



Broad Agency Announcement

Harnessing Enzymatic Activity for Lifesaving Remedies (HEALR)

BIOLOGICAL TECHNOLOGIES OFFICE

HR001120S0052

June 24, 2020

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PART I: OVERVIEW INFORMATION

- **Federal Agency Name** – Defense Advanced Research Projects Agency (DARPA), Biological Technologies Office (BTO)
- **Funding Opportunity Title** – **Harnessing Enzymatic Activity for Lifesaving Remedies (HEALR)**
- **Announcement Type** – Initial Announcement
- **Funding Opportunity Number** – HR001120S0052
- **North American Industry Classification System (NAICS)** – 541714
- **Catalog of Federal Domestic Assistance Numbers (CFDA)** – 12.910 Research and Technology Development
- **Dates**
 - Posting Date: June 24, 2020
 - Proposal Abstract Due Date and Time: August 11, 2020, 4:00 PM ET
 - Full Proposal Due Date and Time: September 17, 2020, 4:00 PM ET
 - BAA Closing Date: September 17, 2020
 - Proposers' Day: June 30, 2020

<https://beta.sam.gov>
- **Concise description of the funding opportunity** – The goal of the HEALR program is to develop new medical countermeasures against bacterial pathogens and their toxins by leveraging host degradation and deactivation pathways.
- **Anticipated individual awards** – Multiple awards are anticipated.
- **Types of instruments that may be awarded** – Procurement contract, cooperative agreement, or other transaction.
- **Agency contact**

The BAA Coordinator for this effort may be reached at:
HEALR@darpa.mil
DARPA/BTO
ATTN: HR001120S0052
675 North Randolph Street
Arlington, VA 22203-2114

PART II: FULL TEXT OF ANNOUNCEMENT

1. Funding Opportunity Description

This publication constitutes a Broad Agency Announcement (BAA) as contemplated in Federal Acquisition Regulation (FAR) 6.102(d)(2) and 35.016 and 2 CFR § 200.203. Any resultant award negotiations will follow all pertinent law and regulation, and any negotiations and/or awards for procurement contracts will use procedures under FAR 15.4, Contract Pricing, as specified in the BAA.

The Defense Advanced Research Projects Agency (DARPA) often selects its research efforts through the Broad Agency Announcement (BAA) process. The BAA will appear first on the beta.SAM.gov website, <https://beta.sam.gov>, and the Grants.gov website <http://www.grants.gov/>. The following information is for those wishing to respond to the BAA.

DARPA is soliciting innovative proposals to develop (1) new therapeutics against Department of Defense (DoD)-priority bacterial threats that leverage host-driven protein degradation or deactivation pathways; and (2) a platform capability to rapidly develop, screen, and optimize therapeutics against emerging bacterial threats.

1.1. PROGRAM OVERVIEW

Microbial infections are a problem of particular concern to the DoD. The DoD has long recognized the warfighter's outsized risk of exposure to infectious disease, including the rise of antimicrobial resistant (AMR) and multidrug resistant (MDR) pathogens that have challenged military wound care in Iraq and Afghanistan. Furthermore, the responsibility of the DoD to protect the homeland encompasses biological threat agents, including many bacterial threat agents and their associated toxins, for which there are few effective countermeasures or narrow time windows for countermeasure delivery.

The development of new therapeutics for addressing microbial infections is not only a military health challenge but also a growing public health issue. Reports show that antibiotic resistance is on the rise and is an imminent global health threat. In 2019, the United States (U.S.) Military Infectious Diseases Threat Prioritization Panel ranked MDR organisms as a Tier 1 threat to the U.S. military from among > 60 global diseases. Despite this looming crisis, there has been a notable exodus of pharmaceutical companies from the antibiotic space, as well as several high profile failures of biotechnology companies focused on antibiotic development.

Common chemo- and bio-therapeutic strategies for treating microbial infections include small molecules, biologics, and vaccines. HEALR seeks to establish an orthogonal approach to treating microbial infections by harnessing advancements in recruiting native cellular host machinery to recognize and eliminate disease-related targets. Specifically, HEALR will develop new medical countermeasures (MCMs) that result in *host-driven degradation or deactivation of bacterial targets*. By harnessing innate cellular processes, approaches such as proteolysis targeting chimeras (PROTACs) and similar methods can achieve superior outcomes over existing therapies.

PROTACs molecules are referred to as ‘chimeras’ because they are comprised of two *ligands* connected by a *linker*; one ligand binds the target protein (i.e., *threat-binding ligand*) and the second ligand binds a host protein (i.e., *host-binding ligand*). In the case of PROTACs, the host-binding ligand binds to an enzyme known as an ubiquitin ligase. When PROTACs molecules bind both the target protein and ubiquitin ligase, the ligase ‘tags’ the target protein for cellular degradation. Existing studies using PROTACs against oncology targets have demonstrated the feasibility of the HEALR approach. PROTACs studies have also shown that their distinct mechanism-of-action (MOA) may be effective at addressing emerging drug resistance. Finally, compared to conventional therapeutics, which must remain persistently bound to the target, HEALR therapeutics have the potential to utilize lower drug doses and increase safety because these MCMs only require transient target binding and can then be ‘recycled’ to act on additional targets.

HEALR aims to develop: (1) tools to target microbial pathogens via protein degradation (i.e., target-binding ligand development); (2) innovative modalities to enable new pathways to protein degradation or deactivation; and (3) a platform that leverages these advances to permit flexible and rapid response to emerging threats.

1.2. TECHNICAL APPROACH AND PROGRAM STRUCTURE

1.2.1. TECHNICAL AREAS

The HEALR program includes three technical areas (TAs) that will run concurrently for the duration of the program. **Proposals that do not address all TAs as characterized within this section will be deemed non-conforming and may not be considered for review.**

The three technical areas are:

1. **Technical Area 1 (TA1): Microbial Targeting.** Develop and demonstrate innovative methods to screen and identify new threat-binding ligands against microbial targets.
2. **Technical Area 2 (TA2): Host Machinery Engagement.** Develop and demonstrate new strategies to engage cellular processes to degrade or deactivate targets.
3. **Technical Area 3 (TA3): Platform Integration.** Develop the tools to integrate threat- and host-binding ligands to rapidly construct, optimize, and deliver safe and effective countermeasures against new microbial threats.

TA1. Microbial Targeting

TA1 will develop the technologies needed to establish PROTACs as a novel type of antimicrobial MCM through ligand generation capabilities that will enable a response platform for new and emerging threats. This requires the development of innovative methods to identify and screen new threat-binding ligands that will engage target proteins in order to neutralize important microbial pathogens. TA1 objectives include (a) identification of suitable microbial and toxin (threat) targets; (b) threat-binding ligand discovery, design, and screening approaches;

and (c) demonstration of a degradation or deactivation MOA in increasingly complex cellular environments.

Proposers will select specific threats against which to design their TA1 assets ([Section 1.2.3](#)), but will also be expected to look more broadly at how to create a system for ligand design that will allow for a flexible and rapid response to changing targets. This component of TA1 will feed into the development of an Integrated Platform (TA3) that performers will demonstrate by generating countermeasures to DARPA-selected threats.

Target Identification. Proposers must develop approaches to quickly identify threat targets. Targets must be specific to the pathogen(s) of interest, addressable by appropriate ligands, and be addressable by a host machinery pathway. Targets should be selected such that deactivation or degradation by host machinery results in effective elimination of the pathogen or pathogen-derived threat. Targets need not serve a specific metabolic role for the pathogen, as long as deactivation or degradation of the target results in the desired therapeutic outcome. Methodologies to identify both known and new targets amenable to chimeric approaches are desired. Structural biology, cheminformatics, bioinformatics, and machine learning to enable in silico methods for predicting viable targets, as well as new threat-binding ligands and compatible ligand-linker-machinery combinations, are possible elements of the proposed work.

Threat-Binding Ligand Discovery, Design, and Screening. Rapid methods for screening, discovering, and optimizing threat-binding ligands will be developed as part of TA1. Ligand discovery methods may include, but are not limited to, virtual screening, high-throughput screening (HTS) of chemical libraries, and Isotopic Tandem Orthogonal Proteolysis-enabled Activity-based Protein Profiling (IsoTOP-ABPP). Ligand discovery methods should exploit the fact that chimeras need not bind at target active sites, and, as such, can leverage a greater target landscape when compared to conventional small molecule inhibitors.

Deactivation or degradation MOA. Proposers must demonstrate that their identified target(s) can be engaged using their threat-binding ligand protocol with a complete chimera molecule. The chimera for TA1 can utilize known host pathways for degradation (i.e., PROTACs), but should demonstrate that the MOA is via the selected pathway. Demonstration of target engagement by novel chimeras should be performed in an increasingly complex cellular environment.

The following information should be included in the proposal to address TA1 challenges:

- Approach to target identification;
- Process for target ligand discovery;
- Proposed strategies for target ligand optimization to maximize target binding, achieve good target selectivity, and minimize the emergence of resistance;
- Fabrication and demonstration of chimera(s) that shows on-target activity; and
- Evidence for target engagement by chimera(s) resulting in activity consistent with the desired MOA.

TA2. Host Machinery Engagement

The PROTACs approach uses cellular machinery that resides inside of a host cell and will, therefore, not be effective against extracellular bacterial threats. To overcome this and other

possible limitations of PROTACs, TA2 will focus on engaging alternative host machinery to degrade or deactivate targets by developing new chimeric strategies (i.e., ‘NewTACs’) to address a wider scope of microbial diseases. TA2 objectives include: (a) host-binding ligand design and discovery for engaging NewTACs cellular machinery, (b) preparation of chimeric molecules to demonstrate NewTACs efficacy against pathogen targets, and (c) demonstration of NewTACs MOA in increasingly complex cellular environments.

NewTACs Pathway Identification. Proposers may target a variety of possible host pathways, including, but not limited to, phosphatases (‘PhosTACs’), lysosomes (‘LYTACs’), and PROTACs involving engagement of non-standard E3 ligases (beyond Celebron and VHL). Selected pathways need not result in target degradation but can involve deactivation or modification pathways that disable the target. For example, PhosTACs could be designed to couple a target with phosphatases, rather than tagging and degrading the target, as in PROTACs, which would deactivate the target protein via dephosphorylation. Similarly, LYTACs employs molecules that bind target proteins and chaperone them to lysosomes within the cell for degradation. Unlike PROTACs, which only acts on proteins within a host cell, LYTACs degrades target proteins outside of cells by internalizing targets into lysosomes. This approach could be critical to combat bacterial pathogens that attack and reside outside the cell. Overall, selection of NewTACs pathways should be justified based on the clear advantages they afford over existing TACs (e.g., PROTACs) and how they enable engagement of a broader range of pathogenic targets (i.e., extracellular targets). Methods to characterize and provide evidence for engagement of the selected pathway/machinery should be explicitly described.

Host-Binding Ligand Discovery, Design, and Screening. Rapid methods for screening, discovering, and optimizing host-binding ligands will be developed as part of TA2. Ligand discovery methods may include, but are not limited to, virtual screening and HTS of chemical libraries. Ligands for engaging untapped host machinery must be designed so they can be modified with suitable linkers, while retaining host activity, for development into full chimera molecules. It is expected that performers will demonstrate host ligand optimization that maximizes the efficacy of chimeras while maintaining a high degree of selectivity for the desired host machinery pathway.

NewTAC MOA. Proposers must demonstrate that the proposed NewTACs achieve the desired MOA by integrating the host-binding ligand into a complete chimera molecule. The chimera molecule for TA2 can utilize known threat-binding ligands but should demonstrate that the MOA is via the selected pathway. Demonstration of target engagement by NewTACs chimeras should be performed in an increasingly complex cellular environment.

The following information should be included in the proposal to address TA2 challenges:

- Description of selected host machinery/pathways;
- Process for host ligand design and discovery;
- Proposed strategies for host ligand optimization to maximize binding and selectivity;
- Methods to characterize and demonstrate host ligand engagement with target machinery;
- Fabrication and demonstration of NewTACs that shows on-target activity; and
- Evidence of target engagement by NewTACs resulting in activity consistent with the desired MOA.

TA3. Platform Integration

TA3 seeks to enable a platform for flexible, threat-agnostic response to emerging bacterial pathogens (e.g., emerging AMR, novel biological threats). From the outset of the program, work should commence in the development and optimization of linkers to bridge the threat-targeting ligand and the host-targeting ligand, determination of cellular kinetics and pharmacodynamics associated with the use of HEALR therapeutics, and optimization of formulation, delivery, and bioavailability.

