/programs/best-bioelectronics

3. **Is Dr. Tender available for a call or meeting to discuss how our technology may align with the program?**
   A: In the interest of fairness to all potential proposers, as Dr. Tender will not have the availability in his schedule to honor all requests, we will not be scheduling any program-related calls or meetings outside of the sidebars held in conjunction with the BEST Industry Day. The best way to receive feedback on an approach is through the submission of a proposal abstract prior to the deadline specified in the Program Solicitation (PS). The PS describes the program, including metrics, in detail. Specific questions may be submitted by email to BEST@darpa.mil. Proposers should be aware that submitted questions and answers may be published on a FAQ page, with revisions to remove proprietary information.

4. **Is teaming required?**
   A: While teaming is not required, it is strongly encouraged to provide the expertise and capabilities needed to achieve the BEST program goals. Proposing teams should have a plan in place for managing team interactions and future technology transitions. Prior DARPA experience is not a requirement for proposers.

5. **What is the ideal team size?**
   A: It is up to the proposers to determine and justify the size of the team needed to complete their proposed tasks. All teams must have expertise to complete the technical, regulatory, and commercialization objectives of the BEST program.

6. **Can individuals be part of multiple proposals under this solicitation, or are there any restrictions regarding team member overlap across different submissions?**
   A: Yes. Teams can be subcontractors on multiple efforts. However, 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 tasking.

7. **Several BEST Industry Day presentations were given by Government laboratories and resources about technologies they have, animal models, etc. Do we need to reach out to them and include them in the**

proposal writing process (including their costs), or can we propose working with them using the presented capabilities without needing to formally include them in the proposal?
A: Members of the BEST Government team are not allowed to join individual, competitive proposals in response to the Program Solicitation. Proposers must address all aspects of the program described in the solicitation without dependence upon these organizations or other Government Entities (see Section 3.1.1 for eligibility information).

8. **Could more information be provided about the form and format of justifying unique capabilities of a potential National Lab participant?**
A: As described in Section 3.1.1 of the Program Solicitation, Government Entities – Government Laboratories, FFRDCs, UARCs – are subject to limitations in participating as competitive performers in the BEST program. These entities are *strongly discouraged* from proposing (as prime entity or subawardee) against this solicitation as awards to Government Entities will only be made by exception. Government Entities interested in this solicitation, either as a prime or a subcontractor, should contact the Agency Point of Contact (POC) listed in the Program Solicitation's 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. There is not a specific form or format for including a Government Entity in a competitive proposal, as a prime or a subcontractor organization; this would need to be heavily justified in the proposal with the understanding that "awards to Government Entities will only be made by exception."

9. **We currently collaborate with a Government Entity. Are we in conflict for the BEST program?**
A: Current collaborations outside of the BEST program are not in conflict. However, with respect to participating as part of the performer team for the BEST program, Government Entities – Government Labs, FFRDCs, UARCs – are subject to limitations as described in Section 3.1.1 of the Program Solicitation. These entities are *strongly discouraged* from proposing against this solicitation as awards to Government Entities will only be made by exception. Government Entities interested in this solicitation, either as a prime or a subcontractor, should contact the Agency Point of Contact (POC) listed in the Program Solicitation's 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.

10. **Can foreign entities/organizations participate in the program?**
A: Yes. As stated in Section 3.1.2 of DARPA-PS-25-12, "Non-U.S. organizations and/or individuals may participate in accordance with applicable laws, regulations, and policies, including those pertaining to export controls and security."

11. **Can you provide an update on advancements in wound healing monitoring strategies and treatments that were developed by other DARPA programs, such as the BioElectronics for Tissue Regeneration (BETR) program? It would be helpful to understand the key takeaways and developments from BETR or other programs.**
A: The BETR program is ongoing, so DARPA encourages any interested proposers to directly contact BETR performers for specific information about the technologies in development. DARPA is not requiring that BEST proposals build directly off results or technologies from the BETR program.

12. **The BEST program seems to cover different phases of wound care. Can an organization or investigator submit different abstracts that address these different phases?**
A: The BEST program is specifically focused on preventing and managing wound infections. All abstracts and proposals should address this need. Any approach related to wound care beyond infection is out of scope.

Contracting and Cost

13. **How much funding is available for the BEST program? What is the expected size of an award? Approximately how many projects is DARPA planning to fund?**
    A: DARPA has approximately $22.8M total for performer awards and anticipates making multiple awards. DARPA has not predetermined individual award amounts. Proposers are required to provide a well-justified budget that covers the scope of the proposed work with tasks described and budgets requested to meet the BEST program objectives. Budgets will be examined in detail for appropriateness. If the proposal is selected for award, a Government contract officer will negotiate the terms of the contract. During this negotiation, every aspect of the proposed work plan and cost proposal will be reviewed. Please follow all instructions and use all templates or attachments provided with the BEST Program Solicitation (DARPA-PS-25-12).