As the program matures, it is also expected that outputs from TA1 and TA2 will feed into an Integrated Platform developed as part of TA3. TA1 will enable the development of libraries and screening methods that facilitate the identification of threat-binding ligands against pathogen targets, and TA2 will develop new protein degradation or deactivation pathways that will expand the range of threats that can be addressed by cellular machinery, including the addition of pathways that enable targeting of extracellular threats. Because the aim of this program is to provide a rapid and flexible means to develop a therapeutic against a new microbial threat, the ability to both generate new threat-targeting ligands and to pair them with appropriate host degradation strategies will be necessary to succeed in TA3.

The platform developed in TA3 will be tested against DARPA-selected microbial threats for rapid generation of effective therapeutic molecules in two Pressure Tests during Phase II of the program (see Section 1.3).

Linker Development and Chimeric Molecule Assembly. The length, chemical composition, and structure of linkers are essential to the function of TACs. Proposals should include rapid and effective methods to identify, optimize, and synthesize linkers for connecting threat- and host-binding ligands to obtain fully functioning chimeras. Methods to select linkers that maximize the drug-likeness of resulting chimeras should also be incorporated into these efforts.

System Dynamics. The use of TACs requires an understanding of the rates at which three or more distinct molecules come together, interact, and dissociate. These binding affinities and kinetics are needed to predict and control the rate at which a target is degraded/deactivated. Methods to model multibody binding equilibria have been developed and can be adapted to understand TACs kinetics. Proposers should develop relevant models that predict the optimal performance of TACs based on binding equilibria and kinetics of binding interactions. These models should inform threat ligand, host ligand, and linker design to optimize chimera design for achieving optimal therapeutic outcomes.

Formulation and Delivery. Compared to conventional small molecules, the larger molecular size of chimeras underscores the importance of TACs formulation and delivery in the context of therapeutic use. Proposals should include novel and effective strategies to formulate and deliver TACs for optimal bioavailability, pharmacokinetics, therapeutic index, and overall efficacy in animal models of infection. Strategies may include, but are not limited to, conventional formulation, nanodelivery systems, or the design of molecular glues ('monovalent degraders') that may overcome the challenges associated with conventional chimeras.

Integrated Platform. Ultimately, performers should develop a complete Integrated Platform in TA3 that allows for rapid and effective identification, preparation, and evaluation of TACs-based MCMs. When presented with a potential threat, the Integrated Platform should be able to swiftly identify the best threat targets and host machinery to engage, generate threat- and host-binding ligands, and suitable linker groups for combining ligands, such that an effective TACs-based MCM can be quickly identified and validated. The Integrated Platform should be able to produce TACs-based MCMs in a manner that allows performers to mount a successful response to the Pressure Tests (PTs) in the HEALR program.

The following information should be included in the proposal to address TA3 challenges:

- Strategy for rapid linker discovery and optimization;
- Methods for TACs modeling;
- Methods to formulate and deliver TACs-based therapeutics; and
- Description of an Integrated TACs Platform that can rapidly and effectively respond to Capability Demonstrations and Pressure Tests.

1.2.2. PROGRAM STRUCTURE

HEALR is divided into three sequential phases: Phase I (Base) for 24 months; Phase II (Option 1) for 18 months; and Phase III (Option 2) for 12 months (Figure 1). Proposers must present a plan for no more than 54 months that includes a comprehensive approach for meeting all program metrics and objectives. Progression from Phase I to Phase II and from Phase II to Phase III is dependent on funding availability and demonstrated success in meeting program metrics and objectives, as described in Section 1.3.

Phase I (Base, 24 months)

During the 24-month Phase I, performers will complete an analysis of suitable target space and develop new target-binding ligands to enable PROTACs for microbial targets (TA1). Performers will further develop new host-binding ligands to engage novel cellular machinery and demonstrate activity against microbial targets (TA2). These activities will be demonstrated in vitro and in cell culture through a Capability Demonstration (CD1). Performers will also develop a strategy for HEALR therapeutic assembly (e.g., linker development and optimization) and delivery as part of TA3.

Phase II (Option 1, 18 months)

During the 18-month Phase II, performers will advance the assets developed in Phase I of the program with in vivo studies in an appropriate model. The Phase I (TA1 and TA2) assets should be benchmarked against state-of-the-art (SOA) MCM activity, with improvements expected to focus on host functionality and survival, including, but not limited to, improved level of protection (e.g., survival rate or colonization), time to protection, frequency of resistance, and breadth of threats covered (e.g., broad spectrum activity against multiple mutants/universality). The improvements should be shown in two Capability Demonstrations in the middle and at the end of Phase II (CD2, CD3). Performers will be expected to engage with the Food and Drug Administration (FDA) for TA1 and TA2 assets during Phase II at a pre-Investigational New Drug (IND) level.

TA3 in Phase II should continue to develop linker molecules and advance kinetics, formulation, and bioavailability considerations for HEALR therapeutics. It is also expected that Phase I advancements made in TA1 and TA2 will feed into the development of an Integrated Platform. The platform should enable performers to integrate the microbial-targeting component of TA1 with the novel cellular machinery engagement developed in TA2. The Integrated Platform should be capable of responding to a range of microbial threats (including their toxins) in intracellular and/or extracellular environments. Proposers should plan for two PTs of their Integrated Platform during Phase II to demonstrate the ability to rapidly develop and screen molecules against previously untested threat target proteins.

Phase III (Option, 12 months)

During the 12-month Phase III, performers who have demonstrated in vivo safety and efficacy and otherwise met program metrics and objectives will focus on IND-enabling studies and continued engagement with the FDA to prepare for IND filing at the end of Phase III. A final Capability Demonstration (CD4) will also take place by the end of Phase III.

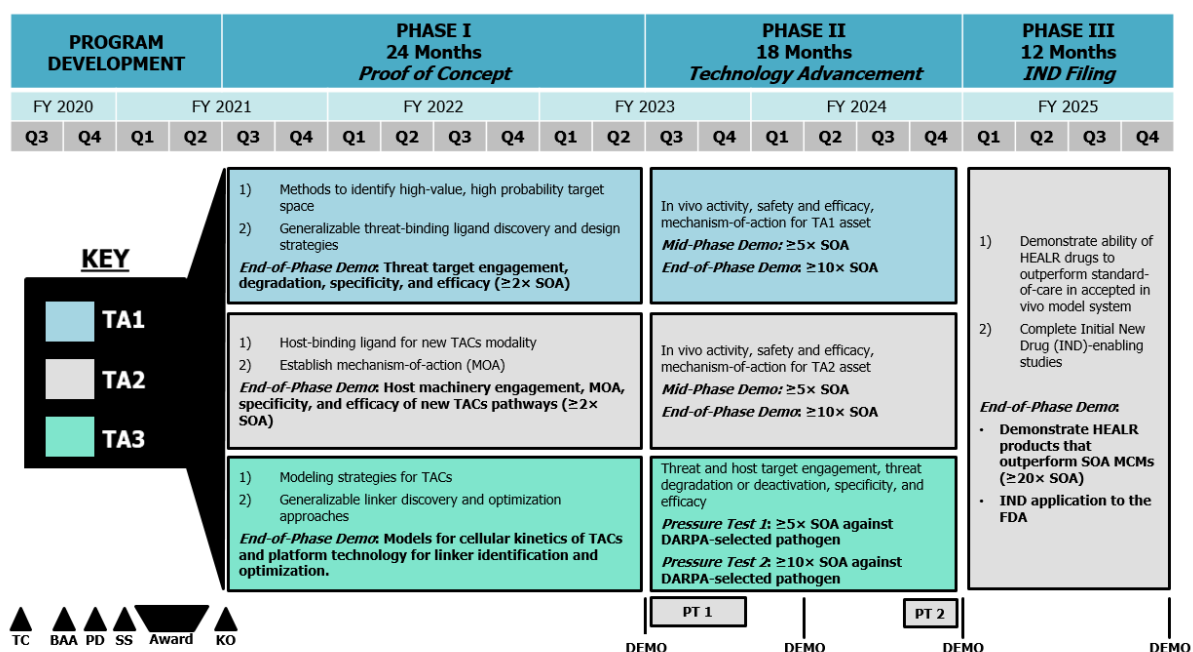


Figure 1. Program Schedule and General Overview

1.2.3. TARGET SELECTION

Proposers are required to designate specific targets for threat-binding and host-binding ligands. Proposers should select targets that enable them to achieve – and demonstrate achievement of – the objectives and metrics for TA1 and TA2. The DARPA team will select targets for the TA3 PT.

TA1 Targets

Because the focus of TA1 is the development of threat-binding ligands, it is recommended that the proposer specify a previously well-established host-binding ligand and host target (e.g.,

proteolysis and PROTACs-related proteins, such as an E3 ubiquitin ligase). The proposer should suggest a minimum of **two** threats from the threat priority list in the BAA ([Table 1](#)) for which ligand development will take place during Phase I of TA1; proposers may choose to pursue more than two threats. Proposers may suggest multiple protein targets associated with each of the threats and/or outline a screening strategy that will allow the proposer to define the protein targets associated with a given threat.

TA2 Targets

The focus of TA2, new host machinery engagement, requires the development of new host-binding ligands. Proposers should select a minimum of **one** protein degradation or deactivation pathway for which to develop ligands during Phase I; proposers may choose to pursue more than one degradation or deactivation pathway. The pathway(s) may have multiple host targets (e.g., a proposer seeking to further develop PROTACs could suggest multiple E3 ubiquitin ligases), which should be explicitly identified in the proposal. Proposed pathways that target degradation of extracellular threats are also of significant interest to HEALR.

Proposers should use the following guidelines to select pathway(s):

- Proposers may seek to advance mechanisms and machinery that leverage proteolysis and the proteasome through new host targets (e.g., E3 ubiquitin ligases that have not yet been studied), but at least one proteasome-independent degradation or deactivation pathway should be proposed as well (i.e., those proposals should present a minimum of two pathways).
- Proposers may leverage mechanisms and machinery that target protein degradation or deactivation capabilities of a pathogen rather than the host, but at least one new host-based protein degradation or deactivation pathways should be proposed (i.e., those proposals should present a minimum of two pathways).
- Proposers may leverage techniques such as molecular glues that act through mechanisms other than protein degradation, but at least one chimeric/heterobifunctional molecule should be proposed.

The selection of threat targets will need to be tailored to the proposed mechanism (e.g., an intracellular degradation method should be paired with an intracellular threat target). Because the goal of TA2 is to test the host machinery engagement rather than the threat-binding ligand of the construct, the proposer may select previously established targets and threat-binding ligands, where available; however, these must still come from the list of threats included in the BAA ([Table 1](#)).

Host-Binding Ligands

For the development of host-binding ligands, proposers should clearly specify the proposed degradation or deactivation strategy and identify any specific targets that would allow access to the relevant cellular machinery. For example, a proposer suggesting a proteolysis pathway might point to several E3 ubiquitin ligases as potential targets. Proposers should be as specific as possible in their identification of host targets (proteins) or, where specificity is not possible, should provide a detailed description of how host targets will be identified.

Threat-Binding Ligands

Proposers should identify known protein targets whenever possible. If the threat protein targets are not known, proposers should provide a detailed description of their strategy to identify them. For threat-binding ligands, performers should select threats from the following list:

Table 1. Threat selection list

Category	Threat
AMR	<i>Acinetobacter baumannii</i>
AMR	<i>Enterobacter</i> spp.
AMR	<i>Enterococcus</i> spp.
AMR	<i>Klebsiella pneumoniae</i>
AMR	<i>Mycobacterium tuberculosis</i>
AMR	<i>Pseudomonas aeruginosa</i>
AMR	<i>Staphylococcus</i> spp. (especially <i>S. aureus</i>)
Biothreat	<i>Burkholderia</i> spp.
Biothreat	<i>Francisella tularensis</i>
Biothreat	<i>Yersinia pestis</i>
Bacterial toxin	Anthrax toxin
Bacterial toxin	Botulinum neurotoxin (BoNT)

DARPA-Selected Targets

Performers will be challenged to complete PTs (described in detail in Section 1.3) in Phase II of the program to demonstrate the adaptability of their Integrated Platform (TA3). Performers will be assigned one or more threats, which may or may not be listed in Table 1.

1.3. PROGRAM METRICS

For the Government to evaluate how effectively a proposed solution achieves the stated program objectives, the Government hereby promulgates the following program metrics that may serve as the basis for determination of satisfactory progress to warrant continued funding. The Government has identified these goals with the intention of bounding the scope of effort while affording the maximum flexibility, creativity, and innovation to proposed solutions to the stated problem.

Quantitative performance metrics are expected to vary for each proposer-selected threat and host target. Proposers to the HEALR program are required to define ambitious, specific, and quantitative metrics in support of program goals, including intermediate metrics, to help further evaluate progress. Some exemplary milestones and metrics are included below, but proposers should adjust according to their proposed work. Final metrics are to be determined at time of award negotiation and are subject to DARPA approval. Proposers should note that program metrics may serve as the basis for determining whether satisfactory progress is being made to warrant continued funding of the program.

1.3.1. CAPABILITY DEMONSTRATIONS

Performance metrics should focus on improvements in host functionality and survival, including, but not limited to, the following categories:

- Enhanced protection/survivability (e.g., reduced colonization or increased survival)
- Improved survivability at increased threat exposures/doses
- Time to protection from MCM administration
- Time window for effective treatment (i.e., time window between threat exposure and administration of MCM with maximal efficacy)
- Breadth of threats covered at maximum protection (e.g., broad activity against multiple strains/drug-resistant organisms)
- Reduced frequency of resistance

Proposers must clearly indicate their target performance metrics for each CD. These metrics must describe the SoA MCM that will be used to benchmark performance, define in quantitative and qualitative terms what is considered threat “protection” in vivo, and describe how protection metrics will be measured. **Successful completion of all CDs should yield MCMs with at least 20× improved performance in vivo over SoA for a given threat in at least one performance category.**

Examples of proposed performance metrics relative to SoA MCMs that must be provided by each proposer team are shown in Table 2. Proposers may select more than one performance category to exceed SoA MCMs, but must meet *at least* one performance category at $\geq 2\times$ SoA for CD1; $\geq 5\times$ SoA for CD2; $\geq 10\times$ SoA for CD3; and $\geq 20\times$ SoA for CD4. Teams that propose therapeutics solutions that exceed 2×, 5×, 10×, and 20× SoA for more than one performance category will be viewed more favorably.

Table 2. Performance Metrics Examples¹

Performance Category	Threat	SoA MCM	CD1	CD2	CD3	CD4
			Initial Target	Improved Target	Optimize Target	Final Target
Potency	<i>Klebsiella pneumonia</i> (Gram-negative) ²	Colistin	MIC 4 µg/mL ⁴	MIC 1.6 µg/mL ⁴	MIC 0.8 µg/mL ⁴	MIC 0.4 µg/mL ⁴
		MIC ³ 8 µg/mL				
	<i>Staphylococcus aureus</i> (MRSA, Gram-positive)	Vancomycin	MIC 4 µg/mL ⁴	MIC 1.6 µg/mL ⁴	MIC 0.8 µg/mL ⁴	MIC 0.4 µg/mL ⁴
		MIC ³ 8 µg/mL				
Breadth of Coverage	<i>Acinetobacter baumannii</i> (MDR, Gram-negative)	Small molecule antibiotics ⁵	Efficacy against 75% of known <i>A. baumannii</i> strains	Efficacy against 80% of known <i>A. baumannii</i> strains	Efficacy against 90% of known <i>A. baumannii</i> strains	Efficacy against >95% known <i>A. baumannii</i> strains
		Resistance developed to all antibiotics in CENTCOM formulary				
Therapeutic Window	Botulinum Neurotoxin ⁶	Botulinum Antitoxin	>75% survival @ 4 hours ^{7,8}	>80% survival @ 6 hours ^{7,8}	>85% survival @ 8 hours ^{7,8}	>90% survival @ 10 hours ^{7,8}
		75% survival @ 2 hours ⁷				

¹Not all examples given reach the 2×, 5×, 10×, and 20× SoA threshold and therefore would require an additional performance category that does meet these improvements in order to meet the BAA guidance

²Includes antimicrobial resistant strains

³MIC = Minimum inhibitory concentration, varies greatly by strain (*Klebsiella* 0.25 to 128 µg/mL; MRSA 1.0 to 138 µg/mL)

⁴Against a panel of >30 resistant strains

⁵Tobramycin shows efficacy against 68% of MDR strains isolated in Role 3 facility; no other antibiotic shows efficacy against >25% of MDR strains (Craig Joint Theater Hospital, Afghanistan)

⁶Type E, rabbit model

⁷Post-symptomatic administration

⁸Mean time-to-death for untreated infection is 17.5 hours after symptom onset; therapeutic window scaled accordingly

The CDs are scheduled to take place at the end of Phase I, throughout Phase II, and again at the end of Phase III, as shown in Table 3.

Table 3. Capability Demonstration Schedule

CD	Program Phase	Program Month
CD1; ≥2× SoA	Phase I	Month 24
CD2; ≥5× SoA	Phase II	Month 33
CD3; ≥10× SoA	Phase II	Month 42
CD4; ≥20× SoA	Phase III	Month 54

1.3.2. PLATFORM INTEGRATION AND PRESSURE TESTS

Proposers should outline a clear plan for development of the Integrated Platform, including optimization steps, expected risks, and risk mitigation strategies. The component capabilities generated from each TA (including those developed for TA3 during Phase I of the program)

should work as an integrated whole to generate therapeutics against DARPA-selected bacterial threats. Performance of the Integrated Platform developed in TA3 will be assessed by PTs in Phase II of the program.

PT1 will begin by Month 24 of the program and will consist of one DARPA-assigned challenge threat. Performers will be expected to identify a suitable target for threat degradation, determine an appropriate mechanism for degradation/deactivation, screen and optimize threat-binding ligands, assemble a complete HEALR therapeutic using an appropriate linker, and demonstrate efficacy of the therapeutic in vitro, in cell culture, and in vivo over the span of 6 months.

PT2 will begin by Month 39 of the program with the assignment of one challenge threat. The parameters of PT2 will be identical to PT1; however, the timeframe for completing PT2 will be shortened to 3 months.

The therapeutics developed in each PT will be benchmarked in the same manner as the CDs; that is, the therapeutics will be expected to meet or exceed $\geq 5\times$ SoA (PT1) or $\geq 10\times$ SoA (PT2), with a focus on improvements in host functionality and survival, including, but not limited to, the following categories:

- Enhanced protection/survivability (e.g., reduced colonization or increased survival)
- Improved survivability at increased threat exposures/doses
- Time to protection from MCM administration
- Time window for effective treatment (i.e., time window between threat exposure and administration of MCM with maximal efficacy)
- Breadth of threats covered at maximum protection (e.g., broad activity against multiple strains/drug-resistant organisms)
- Reduced frequency of resistance

For each PT, proposers must compare the performance of the HEALR therapeutics head-to-head against SoA MCMs for a given threat in order to demonstrate improved performance compared to SoA MCMs. Performers are not expected to specify the performance categories they will pursue until the beginning of the PT, and they may choose to revise their performance categories during the PT as needed.

1.3.3. PROGRAM METRICS BY TA

Proposers should consider program metrics, objectives, and deliverables, as outlined below. Proposers should address these metrics in the proposal specifically and quantitatively wherever possible.

Table 4. TA1 metrics

TA1: Microbial Targeting (Phase I)	
Milestones and Deliverables	Program Metrics
<ul style="list-style-type: none"> Identify suitable microbial and toxin (threat) targets Develop threat-binding ligand discovery, design, and screening approaches, including against novel targets Demonstrate degradation or deactivation MOA against targets in increasingly complex cellular environments 	<p>Proposers must define quantitative performance metrics for each Capability Demonstration (CD):</p> <ul style="list-style-type: none"> Criteria for selection and prioritization of targets for a given threat Criteria for screening and optimization of threat-binding ligand Efficacy in vitro and in cell culture: e.g., reduction in target activity <ul style="list-style-type: none"> CD1: $\geq 2 \times$ SoA MCM Specificity: e.g., no off-target effects compared to suitable controls Safety: therapeutic index > 5
TA1: Microbial Targeting (Phase II)	
Milestones and Deliverables	Program Metrics
<ul style="list-style-type: none"> Refine microbial and toxin (threat) targets identification Optimize threat-binding ligand discovery, design, and screening approaches, including against novel targets Demonstrate degradation or deactivation MOA against targets in appropriate animal models Engage in pre-IND activities with FDA 	<p>Proposers must define quantitative performance metrics for each metric category below for each Capability Demonstration (CD):</p> <ul style="list-style-type: none"> Efficacy: e.g., protection or survival exceeding that of SoA MCMs for threat relevant duration <ul style="list-style-type: none"> CD2: $\geq 5 \times$ SoA MCM CD3: $\geq 10 \times$ SoA MCM Specificity: no off-target or off-tissue effects compared to suitable controls Safety: no adverse effects in a healthy animal model, including toxicity, immunogenicity, weight loss, etc. Safety: therapeutic index > 10

Table 5. TA2 metrics

TA2: Host Machinery Engagement (Phase I)	
Milestones and Deliverables	Program Metrics
<ul style="list-style-type: none"> Identify NewTAC approaches, including targets for engagement of host cellular machinery Develop host-binding ligand discovery, screening, and optimization approaches Demonstrate degradation or deactivation MOA against targets in increasingly complex cellular environments 	<p>Proposers must define quantitative performance metrics for each Capability Demonstration (CD):</p> <ul style="list-style-type: none"> Criteria for selection of protein targets for cell machinery engagement Criteria for screening and optimization of host-binding ligand Efficacy in vitro and in cell culture: e.g., reduction in target activity <ul style="list-style-type: none"> CD1: $\geq 2 \times$ SoA MCM Specificity: no off-target effects compared to suitable controls Safety: therapeutic index > 5 Experimental validation of NewTACs MOA
TA2: Host Machinery Engagement (Phase II)	
Milestones and Deliverables	Program Metrics
<ul style="list-style-type: none"> Refine and optimize host-binding ligand Demonstrate degradation or deactivation MOA against targets in appropriate animal models Engage in early pre-IND activities with FDA 	<p>Proposers must define quantitative performance metrics for each metric category below for each Capability Demonstration (CD):</p> <ul style="list-style-type: none"> Efficacy: e.g., protection or survival exceeding that of SoA MCMs for threat relevant duration <ul style="list-style-type: none"> CD2: $\geq 5 \times$ SoA MCM CD3: $\geq 10 \times$ SoA MCM Specificity: no off-target or off-tissue effects compared to suitable controls Safety: therapeutic index > 10 Safety: no adverse effects in a healthy animal model, including toxicity, immunogenicity, weight loss, etc.

Table 6. TA3 Metrics

TA3: Integrated Platform (Phase I)	
Milestones and Deliverables	Program Metrics
<ul style="list-style-type: none"> Develop linker design, screening, and optimization approaches for joining threat- and host-binding ligands to form new chimeric molecules Determine cellular kinetics and pharmacodynamics of HEALR therapeutics Develop formulation and delivery strategies 	<p>Proposers must define quantitative performance metrics for:</p> <ul style="list-style-type: none"> Predictive modeling for optimal chimera dosing Rapid prediction of linker design and length for optimal chimera performance Demonstration of necessary biodistribution to elicit TACs effect
TA3: Integrated Platform (Phase II)	
Milestones and Deliverables	Program Metrics
<ul style="list-style-type: none"> Refine linker design, screening, and optimization approaches for joining threat- and host-binding ligands to form new chimeric molecules Integrate ligand-screening capabilities (TA1) and host engagement mechanisms (TA2) with linker development (TA3) for rapid generation of HEALR therapeutic molecule candidates against new threats for two Pressure Tests Demonstrate efficacy of candidates in an appropriate animal model Screen for and optimize bioavailability of HEALR therapeutic candidates Refine formulation and delivery strategies 	<p>Proposers will be expected to define and meet quantitative performance metrics for each metric category below within the PT timeframe (6 months for PT1, 3 months for PT2)</p> <ul style="list-style-type: none"> Efficacy: e.g., protection or survival exceeding that of SoA MCMs for threat relevant duration against a DARPA-issued challenge pathogen <ul style="list-style-type: none"> PT1: $\geq 5 \times$ SoA MCM PT2: $\geq 10 \times$ SoA MCM Specificity: no off-target or off-tissue effects compared to suitable controls Safety: in vivo therapeutic index >10 Safety: no adverse effects in a healthy animal model, including toxicity, immunogenicity, weight loss, etc. Bioavailability and adsorption, distribution, metabolism, and excretion (ADME) properties

Table 7. Phase III Metrics for All TAs

All TAs (Phase III)	
Milestones and Deliverables	Program Metrics
<ul style="list-style-type: none"> • Refine and optimize best Phase II HEALR therapeutics (all TAs) for IND submission • Complete IND-enabling studies • Demonstrate performance of optimized HEALR 	<p>Proposers must define quantitative performance metrics for each metric category below for each Capability Demonstration (CD):</p> <ul style="list-style-type: none"> • Efficacy: e.g., protection or survival exceeding that of SoA MCMs for threat relevant duration <ul style="list-style-type: none"> ◦ CD4: $\geq 20 \times$ SoA MCM • Specificity: no off-target or off-tissue effects compared to suitable controls • Safety: in vivo therapeutic index >100 • Safety: no adverse effects in a healthy animal model, including toxicity, immunogenicity, overall health effects, etc. • Formulation, bioavailability, and ADME properties

1.3.4. INDEPENDENT VERIFICATION AND VALIDATION

While preparation for IND submission and FDA engagement will establish the necessary framework for the program, HEALR therapeutics may undergo additional Independent Verification and Validation (IV&V) using team(s) established by DARPA to help test and validate progress. The IV&V team will consist of subject matter experts from Government organizations, Federally Funded Research and Development Centers (FFRDCs), and/or other relevant domains. IV&V may include verification of safety and efficacy in cells and established animal models for relevant threats.