14. **Can DARPA partially fund a proposal?**
    A: Yes, DARPA reserves the right to fully or partially fund a proposal.

15. **Is there flexibility within the program budget? Can performers address changes in cost throughout the effort?**
    A: It is important to prepare the budget for the work you propose with sufficient justification, as described in the solicitation. This can include risk mitigation (for example, budgeting for multiple ways to accomplish a task that constitutes a technical break through).

16. **Should the estimated budget be broken down by performance site as well as by phase, labor, and non-labor costs?**
    A: For abstracts, please follow the guidance provided in Attachment B (Abstract Template) and provide the budget breakdown for each participating organization (prime and subcontractors). For the full proposal, please complete Attachments D (Volume II) and E (Standard Cost Proposal Spreadsheet) for each participating organization (prime and subcontractors).

17. **Can DARPA clarify the indirect cost rate options available to proposers?**
    A: Depending on the performer's status, the indirect rate can be negotiated or the Government would rely on a current federal negotiated indirect cost rate agreement. The rate agreement is usually provided by a government agency (e.g., DCAA, ONR, DHHS, etc.).

    For recipients and subrecipients that do not have a current federal negotiated indirect cost rate, they may elect to charge a de minimis rate of up to 15 percent of modified total direct costs (MTDC). The recipient or subrecipient is authorized to determine the appropriate rate up to this limit. Recipients and subrecipients are not required to use the de minimis rate. When applying the de minimis rate, costs must be consistently charged as either direct or indirect costs and may not be double charged or inconsistently charged as both. The de minimis rate does not require documentation to justify its use and may be used indefinitely. However, once elected, the recipient or subrecipient must use the de minimis rate for all federal awards until the recipient or subrecipient chooses to receive a negotiated rate.

18. **For budgeting purposes, what is the expected start date of the BEST program?**
    A: In preparing your cost proposal, please use 1 October 2025 as the project start date. Please keep in mind that this is just an estimate, and funding may be awarded before or after that date.

19. **For budgeting purposes, how many days are anticipated to be spent at BEST Technical Interchange Meetings in each of the travel locations – Boston, San Francisco, and Arlington?**

A: Please estimate a maximum of 3 days per trip for BEST Technical Interchange Meetings.

20. **In the regulatory milestones, it states that biocompatibility studies will be conducted by a Contract Research Organization (CRO). Is this something to include in the proposed budget?**
A: Any biocompatibility studies for the BEST program will be conducted by a CRO selected and paid for by the performer team, so please include associated cost estimates and quotes in the cost proposal.

21. **For the tabs in the Cost Proposal Spreadsheet, which one applies to Phase II?**
A: Please use the "Base" tab for Phase I costs and "O1" for Phase II costs. The "O" denotes that this is an Option, and the PS states that Phase II is a "Costed Option" (header of Section 1.5.4).

22. **What is Cost Realism?**
A: Please refer to Section 5.3 in the Program Solicitation for the full definition of Cost Realism as well as other evaluation criteria.

23. **What types of award mechanisms will be executed under the BEST program?**
A: Other Transaction for Prototype.

Program Structure

24. **How do performers address changes to the originally proposed approach during the life of the project?**
A: Proposals will be evaluated as submitted. It is beneficial to be sufficiently flexible in your proposal and Task Description Document to meet all program metrics while accommodating potential alternatives and risk mitigation strategies where appropriate.

25. **What is an expected period of performance to reach TRL6?**
A: The Period of Performance is described in Section 1.4 of the Program Solicitation. Phase I is 24-months, and the developed technologies are expected to reach TRL5 on the Medical Devices scale (https://medicalcountermeasures.gov/trl/trls-for-medical-devices/). Phase II is 12-months, and technologies are expected to reach TRL6 on the Medical Devices scale.

26. **Can proposers address only one Focus Area or one Phase?**
A: Proposals must address all three Focus Areas and both Phases to be considered compliant for review.

Abstracts and Proposals

27. **Is submitting an abstract required? What is the advantage of submitting an abstract? Does the abstract need to match the full proposal submitted?**
A: Proposers are strongly encouraged, but not required, to submit an abstract. DARPA will provide feedback for each abstract submitted. DARPA will attempt to respond to abstracts with a statement indicating whether DARPA is interested in the proposed idea. Regardless of DARPA's response to an abstract, proposers may submit a full proposal. DARPA will review all full proposals submitted using the published evaluation criteria and without regard to any comments resulting from the review of an abstract. Proposers should endeavor to follow the constructive feedback provided following abstract review. Finally, DARPA understands that final concepts and team make-up may change from abstract phase to final proposal as the technical approach is solidified. Please refer to Section 4 in the Program Solicitation for information on abstracts and Section 5 for information on full proposals.