To avoid potential conflicts of interest, HEALR performers will not be allowed to compete for the IV&V contract. DARPA is not soliciting proposals for IV&V under HR001120S0052. Government teams interested in participating in IV&V should not respond to this BAA but should rather indicate their interest in the HEALR program by reaching out directly to the DARPA Program Manager.

1.4. GENERAL REQUIREMENTS

1.4.1. PROPOSING TEAMS

It is expected that proposals will involve multidisciplinary teams with expertise from distinct, complementary disciplines. Specific content, communications, networking, and team formation

are the sole responsibility of the proposer teams. Proposer teams must submit a single, integrated proposal led by a single Principal Investigator under a single prime contractor that addresses all program technical areas and phases, as applicable. Proposer teams (from the same or different institutions) should be assembled as a single research entity, and report as such. Proposer teams must include a dedicated Project Coordinator for administrative, financial, and management oversight of the proposed program.

DARPA will hold a Proposers Day (see Section 8, Other Information) to facilitate the formation of proposer teams with the expertise necessary to meet the goals of the program and will share information among interested proposers through the DARPA Opportunities Page.

1.4.2. COMMERCIALIZATION AND TECHNOLOGY TRANSFER PLAN

Proposers are required to propose a [commercialization and technology transfer plan](#) to ensure transition of the therapeutics developed through the HEALR program and the associated platform capabilities. Such a plan might include partnership with an existing commercial entity to fund work beyond IND submission, formation of a company to continue developing NewTACs therapeutics, or other efforts to leverage anticipated results from the program. In order to ensure a path to technology transfer after the program, proposers are strongly encouraged to seek a partnership to provide a Phase III cost share and to describe how this cost share will help support transition.

1.4.3. EMBEDDED ENTREPRENEURSHIP INITIATIVE (EEI) OPTION

The mission of DARPA's Embedded Entrepreneurship Initiative (EEI) is to eliminate problematic foreign investment and involvement in DARPA performers by building stronger companies that have a higher likelihood of securing U.S. investment, growing domestically, and providing new capabilities for national security. The resources provided by EEI enable teams to complete foundational entrepreneurial work that is required to achieve successful transition of dual-use technologies. Resources include up to \$250,000 to complete milestones (see below for example milestones), quarterly access to a senior commercialization advisor, and at the appropriate time, connection to key transition partners and investors. The determination for participation in EEI will be made independently by the Government following selection for an award. Selection for award does not imply selection for participation in EEI.

Participation in DARPA's EEI is voluntary and will be included in the award as an Option that can be employed, by the Government, at any point in time during the period of performance. EEI tasks and deliverables must be provided as an option in the Statement of Work submitted in response to this BAA. EEI funding requests should be consistent with the proposed work scope and proposed timeline but are anticipated to be in the range of \$250,000 per performer. The EEI option will be exercised at the discretion of the Government based on a performer's technical accomplishments and progress towards development of a technology with transition and commercialization potential and subject to the availability of funding.

Proposers wishing to be considered for participation in EEI must:

1. Include in their proposal a separately costed task for up to \$250,000. A typical

timeframe for the EEI work is between one and two years.

2. Include milestones required to produce a robust “Go to Market” strategy (i.e., Transition Plan). Please see below the list of typical EEI milestones. Please propose your best assessment of what entrepreneurial work would be required for successful transition, or simply copy and paste the typical milestones below. Because it is difficult to know early in a research effort what work would be relevant or needed in order to transition the technology, these milestones may be modified at the time of award of the Option.

Typical Embedded Entrepreneurship Initiative (EEI) Milestones include:

1. **Hire EEI lead:** Find and engage a seasoned entrepreneur, with experience transitioning early technologies into products within the relevant markets of interest. This individual will execute the milestones below. DARPA will provide a “non-object” to engage this person. In some cases, different skill sets may need to be engaged. For example, a portion of the funding could be utilized to hire a seasoned entrepreneur, and another portion could be utilized to hire a regulatory expert.
2. **Identify Target Markets:** Often, there are multiple, distinct market segments that an early technology can target for transition. Different market segments have different barriers to entry, value propositions, cost points, revenue streams, estimated returns on investment (ROIs), potential business models, channels to market, customer acquisition costs, competitors, launch volumes, etc. Assess each potential market of entry based on key criteria (such as those listed above). Conduct interviews with key stakeholders in each potential market. Downselect to a single market of first entry or a viable subset of target markets that balances your vision with the reality of logistically entering multiple markets as well as needed financing to execute. Describe the decision process. At least one market analyzed must be for national security applications.
3. **Market Analysis and Value Chain Mapping:** For the identified first market of entry, map the key players throughout the value chain, their current partnerships, business models, price points and margins.
4. **Competitive Analysis:** Complete a robust competitive analysis, including indirect competitors as well as emerging competitors, still in the lab today, that target a similar value proposition. Include a summary of key findings for each product, by market segment, and with an appendix of tabulated data on competing companies and technologies. In a format similar to a Strengths, Weaknesses, Opportunities, and Threats (SWOT) analysis, include features, strategies utilized to enter their market segments, partnerships and business models of potential competitors, estimated margins and market share, and strategies utilized to attract customers.
5. **Techno-Economic Analysis:** Produce a written document and/or a robust Excel doc to capture and validate the following:
 - i) A basic Bill of Materials cost model for your potential product.

- ii) A substantial business, financial model including Operating Expenditures (OPEX) and Capital Expenditures (CAPEX).
 - iii) A sensitivity analysis on overall cost structure with key variables such as market penetration assumptions, necessary cost points, and volume pricing of components.
6. **Manufacturing and Scale-up Plan:** Plan to include estimated financing required, identified supply chain partners with an emphasis on domestic suppliers, and timeline.
7. **IP Strategy:** Produce a written document outlining strategy for protecting the technology investment. Assessment should consider the following:
- i) Patent strategy (domestic and international), trade secret strategy.
 - ii) Freedom to operate analysis.
 - iii) Exploration of the value of novelty destroying publications, creative patenting approaches (Markush lists, claims, etc.).
 - iv) How these strategies affect the approach towards broader markets, higher prices and drive market share, as well as how this DARPA-funded effort would maintain a domestic technological advantage.
8. **Dual-Use (commercial and defense) Go to Market Strategy:** Based on learnings from the above milestones, deliver a robust plan to go to market. Include a proposed business model, target market of entry, value proposition, estimated product cost structure, financing mechanisms, customer acquisition strategy, manufacturing and scale-up plan, required partnerships, timeline, IP strategy, regulatory milestones, etc.

1.4.4. DELIVERABLES

All products, material and otherwise, to be provided to the Government as outcomes from conducted research should be defined in the proposal. Performers need to allot time and budget to fulfill obligations for travel to and from review meetings, and the transmission of report documentation.

Monthly financial reports: Performers are required to provide financial status updates. The prime Performer shall include information for itself and all subawardees/subcontractors. These reports should be in the form of an editable Microsoft (MS) Excel™ file, and should provide financial data including, but not limited to:

- Program spend plan by phase and task
- Incurred program expenditures to date by phase and task
- Invoiced program expenditures to date by phase and task

Monthly technical progress reports: Performers are required to provide monthly research updates in the form of a standardized slide presentation given to DARPA and discussed with the program management team via teleconference. Length and detail level is at the discretion of the Program Manager.

Semi-annual program reviews: Leadership from each performer team (with additional key

personnel at the discretion of the Principal Investigator [PI]) will be required to present research progress in person at program review meetings. The purpose of these reviews is to ensure adequate engagement with the DARPA team, to discuss details that might otherwise fall outside the scope of a routine technical brief, and provide opportunities to discuss progress towards milestones and scientific goals and any ongoing technical or programmatic challenges that must be overcome to achieve the overarching goals of the program.

End of Phase report: Three months prior to the end of Phase I and Phase II (i.e., at Month 21 and Month 39), performers must draft and present to DARPA a written report of all research activities and metrics satisfied. This report should contain as much supporting data as possible.

Final Program Report: When the final funding phase closes out, performer teams must provide a final report summarizing all research activities, outcomes, and materials discovered during the program, publications, research presentations, patent applications that result from the research pursued, and any additional deliverables requested by the DARPA contracting agent for this program.

2. Award Information

2.1. GENERAL AWARD INFORMATION

Multiple awards are possible. The amount of resources made available under this BAA will depend on the quality of the proposals received and the availability of funds.

The Government reserves the right to select for negotiation all, some, one, or none of the proposals received in response to this solicitation and to make awards without discussions with proposers. The Government also reserves the right to conduct discussions if it is later determined to be necessary. If warranted, portions of resulting awards may be segregated into pre-priced options. Additionally, DARPA reserves the right to accept proposals in their entirety or to select only portions of proposals for award. In the event that DARPA desires to award only portions of a proposal, negotiations may be opened with that proposer. The Government reserves the right to fund proposals in phases with options for continued work, as applicable.

The Government reserves the right to request any additional, necessary documentation once it makes the award instrument determination. Such additional information may include but is not limited to Representations and Certifications (see Section VI.B.2., “Representations and Certifications”). The Government reserves the right to remove proposers from award consideration should the parties fail to reach agreement on award terms, conditions, and/or cost/price within a reasonable time, and the proposer fails to timely provide requested additional information. Proposals identified for negotiation may result in a procurement contract, cooperative agreement, or other transaction, depending upon the nature of the work proposed, the required degree of interaction between parties, whether or not the research is classified as Fundamental Research, and other factors.

Proposers looking for innovative, commercial-like contractual arrangements are encouraged to consider requesting Other Transactions. To understand the flexibility and options associated with

Other Transactions, consult <http://www.darpa.mil/work-with-us/contract-management#OtherTransactions>.

In accordance with 10 U.S.C. § 2371b(f), the Government may award a follow-on production contract or Other Transaction (OT) for any OT awarded under this BAA if: (1) that participant in the OT, or a recognized successor in interest to the OT, successfully completed the entire prototype project provided for in the OT, as modified; and (2) the OT provides for the award of a follow-on production contract or OT to the participant, or a recognized successor in interest to the OT.

In all cases, the Government contracting officer shall have sole discretion to select award instrument type, regardless of instrument type proposed, and to negotiate all instrument terms and conditions with selectees. DARPA will apply publication or other restrictions, as necessary, if it determines that the research resulting from the proposed effort will present a high likelihood of disclosing performance characteristics of military systems or manufacturing technologies that are unique and critical to defense. Any award resulting from such a determination will include a requirement for DARPA permission before publishing any information or results on the program. For more information on publication restrictions, see the section below on Fundamental Research.

2.2. FUNDAMENTAL RESEARCH

It is DoD policy that the publication of products of fundamental research will remain unrestricted to the maximum extent possible. National Security Decision Directive (NSDD) 189 defines fundamental research as follows:

‘Fundamental research’ means basic and applied research in science and engineering, the results of which ordinarily are published and shared broadly within the scientific community, as distinguished from proprietary research and from industrial development, design, production, and product utilization, the results of which ordinarily are restricted for proprietary or national security reasons.

As of the date of publication of this BAA, the Government expects that program goals as described herein may be met by proposers intending to perform fundamental research and does not anticipate applying publication restrictions of any kind to individual awards for fundamental research that may result from this BAA. Notwithstanding this statement of expectation, the Government is not prohibited from considering and selecting research proposals that, while perhaps not qualifying as fundamental research under the foregoing definition, still meet the BAA criteria for submissions. If proposals are selected for award that offer other than a fundamental research solution, the Government will either work with the proposer to modify the proposed statement of work to bring the research back into line with fundamental research or else the proposer will agree to restrictions in order to receive an award.

Proposers should indicate in their proposal whether they believe the scope of the research included in their proposal is fundamental or not. While proposers should clearly explain the intended results of their research, the Government shall have sole discretion to determine whether the proposed research shall be considered fundamental and to select the award

instrument type. Appropriate language will be included in resultant awards for non-fundamental research to prescribe publication requirements and other restrictions, as appropriate. This language can be found at <http://www.darpa.mil/work-with-us/additional-baa>.

For certain research projects, it may be possible that although the research to be performed by a potential awardee is non-fundamental research, its proposed subawardee's effort may be fundamental research. It is also possible that the research performed by a potential awardee is fundamental research while its proposed subawardee's effort may be non-fundamental research. In all cases, it is the potential awardee's responsibility to explain in its proposal which proposed efforts are fundamental research and why the proposed efforts should be considered fundamental research.

3. Eligibility Information

3.1. ELIGIBLE APPLICANTS

All responsible sources capable of satisfying the Government's needs may submit a proposal that shall be considered by DARPA.

3.1.1. Federally Funded Research and Development Centers (FFRDCs) and Government Entities

FFRDCs

FFRDCs are subject to applicable direct competition limitations and cannot propose to this BAA in any capacity unless they meet the following conditions. (1) FFRDCs must clearly demonstrate that the proposed work is not otherwise available from the private sector. (2) FFRDCs must provide a letter, on official letterhead from their sponsoring organization, that (a) cites the specific authority establishing their eligibility to propose to Government solicitations and compete with industry, and (b) certifies the FFRDC's compliance with the associated FFRDC sponsor agreement's terms and conditions. These conditions are a requirement for FFRDCs proposing to be awardees or subawardees.

Government Entities

Government Entities (e.g., Government/National laboratories, military educational institutions, etc.) are subject to applicable direct competition limitations. Government Entities must clearly demonstrate that the work is not otherwise available from the private sector and provide written documentation citing the specific statutory authority and contractual authority, if relevant, establishing their ability to propose to Government solicitations and compete with industry. This information is required for Government Entities proposing to be awardees or subawardees.

Authority and Eligibility

At the present time, DARPA does not consider 15 U.S.C. § 3710a to be sufficient legal authority to show eligibility. While 10 U.S.C. § 2539b may be the appropriate statutory starting point for some entities, specific supporting regulatory guidance, together with evidence of agency approval, will still be required to fully establish eligibility. DARPA will consider FFRDC and Government Entity eligibility submissions on a case-by-case basis; however, the burden to prove eligibility for all team members rests solely with the proposer.

3.1.2. NON-U.S. ORGANIZATIONS

Non-U.S. organizations and/or individuals may participate to the extent that such participants comply with any necessary nondisclosure agreements, security regulations, export control laws, and other governing statutes applicable under the circumstances.

3.2. ORGANIZATIONAL CONFLICTS OF INTEREST

FAR 9.5 Requirements

In accordance with FAR 9.5, proposers are required to identify and disclose all facts relevant to potential OCIs involving the proposer's organization and *any* proposed team member (subawardee, consultant). Under this Section, the proposer is responsible for providing this disclosure with each proposal submitted to the BAA. The disclosure must include the proposer's, and as applicable, proposed team member's OCI mitigation plan. The OCI mitigation plan must include a description of the actions the proposer has taken, or intends to take, to prevent the existence of conflicting roles that might bias the proposer's judgment and to prevent the proposer from having unfair competitive advantage. The OCI mitigation plan will specifically discuss the disclosed OCI in the context of each of the OCI limitations outlined in FAR 9.505-1 through FAR 9.505-4.

Agency Supplemental OCI Policy

In addition, DARPA has a supplemental OCI policy that prohibits contractors/performers from concurrently providing Scientific Engineering Technical Assistance (SETA), Advisory and Assistance Services (A&AS) or similar support services and being a technical performer. Therefore, as part of the FAR 9.5 disclosure requirement above, a proposer must affirm whether the proposer or *any* proposed team member (subawardee, consultant) is providing SETA, A&AS, or similar support to any DARPA office(s) under: (a) a current award or subaward; or (b) a past award or subaward that ended within one calendar year prior to the proposal's submission date.

If SETA, A&AS, or similar support is being or was provided to any DARPA office(s), the proposal must include:

- The name of the DARPA office receiving the support;
- The prime contract number;
- Identification of proposed team member (subawardee, consultant) providing the support; and
- An OCI mitigation plan in accordance with FAR 9.5.

Government Procedures

In accordance with FAR 9.503, 9.504 and 9.506, the Government will evaluate OCI mitigation plans to avoid, neutralize or mitigate potential OCI issues before award and to determine whether it is in the Government's interest to grant a waiver. The Government will only evaluate OCI mitigation plans for proposals that are determined selectable under the BAA evaluation criteria and funding availability.

The Government may require proposers to provide additional information to assist the Government in evaluating the proposer's OCI mitigation plan.

If the Government determines that a proposer failed to fully disclose an OCI; or failed to provide the affirmation of DARPA support as described above; or failed to reasonably provide additional information requested by the Government to assist in evaluating the proposer's OCI mitigation plan, the Government may reject the proposal and withdraw it from consideration for award.

3.3. COST SHARING/MATCHING

Cost sharing is not required. However, it will be carefully considered where there is an applicable statutory condition relating to the selected funding instrument. Cost sharing is encouraged where there is a reasonable probability of a potential commercial application related to the proposed research and development effort.

4. Application and Submission Information

4.1. ADDRESS TO REQUEST APPLICATION PACKAGE

This announcement, any attachments, and any references to external websites herein constitute the total solicitation. If proposers cannot access the referenced material posted in the announcement found at <http://www.darpa.mil>, contact the administrative contact listed herein.

4.2. CONTENT AND FORM OF APPLICATION SUBMISSION

All submissions, including abstracts and proposals, must be written in English with type no smaller than 12-point font. A smaller font may be used for figures, tables, and charts. The page limitation includes all figures, tables, and charts. All pages shall be formatted for printing on 8-1/2 by 11-inch paper. Margins must be 1-inch on all sides. Copies of all documents submitted must be clearly labeled with the DARPA BAA number, proposer organization, and proposal title/proposal short title.

4.2.1. PROPOSAL ABSTRACT FORMAT

Proposers are strongly encouraged to submit an abstract in advance of a full proposal to minimize effort and reduce the potential expense of preparing an out of scope proposal. DARPA will respond to abstracts providing feedback and indicating whether, after preliminary review, there is interest within BTO for the proposed work. DARPA will attempt to reply within 20 calendar days of receipt. Proposals may be submitted irrespective of comments or feedback received in response to the abstract. Proposals are reviewed without regard to feedback given as a result of abstract review. The time and date for submission of proposal abstracts are specified in Part I above.

The abstract is a concise version of the proposal comprising a maximum of **eight (8)** pages including all figures, tables, and charts. All submissions must be written in English with type no smaller than 12-point font. A smaller font may be used for figures, tables, and charts. All pages shall be formatted for printing on 8-1/2 by 11-inch paper. Margins must be 1-inch on all sides. Copies of all documents submitted must be clearly labeled with the DARPA BAA number, proposer organization, and proposal abstract title.

The page limit does NOT include:

- Official transmittal letter (optional);

- Cover sheet;
- Executive summary slide;
- Resumes (optional, submit no more than two – one must be for the PI); and
- Bibliography (optional).

Abstracts must include the following components:

A. Cover Sheet (does not count towards page limit): Include the administrative and technical points of contact (name, address, phone, fax, e-mail, lead organization). Also include the BAA number, title of the proposed project, primary subcontractors, estimated cost, duration of the project, and the label “ABSTRACT.”

B. Executive Summary Slide (does not count towards page limit): The slide template is provided as **Attachment 1** to the BAA posted at <https://beta.sam.gov>. Use of this template is required.

C. Goals and Impact: Clearly describe what is being proposed and what difference it will make (qualitatively and quantitatively), including brief answers to the following questions:

1. What is the proposed work attempting to accomplish or do?
2. How is it done today? And what are the limitations?
3. What is innovative in your approach, and how does it compare to the current state-of-the-art (SOA)?
4. What are the key technical challenges in your approach, and how do you plan to overcome these?
5. Who will care, and what will the impact be if you are successful?
6. How much will it cost and how long will it take?

D. Technical Plan: Outline and address all technical areas and challenges inherent in the approach and possible solutions for overcoming potential problems. This section should provide specific objectives, metrics, and milestones at intermediate stages of the project to demonstrate a plan for accomplishment of the program goals. Propose additional appropriate qualitative and quantitative metrics specific to the approach, as needed. Outline of intermediary milestones should occur at no greater than 6-month increments.

E. Management and Capabilities: Provide a brief summary of expertise of the team, including subcontractors and key personnel.

A principal investigator for the project and a description of the team’s organization, including a breakdown by Technical Area (TA), must be identified. All teams are strongly encouraged to identify a Project Manager/Integrator to serve as the primary point of contact to communicate with the DARPA Program Manager, IV&V partner, and Contracting Officer’s Representative, coordinate the effort across co-performer, vendor, and subcontractor teams, organize regular performer meetings or discussions, facilitate data sharing, and ensure timely completion of milestones and deliverables.

Include a description of the team's organization, including roles and responsibilities. Team member descriptions should address the Technical Plan, describe the time and percent effort divisions for members participating across multiple TAs, and delineate individuals to avoid duplication of efforts.

Describe the organizational experience in this area, existing intellectual property required to complete the project, and any specialized facilities to be used as part of the project. List Government-furnished materials or data assumed to be available. Describe any specialized facilities to be used as part of the project, the extent of access to these facilities, and any biological containment, biosafety, and certification requirements.

F. Cost and Schedule: Provide a cost estimate for resources over the proposed timeline of the project, broken down by phase and major cost items (e.g., labor, materials, etc.). Include cost estimates for each potential subcontractor (may be a rough order of magnitude).

4.2.2. PROPOSAL FORMAT

All full proposals must be in the format given below. Proposals shall consist of two volumes: 1) **Volume I, Technical and Management Proposal**, and 2) **Volume II, Cost Proposal**. All submissions must be written in English with type no smaller than 12-point font. A smaller font may be used for figures, tables, and charts. The page limitation includes all figures, tables, and charts. All pages shall be formatted for printing on 8-1/2 by 11- inch paper. Margins must be 1- inch on all sides. Copies of all documents submitted must be clearly labeled with the DARPA BAA number, proposer organization, and proposal title/proposal short title. Volume I, Technical and Management Proposal, may include an attached bibliography of relevant technical papers or research notes (published and unpublished) which document the technical ideas and approach upon which the proposal is based. Copies of not more than three (3) relevant papers may be included with the submission. The bibliography and attached papers are not included in the page counts given below. The submission of other supporting materials along with the proposals is strongly discouraged and will not be considered for review. **The maximum page count for Volume I is 35 pages.** The official transmittal letter is not included in the page count. Volume I should include the following components:

NOTE: Non-conforming submissions that do not address both technical areas and/or follow the instructions herein may be rejected without further review.

a. Volume I, Technical and Management Proposal

Section I. Administrative

A. Cover Sheet (LABELED "PROPOSAL: VOLUME I") to include:

1. BAA number (HR001120S0052);
2. Lead organization submitting proposal (prime contractor);

3. Type of organization, selected from among the following categories: “LARGE BUSINESS,” “SMALL DISADVANTAGED BUSINESS,” “OTHER SMALL BUSINESS,” “HBCU,” “MI,” “OTHER EDUCATIONAL,” OR “OTHER NONPROFIT”;
4. Proposer’s reference number (if any);
5. Other team members (if applicable) and type of business for each;
6. Proposal title;
7. Technical point of contact (Program Manager or Principle Investigator) to include: salutation, last name, first name, street address, city, state, zip code, telephone, fax (if available), e-mail (if available);
8. Administrative point of contact (Contracting Officer or Award Officer) to include: salutation, last name, first name, street address, city, state, zip code, telephone, fax (if available), e-mail (if available);
9. Award instrument requested: cost-plus-fixed-fee (CPFF), cost-contract—no fee, cost sharing contract – no fee, or other type of procurement contract (*specify*), cooperative agreement, or other transaction;
10. Place(s) of performance, including all subcontractors and consultants;
11. Period of performance;
12. Total funds requested from DARPA, total funds requested per phase and the amount of any cost share (if any);
13. Proposal validity period; AND
14. Date proposal was submitted.

Information on award instruments is available at <http://www.darpa.mil/work-with-us/contract-management>.

B. Official Transmittal Letter.

C. Executive Summary Slide: The slide template is provided as **Attachment 1** to the BAA posted at <https://beta.sam.gov>. Use of this template is required.