28. **Should I submit via DARPA's BAA Portal or Grants.gov?**
    A: Abstracts and full proposals MUST be submitted via DARPA's BAA Portal (https://baa.darpa.mil). Proposers are strongly encouraged to submit proposals in advance of the deadline. DARPA does not anticipate awarding grants.

29. **How should the development and testing of experimental models that will be used across all Focus Areas be captured in the Task Description Document (TDD, Attachment H)?**
    A: The TDD does not prescribe how a proposing team identifies or organizes their project tasks. It is up to the proposer to determine how to organize and parse out their work plan.

30. **Does each team member need to submit a Model OT Agreement (Attachment G)?**
    A: No – this document is representative of the official agreement between DARPA and the Prime.

31. **Is the Task naming/designation in the TDD (Attachment H) required to be consecutive numbers or can other naming conventions be used?**
    A: The choice of task naming convention is up to the proposers.

32. **What is the difference between Section 6 and 7 in Attachment C (Volume I) as well as Attachment H (TDD)? Which of these are included in the 30-page limit of the proposal?**
    A: Section 7 in Attachment C is included in the 30-page proposal limit and is meant to be a summary of the TDD. It should pull together information from Section 4 and the TDD in a brief way to give the reviewers a sense of the project schedule and milestones. This can be presented in a written or graphical format.

    Section 6 in Attachment C is the same as Attachment H – both are the TDD and are NOT included in the 30-page proposal limit. The TDD is a separate file and should capture a detailed description of the project work plan, milestones, deliverables, and schedule.

33. **Does the Schedule of Milestones and Payments (Attachment I) need to be broken down by site or would it be aggregated into one document?**
    A: The latter – a single document for the proposing team.

34. **What does payment in the context of Attachment I? Who is paying whom?**
    A: DARPA is paying the Prime each specified amount once the exit criteria for the corresponding milestone are met (i.e., once the kickoff meeting deliverables described in B5 have been provided, the amount listed in E5 will be remitted to that organization).

35. **How granular does this have to be?**
    A: As stated in Section 5.2 of DARPA-PS-25-12: "Milestones represent a completed technical event, and the milestone schedule outlines key observable events in the critical path to accomplish the program objectives. Fixed payable milestones are payments made after successful completion of the milestones agreed to in the milestone schedule. Proposals may suggest modifications or additions to the Schedule of Milestones and Payments, though it is not guaranteed that these edits will be accepted by DARPA."

Focus Area 1: Sense

36. **Are the metrics in Figure 2 intended to only directly measure the healing state of the wound, only measure the state of the infection, or measure both the state of the wound and the state of the infection?**
    A: Both the state of the wound and the state of the infection should be monitored and measured.

37. **For "high-resolution" and "continuous" sensing, what sort of time and spatial scales are required for measurement? What is the expected sampling frequency for microbial/pathogen colonization versus non-microbial host biomarkers?**
A: DARPA will rely upon proposers to describe and justify the spatiotemporal decisions for their approaches and system. These should be physiologically relevant to wounds and wound infections as well as able to meet the end of phase metrics described in Section 1.5.1 of the Program Solicitation.

38. **Is a direct pathogen sensor expected as an outcome of the BEST program? How many bacterial strains should the platform be able to sense/detect to meet program requirements?**
A: For *in vitro* demonstrations, the sensing approach(es) will need to detect all ESKAPE pathogens in mono and mixed cultures. For *in vivo* demonstrations, the sensing approach(es) will need to detect one or more ESKAPE pathogens in mono and/or mixed cultures (to be determined by the DARPA team). The metrics can be found in Section 1.5.1, Figure 2 of the Program Solicitation.

39. **Is a single sensor that indicates the presence of an infection responsive to the BEST program goals?**
A: No, the metrics state that demonstrations of the sensing technologies must identify individual and mixed cultures of ESKAPE pathogens. The BEST program seeks revolutionary advances in pathogen sensing and excludes research that primarily results in iterative improvements to the existing state of practice.

40. **Can proposals include more than one sensing modality and then down select or merge them later in the program?**
A: Yes, pursuing multiple approaches in parallel and down selecting or merging them is in scope so long as these efforts are sufficiently justified in the proposal.

41. **Would technologies for non-invasive internal organ diagnostics fall outside the scope of this project?**
A: This program is focused on infections in surface exposed wounds (lacerations, abrasions, blast injuries, burns, compound fractures, etc.), so all approaches must address that topic. Everything else is out of scope. Additionally, we want to emphasize that infectious disease is a broad category, but this program is narrowly focused on wound infections.