Section II. Detailed Proposal Information

A. Executive Summary: Provide a synopsis of the proposed project, including answers to the following questions:

- What is the proposed work attempting to accomplish or do?
- How is it done today, and what are the limitations?
- What is innovative in your approach?
- What are the key technical challenges in your approach, and how do you plan to overcome these?
- Who or what will be affected, and what will be the impact if the work is successful?

- How much will it cost, and how long will it take?

- B. Goals and Impact:** Clearly describe what the team is trying to achieve and the difference it will make (qualitatively and quantitatively) if successful. Describe the innovative aspects of the project in the context of existing capabilities and approaches, clearly delineating the uniqueness and benefits of this project in the context of the state of the art, alternative approaches, and other projects from the past and present. Describe how the proposed project is revolutionary and how it significantly rises above the current state-of-the-art. Describe the deliverables associated with the proposed project and any plans to commercialize the technology, transition it to a customer, or further the work.
- C. Technical Plan:** Outline and address technical challenges inherent in the approach and possible solutions for overcoming potential problems. This section should provide appropriate measurable milestones (quantitative if possible) at intermediate stages of the program to demonstrate progress and a plan for achieving the milestones. The technical plan should demonstrate a deep understanding of the technical challenges and present a credible (even if risky) plan to achieve the program goal. Discuss mitigation of technical risk.
- D. Management Plan:** Provide a summary of expertise of the team, including any subcontractors, and key personnel who will be doing the work. A Principal Investigator (PI) for the project must be identified, along with a description of the team organization, including the breakdown by technical area. All teams are strongly encouraged to identify a Project Manager/Integrator to serve as the primary point of contact to communicate with the DARPA Program Manager, IV&V partner, and Contracting Officer's Representative, coordinate the effort across co-performer, vendor, and subcontractor teams, organize regular performer meetings or discussions, facilitate data sharing, and ensure timely completion of milestones and deliverables.

Provide a clear description of the team's organization including an organization chart that includes, as applicable: the programmatic relationship of team members; the unique capabilities of team members; the task responsibilities of team members, the teaming strategy among the team members; and key personnel with the amount of effort to be expended by each person during each year. Provide a detailed plan for coordination, including explicit guidelines for interaction among collaborators/subcontractors of the proposed effort. Include risk management approaches. Describe any formal teaming agreements that are required to execute this program.

- E. Capabilities:** Describe organizational experience in relevant subject area(s), existing intellectual property, specialized facilities, and any Government-furnished materials or

information. Describe any specialized facilities to be used as part of the project, the extent of access to these facilities, and any biological containment, biosafety, and certification requirements. Discuss any work in closely related research areas and previous accomplishments.

- F. Statement of Work (SOW) (does not count towards page limit):** The SOW should provide a detailed task breakdown, citing specific tasks for each technical area, and their connection to the milestones and program metrics. Each phase of the program should be separately defined. The SOW must not include proprietary information. It is encouraged, though not required, to use the SOW template provided as **Attachment 2**. The SOW is not included in the Volume 1 page count.

For each task/subtask, provide:

- A detailed description of the approach to be taken to accomplish each defined task/subtask.
- Identification of the primary organization responsible for task execution (prime contractor, subcontractor(s), consultant(s), by name).
- A measurable milestone, i.e., a deliverable, demonstration, or other event/activity that marks task completion. Include completion dates for all milestones. Include quantitative metrics.
- A definition of all deliverables (e.g., data, reports, software) to be provided to the Government in support of the proposed tasks/subtasks.

NOTE: It is recommended that the SOW be developed so that each technical area and Phase of the program is separately defined.

Do not include any proprietary information in the SOW.

- G. Schedule and Milestones:** Provide a detailed schedule showing tasks (task name, duration, work breakdown structure element as applicable, performing organization), milestones, and the interrelationships among tasks. The task structure must be consistent with that in the SOW. Measurable milestones should be clearly articulated and defined in time relative to the start of the project. It is encouraged, though not required, to use the Gantt Chart template provided as **Attachment 3**.
- H. Commercialization Plan:** It is envisioned that the selected work will lead to both new therapeutics and transformative tools for therapeutic development, both with commercial potential. For this reason, DARPA strongly encourages proposers responding to this topic to provide relevant cost share, especially in Phase III of the program, and to document these contributions. Provide information regarding the types of partners (e.g., government, private industry) that will be pursued and submit a timeline with incremental milestones toward successful engagement. Proposers

interested in the EEI program should reflect that interest in their commercialization plan in addition to including it in their SOW and cost proposal. The plan should include a description of how DARPA will be included in the development of potential technology transfer relationships. If the Commercialization Plan includes the formation of a start-up company, a business development strategy must also be provided.

a. Volume II, Cost Management Proposal

Cover Sheet (LABELED “PROPOSAL: VOLUME II”):

1. BAA Number (HR001120S0052);
2. Lead organization submitting proposal;
3. Type of organization, selected among the following categories: “LARGE BUSINESS”, “SMALL DISADVANTAGED BUSINESS”, “OTHER SMALL BUSINESS”, “HBCU”, “MI”, “OTHER EDUCATIONAL”, OR “OTHER NONPROFIT”;
4. Proposer’s reference number (if any);
5. Other team members (if applicable) and type of business for each;
6. Proposal title;
7. Technical point of contact (Program Manager or Principal Investigator) to include: salutation, last name, first name, street address, city, state, zip code, telephone, fax (if available), electronic mail (if available);
8. Administrative point of contact (Contracting Officer or Award Officer) to include: salutation, last name, first name, street address, city, state, zip code, telephone, fax (if available), and electronic mail (if available);
9. Award instrument requested: cost-plus-fixed-fee (CPFF), cost-contract—no fee, cost sharing contract – no fee, or other type of procurement contract (*specify*), cooperative agreement, or other transaction;
10. Place(s) of performance, including all subcontractors and consultants;
11. Period of performance;
12. Total proposed cost separated by Task Area and Phase (as defined in Figure 1), and the amount of any cost share (if any);
13. Name, address, and telephone number of the proposer’s cognizant Defense Contract Management Agency (DCMA) administration office (*if known*);
14. Name, address, and telephone number of the proposer’s cognizant Defense Contract Audit Agency (DCAA) audit office (*if known*);
15. Date proposal was prepared;
16. Data Universal Numbering System (DUNS) number (<http://www.dnb.com/get-a-duns-number.html>);
17. Taxpayer ID number (<https://www.irs.gov/Individuals/International-Taxpayers/Taxpayer-Identification-Numbers-TIN>);

18. Commercial and Government Entity (CAGE) code
(<https://cage.dla.mil/Home/UsageAgree>);
19. Proposal validity period

The Government strongly encourages that proposers use the provided MS Excel™ cost proposal spreadsheet (Attachment 4) in the development of their cost proposals. All tabs and tables in MS Excel™ cost proposal spreadsheet should be developed in an editable format with calculation formulas intact to allow traceability of the cost proposal numbers across the spreadsheet. This MS Excel™ cost proposal spreadsheet should be used by the prime organization and all subcontractors. In addition to using the MS Excel™ cost proposal spreadsheet, Volume II still must include all other items discussed below that are not covered by the editable spreadsheet. Subcontractor MS Excel™ cost proposal spreadsheets may be submitted directly to the Government by the proposed subcontractor via e-mail to the address in Part I of this BAA. Using the provided MS Excel™ cost proposal spreadsheet will assist the Government in a rapid analysis of your proposed costs and, if your proposal is selected for award, speed up the negotiation and award execution process.

- (1) Total program, per phase (Phase I (Base), Phase II (Option)) and per task cost broken down by major cost items to include:
 - i. **Direct labor** – provide an itemized breakout of all personnel, listed by name or TBD, with labor rate (or salary), labor hours (or percent effort), and labor category. All senior personnel must be identified by name.
 - ii. **Materials and Supplies** – itemized list, which includes description of material, quantity, unit price, and total price. If a material factor is used based on historical purchases, provide data to justify the rate.
 - iii. **Equipment** – itemized list, which includes description of equipment, unit price, quantity, and total price. Any equipment item with a unit price over \$5,000 must include a vendor quote.
 - iv. **Animal Use Costs** – itemized list of all materials, animal purchases, and per diem costs, associated with proposed animal use; include documentation supporting daily rates.
 - v. **Travel** – provide an itemized list of travel costs to include purpose of trips, departure and arrival destinations, projected airfare, rental car and GSA approved per diem, number of travelers, number of days); provide screenshots from travel website for proposed airfare and rental car, as applicable; provide screenshot or web link for conference registration fee and note if the fee includes hotel cost. Conference attendance must be justified, explain how it is in the best interest of the project. **Plan for two (2) DARPA program review meetings per year.**
 - vi. **Other Direct Costs (e.g., computer support, clean room fees)** – Should be itemized with costs or estimated costs. Backup documentation and/or a supporting cost breakdown is required to support proposed costs with a unit price over \$5,000. An explanation of any estimating factors, including their derivation and application, must be provided. Please include a brief description of the proposers' procurement method to be used.

- vii. **Other Direct Costs** – Consultants: provide executed Consultant Agreement that describes work scope, rate and hours.
 - viii. **Indirect costs** including, as applicable, fringe benefits, overhead, General and Administrative (G&A) expense, and cost of money (see university vs. company specific requirements below).
 - ix. **Indirect costs specific to a University performer:** (1) **Fringe Benefit Rate** (provide current Department of Health and Human Services (DHHS) or Office of Naval Research (ONR) negotiated rate package; if calculated by other than a rate, provide University documentation identifying fringe costs by position or HR documentation if unique to each person); (2) **F&A Indirect Overhead Rate** (provide current DHHS or ONR negotiated rate package); (3) **Tuition Remission** (provide current University documentation justifying per student amount); and (4) **Health Insurance/Fee** (provide current University documentation justifying per student amount, if priced separately from fringe benefits with calculations included in the EXCEL cost file).
 - x. **Indirect costs specific to a Company performer:** (1) **Fee/Profit** (provide rationale for proposed fee/profit percentage using criteria found in DFARS 215.404-70); and (2) **Fringe Benefit/Labor OH/Material OH/G&A Rates** (provide current Forwarding Pricing Rate Proposal (FPRP) or DCMA/DCAA Forward Pricing Rate Recommendation or Agreement (FPRR or FPRA). If these documents are not available, provide company historical data, preferably two years, minimum of one, to include both pool and expense costs used to generate the rates).
- (2) A summary of total program costs by Phase I, II, and III and task.
 - (3) An itemization of Subcontracts. All subcontractor cost proposal documentation must be prepared at the same level of detail as that required of the prime. Subcontractor proposals should include Interdivisional Work Transfer Agreements (IWTA) or evidence of similar arrangements (an IWTA is an agreement between multiple divisions of the same organization). The prime proposer is responsible for compiling and providing all subcontractor proposals for the Procuring Contracting Officer (PCO). The proposal must show how subcontractor costs are applied to each phase and task. If consultants are to be used, proposer must provide consultant agreement or other document that verifies the proposed loaded daily/hourly rate.
 - (4) An itemization of any information technology (IT) purchase (including a letter stating why the proposer cannot provide the requested resources from its own funding), as defined in FAR Part 2.101.
 - (5) A summary of projected funding requirements by month for all phases of the project.
 - (6) A summary of tasks that have animal or human use funding.
 - (7) The source, nature, and amount of any industry cost-sharing. Where the effort consists of multiple portions that could reasonably be partitioned for purposes of funding, these should be identified as options with separate cost estimates for each.

- (8) Identification of pricing assumptions of which may require incorporation into the resulting award instrument (e.g., use of Government Furnished Property/Facilities/Information, access to Government Subject Matter Expert/s, etc.).
- (9) Any Forward Pricing Rate Agreement, DHHS rate agreement, other such approved rate information, or such documentation that may assist in expediting negotiations (if available).
- (10) Proposers with a Government acceptable accounting system who are proposing a cost-type contract must submit the DCAA document approving the cost accounting system.

Per FAR 15.403-4, certified cost or pricing data shall be required if the proposer is seeking a procurement contract award per the referenced threshold, unless the proposer requests and is granted an exception from the requirement to submit cost or pricing data. Certified cost or pricing data” are not required if the proposer proposes an award instrument other than a procurement contract (e.g., a grant, cooperative agreement, or other transaction.)

Subawardee Proposals

The awardee is responsible for compiling and providing all subawardee proposals for the Procuring Contracting Officer (PCO)/Grants Officer (GO)/Agreements Officer (AO), as applicable. Subawardee proposals should include Interdivisional Work Transfer Agreements (ITWA) or similar arrangements. Where the effort consists of multiple portions that could reasonably be partitioned for purposes of funding, these should be identified as options with separate cost estimates for each.

All proprietary subawardee proposal documentation, prepared at the same level of detail as that required of the awardee’s proposal and which cannot be uploaded with the proposed awardee’s proposal, shall be provided to the Government either by the awardee or by the subawardee organization when the proposal is submitted. Subawardee proposals submitted to the Government by the proposed subawardee should be submitted via e-mail to the address in Section I.

Other Transaction Requests

All proposers requesting an OT must include a detailed list of milestones for each phase of the program (I and II). Each milestone must include the following:

- milestone description,
- completion criteria,
- due date, and
- payment/funding schedule (to include, if cost share is proposed, awardee and Government share amounts).

It is noted that, at a minimum, milestones should relate directly to accomplishment of program technical metrics as defined in the BAA and/or the proposer’s proposal. Agreement type, expenditure or fixed-price based, will be subject to negotiation by the Agreements Officer. Do not include proprietary data.

4.2.3. ADDITIONAL PROPOSAL INFORMATION

Proprietary Markings

Proposers are responsible for clearly identifying proprietary information. Submissions containing proprietary information must have the cover page and each page containing such information clearly marked with a label such as “Proprietary” or “Company Proprietary.” NOTE: “Confidential” is a classification marking used to control the dissemination of U.S. Government National Security Information as dictated in Executive Order 13526 and should not be used to identify proprietary business information.

Unclassified Submissions

DARPA anticipates that submissions received under this BAA will be unclassified. However, should a proposer wish to submit classified information, an *unclassified* e-mail must be sent to the BAA mailbox requesting submission instructions from the Technical Office Program Security Officer (PSO). If a determination is made that the award instrument may result in access to classified information, a Security Classification Guide (SCG) and/or DD Form 254 will be issued by DARPA and attached as part of the award.

Disclosure of Information and Compliance with Safeguarding Covered Defense Information Controls

The following provisions and clause apply to all solicitations and contracts; however, the definition of “controlled technical information” clearly exempts work considered fundamental research and therefore, even though included in the contract, will not apply if the work is fundamental research.

DFARS 252.204-7000, “Disclosure of Information”

DFARS 252.204-7008, “Compliance with Safeguarding Covered Defense Information Controls”

DFARS 252.204-7012, “Safeguarding Covered Defense Information and Cyber Incident Reporting”

The full text of the above solicitation provision and contract clauses can be found at <http://www.darpa.mil/work-with-us/additional-baa#NPRPAC>.

Compliance with the above requirements includes the mandate for proposers to implement the security requirements specified by National Institute of Standards and Technology (NIST) Special Publication (SP) 800-171, “Protecting Controlled Unclassified Information in Nonfederal Information Systems and Organizations” (see <https://doi.org/10.6028/NIST.SP.800-171r1>) that are in effect at the time the BAA is issued.

For awards where the work is considered fundamental research, the contractor will not have to implement the aforementioned requirements and safeguards. However, should the nature of the work change during performance of the award, work not considered fundamental research will be subject to these requirements.

Human Subjects Research (HSR)/Animal Use

Proposers that anticipate involving human subjects or animals in the proposed research must comply with the approval procedures detailed at <http://www.darpa.mil/work-with-us/additional-baa>, to include providing the information specified therein as required for proposal submission.

Approved Cost Accounting System Documentation

Proposers that do not have a Cost Accounting Standards (CAS) compliant accounting system considered adequate for determining accurate costs that are negotiating a cost-type procurement contract must complete an SF 1408. For more information on CAS compliance, see <http://www.dcaa.mil/cas.html>. To facilitate this process, proposers should complete the SF 1408 found at <http://www.gsa.gov/portal/forms/download/115778> and submit the completed form with the proposal.

Small Business Subcontracting Plan

Pursuant to Section 8(d) of the Small Business Act (15 U.S.C. § 637(d)) and FAR 19.702(a)(1), each proposer who submits a contract proposal and includes subcontractors might be required to submit a subcontracting plan with their proposal. The plan format is outlined in FAR 19.704.

Section 508 of the Rehabilitation Act (29 U.S.C. § 749d)/FAR 39.2

All electronic and information technology acquired or created through this BAA must satisfy the accessibility requirements of Section 508 of the Rehabilitation Act (29 U.S.C. § 749d)/FAR 39.2.

Intellectual Property

All proposers must provide a good-faith representation that the proposer either owns or possesses the appropriate licensing rights to all intellectual property that will be utilized under the proposed effort.

(1) For Procurement Contracts

Proposers responding to this BAA requesting procurement contracts will need to complete the certifications at DFARS 252.227-7017. See <http://www.darpa.mil/work-with-us/additional-baa> for further information. If no restrictions are intended, the proposer should state “none.” The table below captures the requested information:

Technical Data Computer Software To be Furnished With Restrictions	Summary of Intended Use in the Conduct of the Research	Basis for Assertion	Asserted Rights Category	Name of Person Asserting Restrictions
(LIST)	(NARRATIVE)	(LIST)	(LIST)	(LIST)

(2) For All Non-Procurement Contracts

Proposers responding to this BAA requesting a Cooperative Agreement, Technology Investment Agreement, or Other Transaction for Prototypes shall follow the applicable rules and regulations governing these various award instruments, but in all cases, 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. Proposers are encouraged to use a format similar to that described in the section above. If no restrictions are intended, then the proposer should state "NONE."

System for Award Management (SAM) and Universal Identifier Requirements

All proposers must be registered in SAM unless exempt per FAR 4.1102. FAR 52.204-7, "System for Award Management" and FAR 52.204-13, "System for Award Management Maintenance" are incorporated into this BAA. See <http://www.darpa.mil/work-with-us/additional-baa> for further information.

International entities can register in SAM by following the instructions in this link:

https://www.fsd.gov/fsd-gov/answer.do?sysparm_kbid=dbf8053adb119344d71272131f961946&sysparm_search=KB0013221.

4.2.4. SUBMISSION INFORMATION

DARPA will acknowledge receipt of all submissions and assign an identifying control number that should be used in all further correspondence regarding the submission. DARPA intends to use electronic mail correspondence regarding HR001120S0052. Submissions may not be sent by fax or e-mail; any so sent will be disregarded.

Submissions will not be returned. An electronic copy of each submission received will be retained at DARPA, and all other non-required copies destroyed. A certification of destruction may be requested, provided the formal request is received by DARPA within five (5) business days after notification that a proposal was not selected.

For abstract and proposal submission dates, see Part I., Overview Information. Submissions received after these dates and times may not be reviewed.

Abstracts and Full Proposals sent in response to HR001120S0052 may be submitted via DARPA's BAA Website (<https://baa.darpa.mil>). Visit the website to complete the two-step registration process. Submitters will need to register for an Extranet account (via the form at the URL listed above) and wait for two separate e-mails containing a username and temporary password. After accessing the Extranet, submitters may then create an account for the DARPA BAA website (via the "Register your Organization" link along the left side of the homepage), view submission instructions, and upload/finalize the abstract. Proposers using the DARPA BAA Website may encounter heavy traffic on the submission deadline date; it is highly advised that submission process be started as early as possible.

All unclassified concepts submitted electronically through DARPA's BAA Website must be uploaded as zip files (.zip or .zipx extension). The final zip file should be no greater than 50 MB in size. Only one zip file will be accepted per submission. Classified submissions and proposals requesting or cooperative agreements should NOT be submitted through DARPA's BAA Website (<https://baa.darpa.mil>), though proposers will likely still need to visit <https://baa.darpa.mil> to register their organization (or verify an existing registration) to ensure the BAA office can verify and finalize their submission.

Technical support for BAA Website may be reached at BAAT_Support@darpa.mil, and is typically available during regular business hours, (9:00 AM - 5:00 PM EST Monday - Friday).

Proposers using the DARPA BAA Website may encounter heavy traffic on the submission deadline date; it is highly advised that the submission process be started as early as possible.

For Cooperative Agreements only:

Proposers requesting cooperative agreements must submit proposals through one of the following methods: (1) electronic upload per the instructions at <https://www.grants.gov/applicants/apply-for-grants.html>; or (2) hard-copy mailed directly to DARPA. If proposers intend to use Grants.gov as their means of submission, then they must submit their entire proposal through Grants.gov; applications cannot be submitted in part to Grants.gov and in part as a hard-copy. Proposers using Grants.gov do not submit hard-copy proposals in addition to the Grants.gov electronic submission.

Submissions: Proposers must submit the three forms listed below.

Form 1: SF 424 Research and Related (R&R) Application for Federal Assistance, available on the Grants.gov website at https://apply07.grants.gov/apply/forms/sample/RR_SF424_2_0-V2.0.pdf. This form must be completed and submitted.

To evaluate compliance with Title IX of the Education Amendments of 1972 (20 U.S.C. § 1681 et seq.), the Department of Defense (DoD) is collecting certain demographic and career information to be able to assess the success rates of women who are proposed for key roles in applications in science, technology, engineering or mathematics disciplines. In addition, the National Defense Authorization Act (NDAA) for FY 2019, Section 1286, directs the Secretary of Defense to protect intellectual property, controlled information, key personnel, and information about critical technologies relevant to national security and limit undue influence, including foreign talent programs by countries that desire to exploit United States' technology within the DoD research, science and technology, and innovation enterprise. This requirement is necessary for all research and research-related educational activities. The DoD is using the two forms below to collect the necessary information to satisfy these requirements. Detailed instructions for each form are available on Grants.gov.

The Research and Related Senior/Key Person Profile (Expanded) form will be used to collect the following information for all senior/key personnel, including Project Director/Principal

Investigator and Co-Project Director/Co-Principal Investigator, whether or not the individuals' efforts under the project are funded by the DoD:

- Degree Type and Degree Year.
- Current and Pending Support, including:
 - A list of all current projects the individual is working on, in addition to any future support the individual has applied to receive, regardless of the source.
 - Title and objectives of the other research projects.
 - The percentage per year to be devoted to the other projects.
 - The total amount of support the individual is receiving in connection to each of the other research projects or will receive if other proposals are awarded.
 - Name and address of the agencies and/or other parties supporting the other research projects
 - Period of performance for the other research projects.

Additional senior/key persons can be added by selecting the “Next Person” button at the bottom of the form. Note that, although applications without this information completed may pass Grants.gov edit checks, if DARPA receives an application without the required information, DARPA may determine that the application is incomplete and may cause your submission to be rejected and eliminated from further review and consideration under the BAA. DARPA reserves the right to request further details from the applicant before making a final determination on funding the effort.

Form 2: Research and Related Senior/Key Person Profile (Expanded), available on the Grants.gov website at https://apply07.grants.gov/apply/forms/sample/RR_KeyPersonExpanded_2_0-V2.0.pdf. This form must be completed and submitted.

Form 3: Research and Related Personal Data, available on the Grants.gov website at https://apply07.grants.gov/apply/forms/sample/RR_PersonalData_1_2-V1.2.pdf. Each applicant must complete the name field of this form, however, provision of the demographic information is voluntary. Regardless of whether the demographic fields are completed or not, this form must be submitted with at least the applicant's name completed.

Grants.gov Submissions: Grants.gov requires proposers to complete a one-time registration process before a proposal can be electronically submitted. First-time registration can take between three (3) business days and four (4) weeks. For more information about registering for Grants.gov, see <http://www.darpa.mil/work-with-us/additional-baa>.

Proposal abstracts will not be accepted if submitted via Grants.gov.

Hard-copy Submissions: Proposers electing to submit cooperative agreement proposals as hard copies must complete the SF 424 R&R form (Application for Federal Assistance,) available on the Grants.gov website (https://apply07.grants.gov/apply/forms/sample/SF424_2_1-V2.1.pdf).

Failure to comply with the submission procedures may result in the submission not being evaluated. DARPA will acknowledge receipt of complete submissions via e-mail and assign control numbers that should be used in all further correspondence regarding proposals.

4.3. FUNDING RESTRICTIONS

Not applicable.

4.4. OTHER SUBMISSION INFORMATION

DARPA will post a consolidated Frequently Asked Questions (FAQ) document. To access the posting go to <http://www.darpa.mil/work-with-us/opportunities>. A link to the FAQ will appear under the HR001120S0052 summary. Submit your question(s) via e-mail to HEALR@darpa.mil.

5. Application Review Information

5.1. EVALUATION CRITERIA

Proposals will be evaluated using the following criteria, listed in descending order of importance:

5.1.1 Overall Scientific and Technical Merit; 5.1.2 Potential Contribution and Relevance to the DARPA Mission; and 5.1.3 Cost Realism.

5.1.1. OVERALL SCIENTIFIC AND TECHNICAL MERIT

The proposed technical approach is innovative, feasible, achievable, and complete.