Focus Area 2: Treat

42. **During the Industry Day, it was mentioned that if a wound is going to heal on its own the preference is to leave the wound to heal on its own. What is the reason behind this?**
A: Many wounds go on to heal on their own, including wounds that are highly colonized with bacteria. The current standard of care for battlefield wounds is to provide broad-spectrum and high-dose antibiotics regardless of the infection or healing status of the wound. This can lead to unnecessary treatment of wounds, drive antibiotic resistance, have toxic side effects, and increase the burden on limited resources and military medical professionals. One goal of the BEST program is to predict which wounds will heal versus fail due to infection and be able to provide treatment only when necessary.

43. **Should a non-healing wound be defined as infected?**
A: DARPA will rely upon proposers to define healing versus non-healing wounds as well as infected versus non-infected wounds. These definitions should be justified and align with current clinical practice guidelines.

44. **Is there a difference between microbial contamination and microbial infection?**

A: All wounds contain microbes, but that contamination is not always a hindrance to healing. Successful BEST technologies will be able to distinguish microbial contamination from infection as well as determine which wounds will heal and which will fail.

45. **If the proposed treatment is non-antibiotic, but effective across a broad-range of pathogens, does the device still need to also administer antibiotics?**
A: All novel treatments should be well described and justified in the proposal to ensure alignment with the metrics described in Section 1.5.1 of the Program Solicitation. As stated in Figure 2, antibiotic solutions are meant to provide risk mitigation to the innovations and novel approaches for the Treatment (Focus Area 2) portion of the BEST devices.

46. **Are novel antibiotics in scope as a treatment option?**
A: Section 1.4 in the Program Solicitation provides a description of the types of treatments to be developed in the BEST program. "Treatments are expected to be novel and electronically regulated approaches to alter microbial colonization, virulence, biofilm formation and/or other features of infection to prevent a predicted infection and resolve an existing infection. Using the same or separate hardware, the capability to also deliver established, narrow-spectrum antibiotic drugs will be required for risk mitigation." These treatments need not be directly electrical but should be controllable via an electrical circuit. Furthermore, the solicitation seeks treatments to which microbes cannot develop resistance (Section 1.2 of the Program Solicitation). In this context, any proposed use of novel antibiotics will need to be strongly justified.

47. **Are the narrow-spectrum antibiotics expected to be administered topically or systemically?**
A: The narrow-spectrum antibiotics are intended to be delivered from the BEST device which will be topically applied to the wounds. If this administration of the antibiotics is not supported by current clinical practice guidelines, proposers should consider alternative antibiotics and/or provide justification of a systemic administration. As a reminder, the narrow-spectrum antibiotic treatments are intended as risk mitigation for the novel treatment approaches to be developed under BEST Focus Area 2.

48. **Does the risk mitigation approach for delivering narrow-spectrum antibiotics need to be integrated with the non-antibiotic treatment approach(es) in Phase I?**
A: The end of Phase I demonstrations are for independent devices; therefore, the risk mitigation treatment (narrow-spectrum antibiotics) can be a separate module controlled by human in the loop for delivery in Phase I. It should have the same plans and preparations for integration in Phase II as the non-antibiotic treatment option(s).

49. **Does the term "novel treatments" explicitly rule out the use of established, broadly acting antimicrobials such as silver, copper, iodine, or riboflavin?**
A: Correct, novel treatments should not include the use of established, broadly acting antimicrobials. The BEST program seeks revolutionary advances in antimicrobial treatments and excludes research that primarily results in iterative improvements to the existing state of practice.

50. **Is it permissible for therapeutic delivery to be manually administered by a care provider who is automatically alerted upon infection detection, or will only proposals with entirely automated, bandage-integrated deliveries be selected?**
A: The overall BEST vision is to develop a closed-loop, automated system that can function without user or care provider input. Human-in-the-loop is allowed during Phase I, but all approaches must address the integration into a closed-loop system for Phase II.

51. **If the wound patch has pre-loaded narrow-band antibiotics or other on-board medications, what are the expected storage conditions for the patches in field use? Can we assume that no cooling is available?**
A: Correct, please assume that cooling equipment (refrigerators, freezers, etc.) will not be available.

52. **Are there any restrictions on the types of therapeutic modalities that will be considered in this application (e.g., therapeutic lead molecules which are not mAbs, small molecules, or bacteriophage)?**
A: DARPA is not prescriptive about the potential treatment approaches that can be used to meet the BEST program goals so long as they are "novel and electronically regulated approaches to alter microbial colonization, virulence, biofilm formation and/or other features of infection to prevent a predicted infection and resolve an existing infection. Using the same or separate hardware, the capability to also deliver established, narrow-spectrum antibiotic drugs will be required for risk mitigation."

53. **Are there any requirements on the lead therapeutic molecule being FDA approved or are molecules in advanced preclinical development acceptable?**
A: Proposed treatments do not need to be FDA approved.

54. **Can proposals include more than one treatment modality and then down select or merge them later in the program?**
A: Yes, pursuing multiple approaches in parallel and down selecting or merging them is in scope so long as these efforts are sufficiently justified in the proposal.

55. **For the *in vitro* demonstrations (month 12), are the wound healing metrics relevant, and if so, how should they be addressed?**
A: The ultimate goal of the *in vitro* studies is to enable the appropriate selection of sensors and treatments for testing in the *in vivo* models. To confirm efficacy of the treatments, it is up to the proposer to define the "healing" and "non-healing" wound state in their *in vitro* testbed, if relevant.

56. **When will DARPA select the pathogens for the *in vivo*, end of Phase demonstrations?**
A: In consultation with the Government team, DARPA will select one or more ESKAPE pathogens for performers to address in the *in vivo* demonstrations. A date has not yet been determined, and sufficient time will be provided to the performer teams to prepare for these demonstrations; however, all proposers should be prepared address all ESKAPE pathogens *in vivo*.

57. **Is there a metric for how quickly the wound infection should be resolved?**
A: No, we do not specify a metric for the speed of treatment or infection resolution. This should be described by the proposers and be both physiological as well as feasible for the proposed approaches.

Focus Area 3: Closed-Loop Control

58. **Is closed-loop the same as fully autonomous?**
A: The goal of the BEST program is to have a device that does not require human intervention and can function autonomously for a prolonged period of time, though not indefinitely. The longevity of this autonomous function will need to be determined and described by the proposers.

59. **What amount of human intervention is in scope?**
A: Human-in-the-loop is allowed for the independent devices developed in Phase I. By Phase II, the all technologies are expected to function as a closed-loop, automated system without user input.

60. **Does the solution need to be a single, self-contained system with no user input, or can a solution come as a kit with a user following instructions provided by device?**
A: The overall BEST vision is to develop a closed-loop, automated system that can function without user input. A multi-step kit or instruction process that requires user or medical provider engagement after initial application is not in scope.

61. **Does the program require a distinct intervention step after infection detection, or is a continuous infection management and healing process aligned with the program's intent?**
A: Continual characterization of the wound state and infections as well as automated, real-time delivery of treatments is the intent of the BEST program.

62. **Does the required weight metric (25 g) include all components of the integrated system or just the portion directly covering the wound?**
A: The weight metric described in Figure 2 of the Program Solicitation encompasses the entire, integrated device or system. Total weight is a critical concern for use on the battlefield, and the weight metric is intended to meet that use case.

63. **Is there a need or requirement for data to be stored and logged on the BEST device in order to inform military health professionals (following field care) of the infection status and/or treatment that has been administered with the BEST device?**
A: There is not a requirement for data storage in the BEST program, but the ability to do so would address an important need along the military continuum of care.

64. **Will there be a prototype at the end of the program?**
A: By the end of the program, performers will have a physical device that will be used to demonstrate the ability to achieve the metrics. DARPA will not be acquiring this technology, though it may be delivered to Government partners or others for further testing and development beyond the scope of the BEST program.

Other Technical

65. **Can prior work be leveraged in the BEST proposal?**
A: Yes, though proposals should describe how the BEST project will build upon this prior work as well describe how the proposed approaches and solutions are innovative and can address the metrics.

66. **Is Human Subjects Research (HSR) allowed? What about the use of human tissue specimens?**
A: No, human subjects research is not permitted in the BEST program. If human samples or data are to be used, they must be designated as "not HSR" by an Institutional Review Board as well as the DoD's Office of Human Research Oversight.

67. **Is there a preferred animal model for testing?**
A: Yes, large animal models are required in the BEST program with a preference for porcine and polytrauma models. See Section 1.5 of the Program Solicitation for all references to these models and associated deliverables.

68. **Are small animal models allowed in the BEST program?**
A: Yes, however, we caution that proposing teams utilize small animals selectively and efficiently. We want to avoid efforts that miniaturize devices for use on small animals when the BEST *in vivo* demonstrations need to

be conducted on larger animals and wounds. The use of small animals may be relevant for screening and high-throughput testing, which will need to be described and justified in a full proposal.

69. **Are animal studies allowed during the first 12 months of the program?**
A: Yes, animal studies can begin as soon as is reasonable for the proposed approaches and work plan. The deliverable and milestone timeline in the PS denotes the latest date to complete the demonstrations but does not restrict when any work can begin.

70. **Please clarify the intention of "polytrauma." Is the intent to address wound healing when there is an additional, separate injury or trauma in another location on the body?**
A: Correct. Warfighters often suffer from multiple, simultaneous injuries during combat which can suppress their immune response and complicate their clinical care. Polytrauma animal models are therefore more representative of the military context than single injury trauma models. As a reminder, large animal, polytrauma models are strongly preferred but not required.

71. **Does DARPA have examples of porcine polytrauma models of interest?**
A: There are several large animal polytrauma models in use within DoD laboratories. DARPA will rely upon proposers to describe and justify their proposed animal models (trauma or polytrauma). These models should reflect the injury types and patterns experienced in combat scenarios.

72. **Is each team responsible for proposing and/or developing a large animal model upon which to test and evaluate their particular system components? If so, is it up to each team to define "infected" and "healed" in the context of their own model?**
A: Proposer teams are expected to utilize their own animal models to address the BEST program goals and metrics. Section 1.5 of the Program Solicitation specifically describes the use of large animal models, including end of phase demonstration and validation deliverables (Section 1.5.3.1 and 1.5.4.1). All proposer-developed animal models, experiments, and definitions of wound status and outcomes will need to be clearly described and justified in the proposal.

73. **What is the role of the Government team animal model?**
A: The organizations on the Government team may generate wound infection datasets in large animal models to be shared with BEST performer teams, but it is unlikely that the Government team will conduct experimental evaluation of performer-developed technologies.

74. **Is it possible for BEST performers to be trained on the Government team animal model(s) and/or receive those animal protocols from the Government team in order to conduct animal studies with those models at the performer site?**
A: Proposer teams are expected to utilize their own animal models to address the BEST program goals and metrics. While one example of a polytrauma model was presented at the BEST Industry Day event, there are several large animal polytrauma models in use within DoD laboratories. Should BEST-relevant data be generated by the Government team from any of these models, it will be provided to performers to supplement their projects.

75. **Regarding the machine learning component, will datasets be accessible through the BEST program? Or do we need to collaborate directly with the Government Entities that spoke at the BEST Industry Day as part of our team?**

A: BEST performer teams are expected to provide and generate their own datasets throughout the course of the program. Members of the BEST Government team are not allowed to join individual, competitive proposals in response to the Program Solicitation. Any Government team-generated datasets will be made available to all performers in the BEST program.

76. **What information is in the ESKAPE pathogen dataset? (e.g., genetic information, growth rates, level of antibiotic resistivity, metadata on biofilm structure, etc.)?**
A: The combat wound data provided by the BEST Government team are intended to be supplementary to the work done by BEST performer teams. Specific data related to ESKAPE pathogens that are relevant to the proposed approaches should be gathered or generated within the individual performer projects.

77. **Is there any public information available about the Government dataset that can be provided to proposing teams?**
A: Here are three publications that cover the RNA-seq and metagenomics work the Government team has completed thus far using their combat and trauma wound dataset:
    - "The influence of microbial colonization on inflammatory versus pro-healing trajectories in combat extremity wounds" DOI: 10.1038/s41598-024-52479-5. https://www.nature.com/articles/s41598-024-52479-5
    - "Targeted metagenomic assessment reflects critical colonization in battlefield injuries" DOI: 10.1128/spectrum.02520-23. https://journals.asm.org/doi/10.1128/spectrum.02520-23
    - "Metagenomic features of bioburden serve as outcome indicators in combat extremity wounds" DOI: 10.1038/s41598-022-16170-x. https://www.nature.com/articles/s41598-022-16170-x

78. **Since almost all patients get surgical debridement, what is the dataset that correlates to battlefield/pre-debridement wounds?**
A: To the best of our knowledge, there are no comprehensive datasets and samples collected directly from the battlefield. Therefore, we expect that all datasets – existing or generated in the program – can be extrapolated to the combat scenario. Additionally, this program will rely upon the use of animal models and generation of *in vivo* data, that can include undebrided/pre-debrided wounds. All models must be clearly described in the proposal and aligned to the BEST problem. Any human samples or data used must NOT be considered Human Subjects Research.

79. **Can you use Bluetooth Low Energy (BLE) and a mobile device with an app to provide information to the care provider? Is signature management an issue (i.e., no BLE, WiFi, etc.)?**
A: Signature management is not a direct metric in the BEST program; however, it is an important consideration for eventual use on the battlefield. The overall BEST vision is to develop a closed-loop, automated system, so use of BLE, mobile devices, cloud computing, or other forms of external communication to control or manage the wound is not in scope.

80. **Wounds come in different types (e.g., burns, puncture, lacerations) and sizes. Is there a benchmark wound type or size that should be addressed?**
A: DARPA will rely upon proposers to describe and justify the wound type selected for their proposal so long as it is a surface exposed wound (laceration, abrasion, blast injury, burn, compound fracture, etc.). The metric for the minimum wound size is 25 cm^2 (Section 1.5.1, Figure 2 of the Program Solicitation) and any proposed deviations from this metric should be clearly described and justified.

81. **Is there a depth metric for the wound size?**

A: The wound depth should be relevant to the injury model as well as demonstrate the capabilities of the proposed technologies. If proposing a skin wound model (burn, excision, etc.), it must be full-thickness to most appropriately represent the combat wound scenario.

82. **Do the *in vitro* demonstrations (month 12) need to be completed in a 25 cm^2 area?**
A: There is not a size/spatial metric for the *in vitro* demonstrations. Proposers should describe their *in vitro* testbeds and parameters and justify how these will provide confidence in selecting the technologies and approaches for testing in the *in vivo* model and meeting the end of Phase SWaP metrics.

83. **Is it in scope to propose modifying the packaging to allow the device to be applied to different anatomical locations (extremities, torso, joints, etc.)?**
A: As long as the BEST size, weight, and power (SWaP) metrics are met, this would be in scope.

84. **Is there a preference for the anatomical location of the bandage?**
A: We are agnostic to the anatomical location at this point in the technology development. Proposers should align this choice with their proposed animal model as well as the BEST SWaP metrics.

85. **Is it in scope to address environmental conditions on the battlefield (dirt/debris, moisture, waterproofing, etc.)?**
A: Yes, as long as the BEST SWaP metrics are met.

86. **Is it in scope to address ruggedization and/or protection of the device?**
A: Yes, as long as the BEST SWaP metrics are met.

87. **Is the assumption that the bandage will be applied on the battlefield, post-surgery, or both?**
A: The approaches developed in the BEST program are intended to be used at all levels of medical care – from the battlefield to the clinic. The final form-factor may change depending on the specific factors (wound type, wound size, clinical setting, etc.), but the underlying sensing and treatment modalities should be usable in all clinical scenarios. It is crucial that performer teams propose technologies that when fully developed (i.e., TRL-8, clinical studies, etc.), are reasonably expected to be mass produced at non-prohibitive costs and operate in remote and austere environments including the battlefield.

88. **Is the goal to produce a one-time use bandage?**
A: Yes.

89. **Are there shelf-life requirements for the bandage?**
A: No, we do not specify shelf-life metrics in the BEST program. However, assessing and addressing these concerns (longevity of use, shelf-life, product stability, etc.) may be relevant as part of the Transition tasks.

90. **Should proposers assume that the BEST device can support all combat scenarios described on slide #6 of the Industry Day presentation? Is it a fair assumption that a soldier will only wear a single bandage for 72 hours, but new bandages may need to be applied if the evacuation time and prolonged field care extends beyond 72 hours?**
A: There is not a specific time of use metric in the BEST Program Solicitation; however, given the potential for resource limited conditions in a large-scale combat operation (limited medical personnel, limited supplies and resupply, large numbers of casualties), there is a preference for longer-acting solutions that require

infrequent replacement. Proposers will need to describe and justify the anticipated duration of their approaches and technologies in the proposal.

91. **Which is preferred – aiming for a warfighter return to immediate operations or aiming for a warfighter eventual return to duty?**
    A: This program has not specified a use case and is not prioritizing between these two options. The approaches developed in the BEST program are intended to be used at all levels of medical care – from the battlefield to the clinic – and address multiple injury and clinical scenarios.

92. **If solutions only target a subset of the potential military application spaces or use cases, would that still be in scope?**
    A: It is likely to be in scope, though all proposals should include a description of the limitations for the proposed approaches and solutions.

93. **Is there a defined expectation for how quickly the wound should heal, or should proposers provide that benchmarking criteria?**
    A: Accelerated healing is not in scope for the BEST program. Predicting the healing outcome of a wound and being able to adapt that prediction based on the infection status is in scope and described within the Program Solicitation. Performers are expected to justify their definition(s) of healing status and outcomes to achieve the program goals.

Transition

94. **Do proposing teams need to have their own regulatory and commercialization consultants/experts in addition to support provided by the Government team?**
    A: Yes, each team should have their own regulatory and commercialization personnel to manage those respective deliverables and milestones within the project. Clinical expertise is also strongly recommended to ensure successful transition planning and activities.

95. **The BEST device may be viewed by the Food and Drug Administration (FDA) as a combination device involving diagnostic and therapeutic systems that combine drugs, devices, and/or biological products. Will multiple FDA agencies be involved (CDRH/CDER/CBER) requiring additional testing beyond a device Investigational Device Exemption (IDE)?**
    A: The BEST program has deliverables and milestones related to engagement with the FDA to determine the appropriate regulatory path and FDA organization for a given technology's eventual approval.

96. **How comprehensive will the Regulatory Plan Review (month 4) be?**
    A: The Regulatory Plan Review meeting is happening early in the program and is intended to review the performer's regulatory strategy and planned activities prior to completing the remaining Regulatory Deliverables and Milestones (Section 1.5.3.2). Performers will not be expected to have their regulatory documents or items finalized and ready to go at this point in the project.

97. **What scale is DARPA using to determine the Technology Readiness Levels (TRLs) in BEST?**
    A: DARPA is using the TRL scale for Medical Countermeasure Products (Diagnostics and Medical Devices) as determined by the U.S. Department of Health and Human Services: https://medicalcountermeasures.gov/trl/trls-for-medical-devices

98. IDE approved devices appear to require design control including verification and validation (V&V). Is it anticipated that performers will be required to conduct V&V studies for each device (FA1, FA2, FA3) supportive of an IDE application for each component?
A: One of the transition objectives in the BEST program is for performer teams to prepare a regulatory package (IDE or other) for submission to the FDA. Submission and approval are beyond the scope of the BEST program.

99. For Phase I technologies, IDE submissions require design controls including some level of V&V while TRL-5 does not generally require full V&V testing. Is a "risk based" approach (ISO 14971) to determine the level of V&V for an IDE submission package compliant with TRL-5?
A: Yes, this should be acceptable. The pace of the BEST program will introduce some risk, which is why the performers are required to meet with the FDA midway through Phase I (months 12-17). This engagement with the FDA should address V&V plans and the data acceptable for an IDE/regulatory package, as well as other aspects of the performer's regulatory strategy. The BEST Government team will also provide guidance to performers on their regulatory strategy throughout Phases I and II.

100. Phase II technologies are expected to reach TRL-6 which requires testing in an operational environment. These Beta prototype(s) will require a quality management system (QMS) beyond design controls. Does the requirement to "finalize their QMS" require teams to have a fully implemented QMS that has demonstrated full compliance with a standard such as ISO 13485?
A: For this stage of technology development, the sponsors of the IDE are exempt from quality system regulations except for design controls (21 CFR 820.30). A fully *established* QMS is expected by the end of Phase II (month 35) and will continue to be a living document that can be updated across the product lifecycle. Understanding that some sections of the QMS will not be as relevant and are subject to updates after Phase II, it would be most important to consider the TRL-6 relevant sections as a threshold for *implementation* (Design Controls, Document Controls, Risk Management, CAPA, Records). It is up to the performer to determine if the QMS should be validated against ISO standards.

101. TRL-6 typically marks the earliest appropriate stage to initiate human testing, and by extension, full-scale biocompatibility testing at a contract research organization (CRO). Given that, conducting CRO-led biocompatibility work before a device has reached TRL-6 may be premature, introducing inefficiencies and potentially leading to duplicative or out-of-scope testing if the design evolves significantly prior to clinical readiness. With that in mind, what is the purpose of the biocompatibility testing deliverable in Phase I (months 18-22)?
A: DARPA does not expect full-scale biocompatibility testing of a final form-factor in Phase I. The primary objective for the Phase I biocompatibility testing is to confirm that the materials that will comprise the BEST bandages will not introduce adverse effects to the user with the understanding that additional biocompatibility testing will need to be completed once the bandage is in its final, integrated form-factor (Phase II or beyond the scope of the BEST program, depending upon feedback from the FDA). Proposers should describe their plans for Phase I biocompatibility studies and justify how the results will provide confidence in taking their materials, devices, and/or approaches safely into Phase II.

102. How many non-military applications should be considered when developing commercialization plans?
A: At least one robust civilian and at least one robust military use case should be identified during the commercialization activities. These deliverables are intended to identify the first use cases for a commercialization pathway, not be exhaustive of all potential application opportunities.

103. Developing a robust value proposition requires understanding of the customer, use cases, human factors, etc., which starts with exploratory research (qualitative marketing) conducted with users, decision makers, etc., via individual interviews, focus groups, surveys, etc. This discovery process provides information that inform product definition. Will DARPA provide access to people in the Department of Defense (DoD) community to support this?

A: Performers should propose their own plans for engaging with military stakeholders as part of the commercialization activities and not rely upon DARPA for these connections with DoD personnel. Depending upon gaps and needs identified by DARPA and the Government team, DARPA may assist performers in supplementing these activities with additional contacts, though this is not guaranteed.