The proposed technical team has the expertise and experience to accomplish the proposed tasks.

Task descriptions and associated technical elements provided are complete and in a logical sequence with all proposed deliverables clearly defined such that a final outcome that achieves the goal can be expected as a result of award. The proposal identifies major technical risks and planned mitigation efforts are clearly defined and feasible.

5.1.2. POTENTIAL CONTRIBUTION AND RELEVANCE TO THE DARPA MISSION

The potential contributions of the proposed effort are relevant to the national technology base. Specifically, DARPA's mission is to make pivotal early technology investments that create or prevent strategic surprise for U.S. National Security.

The proposed Commercialization and Technology Transfer plan is feasible, achievable, and identifies potential partners with the necessary expertise and experience. **This includes considering the extent to which any proposed intellectual property restrictions will potentially impact the Government's ability to transition the technology.**

5.1.3. COST REALISM

The proposed costs are realistic for the technical and management approach and accurately reflect the technical goals and objectives of the solicitation. The proposed costs are consistent with the proposer's Statement of Work and reflect a sufficient understanding of the costs and level of effort needed to successfully accomplish the proposed technical approach. The costs for the prime proposer and proposed subawardees are substantiated by the details provided in the proposal (e.g., the type and number of labor hours proposed per task, the types and quantities of materials, equipment and fabrication costs, travel and any other applicable costs and the basis for the estimates).

It is expected that the effort will leverage all available relevant prior research in order to obtain the maximum benefit from the available funding. For efforts with a likelihood of commercial application, appropriate direct cost sharing may be a positive factor in the evaluation. DARPA recognizes that undue emphasis on cost may motivate proposers to offer low-risk ideas with minimum uncertainty and to staff the effort with junior personnel in order to be in a more competitive posture. DARPA discourages such cost strategies.

5.2. REVIEW OF PROPOSALS

Review Process

It is the policy of DARPA to ensure impartial, equitable, comprehensive proposal evaluations based on the evaluation criteria listed in Section V.A. and to select the source (or sources) whose offer meets the Government's technical, policy, and programmatic goals.

DARPA will conduct a scientific/technical review of each conforming proposal. Conforming proposals comply with all requirements detailed in this BAA; proposals that fail to do so may be deemed non-conforming and may be removed from consideration. Proposals will not be evaluated against each other since they are not submitted in accordance with a common work statement. DARPA's intent is to review proposals as soon as possible after they arrive; however, proposals may be reviewed periodically for administrative reasons.

Award(s) will be made to proposers whose proposals are determined to be the most advantageous to the Government, consistent with instructions and evaluation criteria specified in the BAA herein, and availability of funding.

Handling of Source Selection Information

DARPA policy is to treat all submissions as source selection information (see FAR 2.101 and 3.104) and to disclose their contents only for the purpose of evaluation. Restrictive notices notwithstanding, during the evaluation process, submissions may be handled by support contractors for administrative purposes and/or to assist with technical evaluation. All DARPA support contractors performing this role are expressly prohibited from performing DARPA-sponsored technical research and are bound by appropriate nondisclosure agreements.

Subject to the restrictions set forth in FAR 37.203(d), input on technical aspects of the proposals may be solicited by DARPA from non-Government consultants/experts who are strictly bound by the appropriate nondisclosure requirements.

Federal Awardee Performance and Integrity Information (FAPIIS)

Per 41 U.S.C. § 2313, as implemented by FAR 9.103 and 2 CFR § 200.205, prior to making an award above the simplified acquisition threshold, DARPA is required to review and consider any information available through the designated integrity and performance system (currently FAPIIS). Awardees have the opportunity to comment on any information about themselves entered in the database, and DARPA will consider any comments, along with other information in FAPIIS or other systems prior to making an award.

6. Award Administration Information

6.1. SELECTION NOTICES

6.1.1. PROPOSAL ABSTRACTS

6.1.2. FULL PROPOSALS

As soon as the evaluation of all proposals is complete, the proposer will be notified that (1) the proposal has been selected for funding pending award negotiations, in whole or in part, or (2) the proposal has not been selected. These official notifications will be sent via e-mail to the Technical POC and Administrative POC identified on the proposal coversheet.

6.2. ADMINISTRATIVE AND NATIONAL POLICY REQUIREMENTS

6.2.1. MEETING AND TRAVEL REQUIREMENTS

There will be a program kickoff meeting in the Arlington, VA vicinity, and all key participants are required to attend. Performers should also anticipate regular program-wide PI meetings and periodic site visits at the Program Manager's discretion in the Arlington, VA vicinity. Proposers shall include within the content of their proposal the details and costs of any travel or meetings they deem to be necessary throughout the course of the effort, to include periodic status reviews by the government.

6.2.2. FAR and DFARS Clauses

Solicitation clauses in the FAR and DFARS relevant to procurement contracts and FAR and DFARS clauses that may be included in any resultant procurement contracts are incorporated herein and can be found at <http://www.darpa.mil/work-with-us/additional-baa>.

6.2.3. Controlled Unclassified Information (CUI) on Non-DoD Information Systems

Further information on Controlled Unclassified Information on Non-DoD Information Systems is incorporated herein can be found at <http://www.darpa.mil/work-with-us/additional-baa>.

6.2.4. REPRESENTATIONS AND CERTIFICATIONS

In accordance with FAR 4.1102 and 4.1201, proposers requesting a procurement contract must complete electronic annual representations and certifications at <https://www.sam.gov/>. In addition, resultant procurement contracts will require supplementary DARPA-specific representations and certifications. See <http://www.darpa.mil/work-with-us/additional-baa> for further information.

6.2.5. TERMS AND CONDITIONS

For terms and conditions specific to grants and/or cooperative agreements, see the DoD General Research Terms and Conditions (latest version) at <http://www.onr.navy.mil/Contracts-Grants/submit-proposal/grants-proposal/grants-terms-conditions> and the supplemental DARPA-specific terms and conditions at <http://www.darpa.mil/work-with-us/contract-management#GrantsCooperativeAgreements>.

6.3. REPORTING

The number and types of reports will be specified in the award document but will include, at a minimum, monthly financial status reports, monthly technical status reports, annual reports, and an end-of-phase report. The reports shall be prepared and submitted in accordance with the procedures contained in the award document and mutually agreed on before award. Reports and briefing material will also be required, as appropriate, to document progress in accomplishing program metrics. A Final Report that summarizes the project and tasks will be required at the conclusion of the performance period for the award, notwithstanding the fact the research may be continued under a follow-on vehicle.

6.4. ELECTRONIC SYSTEMS

6.4.1. WIDE AREA WORK FLOW (WAWF)

Performers will be required to submit invoices for payment directly to <https://wawf.eb.mil>, unless an exception applies. Performers must register in WAWF prior to any award under this BAA.

6.4.2. I-EDISON

The award document for each proposal selected for funding will contain a mandatory requirement for patent reports and notifications to be submitted electronically through i-Edison (<http://public.era.nih.gov/iedison>).

7. Agency Contacts

Administrative, technical or contractual questions should be sent via e-mail to the mailbox listed below.

Points of Contact

The BAA Coordinator for this effort may be reached at:

HEALR@darpa.mil

DARPA/BTO

ATTN: HR001120S0052

675 North Randolph Street

Arlington, VA 22203-2114

For information concerning agency level protests see <http://www.darpa.mil/work-with-us/additional-baa#NPRPAC>.

8. Other Information

DARPA will host a Proposers Day in support of the HEALR program on June 30, 2020 via webcast. The purpose is to provide potential proposers with information on the HEALR program, promote additional discussion on this topic, address questions, provide a forum to present their capabilities, and encourage team formation.

Interested proposers are not required to attend in order to respond to the HEALR BAA, and relevant information and materials discussed at Proposers Day will be made available to all potential proposers in the form of a FAQ posted on the DARPA Opportunities Page.

An online registration form and various other meeting details can be found at the registration website, <http://events.sa-meetings.com/HEALRProposersDay>.

Participants are required to register no later than **June 26, 2020**. This event is not open to the Press. The Proposers Day will be open to members of the public who have registered in advance for the event; there will be no onsite registration.

Proposers Day Point of Contact:

DARPA-SN-20-51@darpa.mil

ATTN: DARPA-SN-20-51

9. APPENDIX 1 – Volume II checklist

**Volume II, Cost Proposal
Checklist and Sample Templates**

The following checklist and sample templates are provided to assist the proposer in developing a complete and responsive cost volume. Full instructions appear in Section 4.2.2 of HR001120S0052. This worksheet must be included with the coversheet of the Cost Proposal.

1. Are all items from Section 4.2.2 (Volume II, Cost Proposal) of **HR001120S0052** included on your Cost Proposal cover sheet?

☐ **YES** ☐ **NO** **Appears on Page(s)** [Type text]

If reply is “No”, please explain:

2. Does your Cost Proposal include (1) a summary cost buildup by Phase, (2) a summary cost buildup by Year, and (3) a detailed cost buildup of for each Phase that breaks out each task and shows the cost per month?

☐ **YES** ☐ **NO** **Appears on Page(s)** [Type text]

If reply is “No”, please explain:

3. Does your cost proposal (detailed cost buildup #3 above in item 2) show a breakdown of the major cost items listed below:

Direct Labor (Labor Categories, Hours, Rates)

☐ **YES** ☐ **NO** **Appears on Page(s)** [Type text]

Indirect Costs/Rates (i.e., overhead charges, fringe benefits, G&A)

☐ **YES** ☐ **NO** **Appears on Page(s)** [Type text]

Materials and/or Equipment

☐ **YES** ☐ **NO** **Appears on Page(s)** [Type text]

Subcontracts/Consultants

☐ **YES** ☐ **NO** **Appears on Page(s)** [Type text]

Other Direct Costs

☐ **YES** ☐ **NO** **Appears on Page(s)** [Type text]

Travel

☐ **YES** ☐ **NO** **Appears on Page(s)** [Type text]

If reply is “No”, please explain:

4. Have you provided documentation for proposed costs related to travel, to include purpose of trips, departure and arrival destinations and sample airfare?
- ☐ YES ☐ NO **Appears on Page(s)** [Type text]

If reply is "No", please explain:

5. Does your cost proposal include a complete itemized list of all material and equipment items to be purchased (a priced bill-of-materials (BOM))?
- ☐ YES ☐ NO **Appears on Page(s)** [Type text]

If reply is "No", please explain:

6. Does your cost proposal include vendor quotes or written engineering estimates (basis of estimate) for all material and equipment with a unit price exceeding \$5000?
- ☐ YES ☐ NO **Appears on Page(s)** [Type text]

If reply is "No", please explain:

7. Does your cost proposal include a clear justification for the cost of labor (written labor basis-of-estimate (BOE)) providing rationale for the labor categories and hours proposed for each task?
- ☐ YES ☐ NO **Appears on Page(s)** [Type text]

If reply is "No", please explain:

8. Do you have subcontractors/consultants? If YES, continue to question 9. If NO, skip to question 13.
- ☐ YES ☐ NO **Appears on Page(s)** [Type text]

9. Does your cost proposal include copies of all subcontractor/consultant technical (to include Statement of Work) and cost proposals?
- ☐ YES ☐ NO **Appears on Page(s)** [Type text]

If reply is "No", please explain:

10. Do all subcontract proposals include the required summary buildup, detailed cost buildup, and supporting documentation (SOW, Bill-of-Materials, Basis-of-Estimate, Vendor Quotes, etc.)?
- ☐ YES ☐ NO **Appears on Page(s)** [Type text]

If reply is "No", please explain:

11. Does your cost proposal include copies of consultant agreements, if available?
○ YES ○ NO **Appears on Page(s)** [Type text]

If reply is “No”, please explain:

12. If requesting a FAR-based contract, does your cost proposal include a tech/cost analysis for all proposed subcontractors?
○ YES ○ NO **Appears on Page(s)** [Type text]

If reply is “No”, please explain:

13. Have all team members (prime and subcontractors) who are considered a Federally Funded Research & Development Center (FFRDC), included documentation that clearly demonstrates work is not otherwise available from the private sector AND provided a letter on letterhead from the sponsoring organization citing the specific authority establishing their eligibility to propose to government solicitations and compete with industry, and compliance with the associated FFRDC sponsor agreement and terms and conditions.
○ YES ○ NO **Appears on Page(s)** [Type text]

If reply is “No”, please explain:

14. Does your proposal include a response regarding Organizational Conflicts of Interest?
○ YES ○ NO **Appears on Page(s)** [Type text]

If reply is “No”, please explain:

15. Does your proposal include a completed Data Rights Assertions table/certification?
○ YES ○ NO **Appears on Page(s)** [Type text]

If reply is “No”, please explain: