Broad Agency Announcement

Cornerstone

BIOLOGICAL TECHNOLOGIES OFFICE

HR001122S0022

June 2, 2022

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- **Federal Agency Name –** Defense Advanced Research Projects Agency (DARPA), Biological Technologies Office (BTO)
- **Funding Opportunity Title –** Cornerstone
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  - Proposal Abstract Due Date and Time: **June 30, 2022, 4:00 PM ET**
  - Full Proposal Due Date and Time: **August 18, 2022, 4:00 PM ET**
  - BAA Closing Date: **August 18, 2022**
- **Concise description of the funding opportunity:** The Cornerstone program will develop safe and effective Integrated Countermeasures (i.e., countermeasure and delivery system) to prevent brain injury. Military personnel face a high risk of traumatic brain injury (TBI), resulting in a debilitating long-term burden both to the person as well as the healthcare infrastructure. At this time, no treatments for TBI have progressed past Phase II clinical trials. Cornerstone will improve mission execution and warfighter protection by addressing this gap. Cornerstone will consist of two technical areas: (TA1) Identify, optimize, and validate prophylactic countermeasures that prevent relevant targets at sites of injury from initiating injury response(s) to kinetic injury (e.g., blast); and (TA2) Develop clinically relevant spatial and temporal delivery of countermeasures. Ultimately, the development of prophylactic therapeutics that prevent injury by blocking the initiation of harmful signaling [initiating at the sites of injury] will sustain warfighter readiness and facilitate a strategic, operational, and tactical advantage.
- **Anticipated individual awards –** Multiple awards are anticipated.
- **Types of instruments that may be awarded –** Procurement contract or other transaction agreements for prototypes.
- **Agency contact**

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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 C.F.R. § 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) is soliciting innovative proposals to address the development of safe and effective Integrated Countermeasures (i.e., delivery system and countermeasure) to prevent brain injury. Research will be focused on the following areas: (1) Identification, optimization, and validation of prophylactic countermeasures that prevent energetically responsive receptors (i.e., targets) from initiating injury response(s) to kinetic insult(s) inclusive of blast or impact; and (2) Development of Integrated Countermeasures with precise delivery (i.e., spatial and temporal control). Proposed research should investigate approaches that enable revolutionary advances in the prevention of traumatic brain injury (TBI). Proposed approaches should investigate the prevention of the initiation of harmful signaling cascades at sites of injury, for example, in the central and/or peripheral nervous systems (CNS, PNS) and/or vasculature, and develop countermeasures that can be administered prophylactically (i.e., before exposure) to prevent behavioral or cognitive deficit from TBI. By program completion, Cornerstone's Integrated Countermeasures will be capable of instantaneous (seconds post-exposure) protection for the operator against Department of Defense (DoD)-relevant kinetic injury, both from a molecular cascade standpoint, and cognitive and behavioral effect.

Specifically excluded is research that involves:

1. Genetic manipulation of the host in order to aid target engagement or achieve altered downstream signaling as a countermeasure.
2. Sole use of *in vitro* or *in vivo* model systems that are not accepted as representative of kinetic (e.g., blast or impact) injury modes.
3. Treatment strategies focused on interventions delivered beyond five seconds post-injury, with preference for pretreatment-based countermeasures that provide a prophylactic effect.
4. Reliance on invasive medical procedures for Integrated Countermeasure delivery (i.e., pumps, implants, lumbar or cranial injections).
5. Remotely triggered Integrated Countermeasure delivery (i.e., strategies that require user or medic administration post-injury).
6. Approaches not inclusive of real-time and/or highly resolved temporal and spatial techniques to validate targeting, safety, and efficacy of countermeasures.

Proposals that employ the approaches described in the above list may be deemed non-conforming and may not be considered for review.

1.1. PROGRAM OVERVIEW

The goal of the Cornerstone program is to develop an Integrated Countermeasure (i.e., countermeasure and delivery system) that, when administered prophylactically, protects against behavioral and cognitive injury in the context of blast- or impact-induced TBI. Integrated Countermeasures would do this by *preventing the initiation* of harmful signaling cascades through spatially and temporally relevant countermeasure delivery.

There is no Food and Drug Administration (FDA) approved, pharmacological treatment for TBI, leaving rehabilitation protocols as the only option for individuals diagnosed with TBI. Current research in TBI countermeasure development focuses on pharmacological approaches that target a single, late-stage (hours- to days- post-exposure) cellular or molecular event in the background of a multimodal, complex injury response that initiates within seconds post-exposure. This puts any post-exposure treatment in the position of needing to treat multiple injury processes simultaneously to achieve efficacy. Balancing the ability to engage many targets while minimizing off-target effects has presented an insurmountable challenge to all therapies designed for TBI post-exposure treatment. Additionally, even potentially effective and safe treatments may need to cross the blood brain barrier to engage the central nervous system (CNS), which has been an obstacle for many drug delivery and neuropharmacological interventions.

While pharmaceutical-based treatment options are nonexistent for TBI, prevention of TBI is also reliant upon antiquated technology. Currently, the only options for protection against TBI are physical protection measures, such as armored vehicles and bulky helmets, which fail to provide complete protection from injury.

To shift the paradigm, proposals are required to focus on the immediate (i.e., within the first five seconds) biological responder(s) to kinetic insult. Within this time frame there are limited molecular structures with the ability to directly respond to energetics. Energetically responsive receptors include mechano-, voltage-, or sensory-sensitive and are located in the CNS, peripheral nervous system (PNS), and vasculature. These energetic responsive receptors (e.g., targets), therefore, may not only sense the first biological responder(s) in the milliseconds to seconds after kinetic injury but then initiate the complex injury cascade that results in cognitive and physical deficits.

To address the shortcomings of current research (which is unable to adequately characterize these initial responses to drive countermeasure development), proposers are encouraged to embrace emerging technologies in neuroscience that have enabled real-time measurement and visualization of molecular and cellular responses *in vitro*, *ex vivo*, and *in vivo*. For example, technologies that enable the observation of energetically responsive receptors in real time would be extremely valuable in validating countermeasure strategies. Cornerstone performers will successfully pair these highly time-resolved observation capabilities with kinetic exposure models to evaluate causal linkages between interventions and outcomes post-exposure (as defined by validated assays), as part of a comprehensive countermeasure validation strategy.

Cornerstone technologies will address two technical areas (TAs), ultimately developing preventative countermeasures to TBI:

- TA1: Identify and validate countermeasures that prevent relevant targets from initiating downstream signaling injury response(s) to kinetic injury.
- TA2: Develop clinically relevant countermeasure delivery systems that prevent molecular targets from responding to kinetic insult at sites of injury (e.g., CNS, PNS, vasculature, and organ systems).

At program completion, Cornerstone will have developed Integrated Countermeasures (i.e., countermeasure and delivery system) that, at minimum, allow for repeated prophylactic administration, a three-day effective residence time per dose, and provide protection in response to injury at any time within the three-day window. Upon kinetic injury (e.g., blast), Integrated Countermeasures should demonstrate spatial and temporal bioactivity necessary to inhibit the initiation of injury processes (e.g., molecular pathway activation) and protect against the development of canonical neuropathological deficits associated with TBI.

Approaches should be tested iteratively and optimized against various challenges with increasing complexity and performance requirements as the program progresses (see Tables 1 and 2).

Proposals to the Cornerstone program should include approaches to achieve the following:

1. Structure-guided design utilizing high-resolution models of targets (e.g., mechanical, electrical, chemical responsive receptors and channel subtype(s)).
2. Countermeasures with inhibitory signaling downstream of the primary target.
3. Demonstration of strong and specific binding of countermeasures with selected target *in vitro*.
4. Demonstration of spatially and temporally controlled delivery (i.e., injury triggered delivery if appropriate, contextual specificity of temporal and spatial resolution).
5. Demonstration of Integrated Countermeasures without behavioral or physiological anomalies at relevant, repeated, prophylactic doses in the absence of kinetic exposure.
6. Demonstration of Integrated Countermeasures with clear protective effects using robust and widely accepted cognitive and behavioral animal model systems.

Performer test protocols (safety, efficacy) will be required to place Cornerstone-developed approaches on a path towards clinical translation and regulatory approval. Performers will be expected to submit regulatory applications to the FDA by the end of the program. Further, performers will be required to engage with the FDA and other U.S. Government regulatory groups for design guidance within Phase I of the program.

1.2. TECHNICAL AREAS

The Cornerstone program is structured as a five (5) year effort consisting of three (3) phases: (Phase I (Base – 24 months), Phase II (Option One – 24 months), and Phase III (Option Two – 12 months)).

DARPA will utilize an Independent Verification and Validation (IV&V) testing infrastructure to validate and assess protection efficacy of performer-generated technologies.

Proposed efforts must describe a plan to address both of the TAs over the entire program duration (60 months). At the end of Phase II (48 months), performers will have developed a safe and effective Integrated Countermeasure capable of providing > 95% protection against blast-induced molecular, cognitive, and behavioral injury in a minimum of two genetically distinct *in vivo* models. See Program Schedule, Metrics and Milestones for additional details.

Tables 1 and 2 describe the schedule of milestones and program evaluations that will drive programmatic decisions.

The technical areas are described below:

1.2.1. TA1: Identify, Optimize, and Validate Prophylactic Countermeasures

Performers will identify, optimize, and validate approaches that counter the initiation of injury signaling cascades at sites of injury (e.g., CNS, PNS, vasculature) protecting against TBI. Approaches to countering the initiation of pathophysiological pathways *may* include novel small molecules, repurposed pharmaceuticals, natural products, immunotherapies, cell therapies, and/or other approaches capable of preventing targets from initiating molecular injury pathways within seconds of kinetic exposure. TA1 approaches should ensure countermeasures have target specificity (e.g., 10-fold higher than off-target binding) and binding that prevents downstream heterogeneous molecular, cognitive, and behavioral effects in response to kinetic injury. Additionally, countermeasures should prevent initiation of injury pathway(s) within five seconds post-exposure to blast or other energetic threats.

1.2.2. TA2: Develop Spatial and Temporal Delivery

The outcome of TA2 will be the precise and temporally relevant delivery and confirmed bioactivity of TA1 therapeutic payloads at sites of injury. Proposers will demonstrate phenotypic outcomes of cell-type and/or regionally specific targeting of countermeasure(s). Performers *may* choose to leverage approaches including extravasation mechanisms (e.g., oncology approaches), mechanically or chemically triggered mechanisms (e.g., mechanophores, nanoparticles, liposomes), time-resolved release (e.g., chronic or acute), spatially targeted (e.g., cellular and subcellular localized payload release), and/or self-limiting mechanisms to enable the effective and safe delivery of therapeutic payloads. Additionally, TA2 approaches should achieve access to sites of injury (for example, though not exhaustive; CNS, PNS, otoliths, vasculature, etc.) and demonstrate localized bioactivity within five seconds of injury. Lastly, the technology must also provide and maintain protective efficacy for three days, following a single, self-administered, minimally invasive mechanism.

Lastly, chronically bioavailable novel or repurposed drugs, with specific target engagement, theoretical or empirically defined mechanism of action, temporal and spatial localization (without the support of novel delivery systems), and theoretical or demonstrated safety record will be considered.

Proposals that fail to address both TAs will be considered non-conforming and may be rejected without further review.

Fully integrated teams should be assembled early in the proposal process, and the integration of both scientific and managerial responsibilities should be conveyed in the submission. Integrated teams should describe the organizational structure within the team, complete with a dedicated project manager (separate from the principal investigator) to show distribution of responsibilities, lines of communication, and technical tasks throughout the proposal. Teams should structure themselves to support continuous, active engagement with IV&V, U.S. Government stake holders, and regulatory agencies to ensure a path towards clinical translation and regulatory application approvals such as Investigational New Drug (IND) or Emergency Use Authorization (EUA) as appropriate.

1.3. TECHNICAL APPROACH

TA1: Identify, Optimize, and Validate Prophylactic Countermeasures
TA1 objectives must achieve countermeasures that prevent the initiation of injury cascades within the first few milliseconds to five seconds of sustaining a kinetic injury.

In TA1, proposed approaches must include utilization of high-resolution molecular structures of targets to inform the design of novel countermeasures. High-resolution structures of countermeasures must demonstrate selective engagements with the target in a manner that preferentially prevents the activation of TBI-associated downstream signaling pathway(s) and subsequent cognitive or behavioral deficits. Countermeasures should show a greater than 10-fold selectivity for the target receptor over closely related anti-targets. TA1 approaches should develop a pipeline with the capability to iteratively optimize the design and activity of countermeasures. Such a pipeline may contain the following components: (1) Informed selection of targets and/or subtype(s) based on evidence for functional roles in TBI; (2) Structural determination of countermeasures and establishment of docking poses conferring signaling bias; and (3) *In vitro* or *ex vivo* assessment of countermeasure-mediated function and validation of predicted signaling bias. For approaches inclusive of drug discovery, proposals should include, at a minimum: state-of-the-art drug discovery approaches, such as virtual docking, predictive toxicity screens, high throughput, and microphysiological assessments in order to identify molecules that prevent targets from triggering downstream signaling injury responses.

Proposers must provide an explicit rationale for the selected target(s), with regard to the involvement of the energetically responsive molecule(s) in the initiation of the TBI. Proposed efforts should include both practical methods for target structure determination, such as X-ray crystallography and/or cryo-electron microscopy, as well as computational approaches, such as homology modeling and molecular dynamics simulations.

Because successful countermeasure development for this program requires reliable discrimination of binding between potentially closely related targets, such as receptors and ion channels, it is critical that the effort employ empirical and iterative determination of target interactions at the atomic scale.

For example, a novel chemotype of predicted value as a lead compound based on activity profiles *in vitro* must have a clear description of the structural basis of the target interaction determined. In order to prioritize translatability for clinical TBI, target(s) structure determination

must begin with human protein sequences and, if derived from animal protein sequence information, deviate minimally from human protein structure.

Proposers developing novel drugs should leverage novel and canonical drug-discovery approaches to design new chemotypes according to predicted structural conformations with associated binding of specific small molecules (at least 10,000 chemotypes docked *in silico*). Specifically excluded are methods that rely solely on high-throughput phenotypic screening of existing compound libraries as a first step.

Following the generation of countermeasures from the structure-guided design effort, prioritized countermeasures should be characterized *in vitro*. The following includes a minimum of SOA techniques that should be included for, but are not limited to, *in vitro* countermeasure characterization; ligand binding parameters (e.g., Kd, residence time, Bmax, etc.), endogenous ligand displacement, target and or target subtype specificity, profiling the inhibition of target activity during kinetic injury initiated signal transduction (agonist/partial agonist/ antagonist/inverse agonist), and pathway selectivity (e.g., G-protein mediated vs. ß-arrestin).

Proposals should include functional cellular *in vitro* assays that utilize, at a minimum, appropriate targets, target subtypes, and signal transduction machinery expressed either endogenously by, or introduced into, a relevant model system. Additionally, cellular and multicellular systems should be minimally manipulated and appropriate for the output of the assay. Where appropriate, functional consequences of heterotypic target oligomerization should be explored. For instance, where targets are known to form functional complexes with another receptor or molecule, a model system should be employed that enables formation of the endogenously active complex.

The critical end product of TA1 is a countermeasure with specificity and rapid prophylactic activity following kinetic insult. As such, all TA1-generated countermeasures satisfying the criteria must be evaluated in animal behavioral and cognitive TBI models to establish their utility as prophylactic countermeasures. In addition, countermeasures prioritized from TA1 must have clear mechanisms of action (with demonstrations of causality) described in terms of molecular, physiological, and behavioral phenotypes.

To meet the end goals of the Cornerstone program, TA1 countermeasures should exhibit rapid bioactivity (less than five seconds after kinetic injury) and a normalized effect size exceeding the mean of archetypal compounds studied in human clinical populations (Cohen's d of 1.4 relative to control). Proposers must also determine the duration (should it exceed three days) of therapeutic efficacy following a single administration of countermeasure.

TA2: Develop Spatial and Temporal Delivery

We assert that TBI is driven by injury sustained in specific cell types and/or nervous system regions initiated by energetically responsive receptors. Thus, DARPA is interested in methods under TA2 that investigate the precise spatial and temporal bioeffects of countermeasures in specific cell types, brain regions, or other anatomical structures within the body. Proposals must provide real-time and/or highly resolved approaches for determining the countermeasure delivery

to the relevant cell types and regions (e.g., vascular, nervous system (central or peripheral)) along with empirical and/or theoretical rationale for delivery system design.

All proposals must present a plan to demonstrate phenotypic outcomes of cell-type and/or brain-region selective targeting of novel countermeasure(s), compared to non-selective delivery of the same countermeasure(s).

Should proposers include externally triggered delivery approaches, triggers may include mechanical (i.e., shear-stress/strain from the blast/impact event itself) or biochemical stimuli (e.g., pH, calcium, ROS, etc.). Proposed triggered strategies (e.g., mechanical, chemical, etc.) should detail experimental approaches for demonstrating the precisely timed/localized payload release, while explicitly protecting against inappropriate release (i.e., delivery system leakiness or false-trigger). Energetic distribution and mechanical loads/stresses/strains should be described at a resolution of less than 50 μm^3 through finite element modeling, analytical equations, or similar estimation tools.

Finally, the integrated output of TA1 and TA2 (Integrated Countermeasure) will be used to inform the submission of an application for consideration as an IND to the FDA by program end. In order to do such, proposers must also consider and outline methods to optimize and characterize the formulation of lead compound(s) to satisfy requirements towards an IND to include multiple pre-submissions with the FDA before program completion.

Additional Considerations

In light of the heterogeneity in clinical presentations of TBI (molecular, behavioral, cognitive) proposals must include the assessment of therapeutic efficacy (and countermeasure safety) in a minimum of four (4) behavioral and cognitive assessments, and two (2) genetically divergent animal models, as outlined below (See Tests in Section 1.4).

Proposers must demonstrate Integrated Countermeasures are devoid of unintended side effects, such as cognitive or behavioral impairment or stimulation when administered at prophylactic doses in the absence of kinetic injury, no less than 48 hours subsequent to target interactions. Proposals should also include behavioral and cognitive assessments for repeat dosing regimens.

In addition, where selected targets and or subtype(s) differ in amino acid sequence between humans and animal models such as mice, efforts must include transgenic *in vivo* model(s) expressing humanized target(s) in order to recapitulate the human target-driven effect(s).

Differences in inhibition of target subtypes and downstream signaling pathways can lead to distinct phenotypic effects. The molecular mechanisms underlying these disparate outcomes are often not well-understood but may be critical for optimization of therapeutic efficacy. Proposers must characterize the downstream signaling events **no less than six hours** subsequent to target interactions using unbiased profiling methodologies (e.g., protein post-translational modifications (PTMs), synaptoproteomics, and/or transcriptional profiling). Additional relevant information on neurobiological effects such as neuronal morphology (e.g., spine analysis, arborization, and/or neuritogenesis) must also be detailed to further inform the mechanisms underlying phenotypic effects.

Safety and Regulatory

Cornerstone-developed Integrated Countermeasures must be characterized for a variety of performance metrics beyond protection against blast. Metrics are detailed in Table 2.

The execution of safety and efficacy assessments will be conducted by performers. These assessments should provide an in-depth understanding of host-toxicity and other factors that will affect performance/safety of both the delivery system (should it be distinct from the countermeasure), and the Integrated Countermeasure (combined countermeasure plus delivery system). Safety testing should demonstrate that preclinical models administered Integrated Countermeasures at prophylactic levels, in the absence of kinetic injury, remain within pre-defined 'normal physiologies.' The relevant results and analysis accumulated throughout Safety and Regulatory Testing should be used to update the FDA during pre-submission meetings, incorporating FDA feedback in any updates to the testing plan. This entire dataset will then be used as part of the IND or other submissions prior to human testing in accordance with regulatory guidance.

Proposers must include the following safety testing, at minimum:

- TA1
    - Physiological responses raised by countermeasures (e.g., long-residence exposure), including organ toxicity (e.g., neuro-, hepato-, reno-, cardio-, gastro-toxicity) and immune responses (e.g., immune cell activation, inflammatory response, and cytokine release);
    - *In silico* ADME predictions, *in vitro* or *ex vivo* high throughput toxicology studies; and
    - Molecular and histological analyses of *ex vivo*, *in vitro*, and *in vivo* studies.

- TA2
    - Spatial and temporal relevance *in vitro* and *in vivo;*
    - Integrated Countermeasure temporal bioactivity (*in vitro*, *ex vivo*, and *in vivo*);
    - Integrated Countermeasure specific spatial- or specific cell-type bioactivity (*in vitro*, *ex vivo*, and *in vivo*); and
    - As appropriate:
        - Trigger (open/close) capability, and associated toxicities (with open- and closed-states) at the level of cell, tissue, and organ;
        - Physiological responses raised by delivery systems, including immune cell activation, inflammatory response, and cytokine release);
        - Standard toxicology studies; and molecular and histological analyses of tissues.

Testing and Evaluation (T&E) of the Cornerstone System

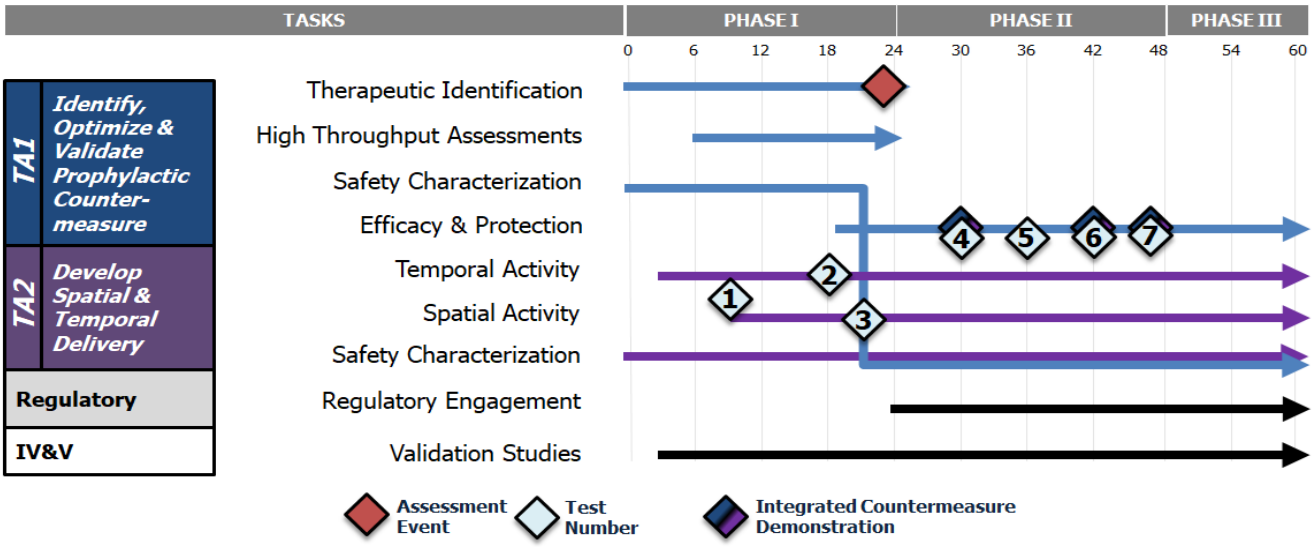
Performers will be required to evaluate *in vitro* and *in vivo* blast models in-house throughout the period of performance. Performer evaluations should include clear molecular, histological, cognitive, and behavioral confirmation of TBI, in addition to clear positive and negative controls

for all experimental approaches. Performers are encouraged to compare Countermeasures and Integrated Countermeasures against SOA as appropriate.

IV&V teams will support Cornerstone as a Government-furnished service to independently validate and verify *in vitro and in vivo* assessments in line with program metrics/milestones. For *in vivo* test challenges performed by IV&V teams, IV&V teams will define clinically relevant injury models, and behavioral/cognitive assessments following injury.

1.4. PROGRAM SCHEDULE, MILESTONES & METRICS

Table 1: PROGRAM SCHEDULE



Phase I (Base Period)
During Phase I, performers will identify and thoroughly characterize a set of first in class countermeasures capable of inhibiting target(s) responsible for initiating injury (molecular, behavioral, cognitive) post-kinetic exposure (e.g., blast) and validate countermeasures *in vitro* or *ex vivo* (TA1). Additionally, performers will develop spatial and temporal delivery with *in vitro* and *in vivo*-demonstrated specificity (TA2). In both TAs, technologies will be evaluated *in vitro* and *in vivo* for safety and toxicity. While tests will focus on select *in vivo* deliverables, proposals should explicitly outline clear performer-led demonstrations and/or timely reporting of deliverables for all metrics and milestones as listed in Table 2. Lastly, in delivery systems inclusive of triggered release, performers will be required to include false pretense exposures. False pretenses are defined as a trigger or injury asymmetrical to kinetic exposure, such as transient inflammation (e.g., LPS, viral, etc.). False pretenses should demonstrate the (1) safety, and (2) specificity of the countermeasure release under 'false' exposure considerations.

Test 1 (9 months) – TA1: Demonstration I: Target causality; II: Spatial relevance; and III: Temporal relevance.

Performers will demonstrate I) the causality; II) spatial relevance; and III) temporal relevance of their selected targets in two genetically divergent blast-appropriate TBI models (molecular, cognitive, behavioral). *In vivo* assessments should include time-resolved (e.g., real-time) data collection, and single-cell resolution characterizing TBI. Performers can select up to three unique targets to evaluate *in vivo*.

Experimental setup, resulting data sets, and analysis will be provided to IV&V teams and DARPA program management in a critical design review at 10 months. The critical review of Test 1 and its outcomes may be leveraged to redesign and modify TA 1 and 2 approaches based on IV&V and DARPA input.

Test 2 (18 months) – TA2: Delivery I: Temporal Precision

Performers will demonstrate in-house temporal delivery *in vivo*. Test 2 will demonstrate countermeasure delivery and/or payload release and bioactivity within five seconds of blast injury. Experimental assessment must include appropriate *in vivo* models. *In vivo* assessment must include detailed, time resolved (e.g., real-time) assessments characterizing the pharmacodynamic and pharmacokinetic payload release and/or bioactivity within five seconds of kinetic injury. Performers may choose to include single-cell resolution to incorporate Test 1 and critical design review feedback as appropriate. Performers may choose payloads to be proof of principal (Luciferase, paramagnets, etc.). Performers with triggerable delivery mechanisms will be required to include a minimum of two false pretenses demonstrating delivery condition specificity. Success will be considered > 80% payload bioactivity within five seconds of blast injury.

Test 3 (20 months) – TA2: Delivery II: Temporal and Spatial Precision

Performed by IV&V, no more than three delivery approaches will be provided to IV&V for testing spatial-specific payload delivery within five seconds of kinetic injury. Delivery systems and/or therapeutic payloads will be assessed for presence and/or bioactivity with cell- or region-specific loci as pre-determined in Test 1. Success will be considered > 80% payload release in targeted loci compared to non-selective delivery of the same payload, within five seconds of kinetic injury. A proof of principal (Luciferase, fluorophores, etc.) payload may be used.

Performers will demonstrate single-cell resolution of spatial specific payload delivery within five seconds of kinetic injury. Performers may choose payloads to be proof of principal (Luciferase, paramagnets, etc.). Performers with triggerable delivery mechanisms will be required to include a minimum of two false pretenses conditions demonstrating delivery spatial and temporal specificity.

Regulatory process

During Phase I, proposers are encouraged to work with the FDA and/or other regulatory agencies. In preparation for active engagement (formal) during Phase II, it is strongly encouraged that all testing in house (inclusive of Safety and Regulatory Testing, Table 1, and

Table 2) is rigorous and carried through with the intent to be used as part of the IND or other submissions prior to human testing in accordance with regulatory guidance.

Phase II (Option One)
During Phase II, proposers will focus on integrating and optimizing the capabilities of Integrated Countermeasures. Each team may move forward into Phase II with up to three countermeasures, integrated into no more than two delivery approaches, informed by earlier test results, safety outcomes, and preliminary formulation assessments. In house testing should include a minimum of two genetically divergent, blast appropriate, TBI animal models and a minimum of four total behavioral/cognitive assessments per Test as appropriate. By Test 6, proposers will further narrow to one countermeasure and minimally invasive formulations for IV&V assessment. Additionally, starting at Test 6, performers will be required to include false pretenses in vivo.

Test 4 (30 months) – TA1: Countermeasure Intervention

Performers will demonstrate in house that administered interventions result in a therapeutic reduction of molecular and cellular injury upon blast exposure. Assessment will consist of prophylactic administration of the countermeasure (either by TA2 delivery systems or IV infusion, lumbar puncture, etc.). Following administration, animals will undergo kinetic injury and highly time-resolved data collection characterizing the downstream molecular and cellular responses of blast injury. No less than three downstream pathway responses must be highly time resolved and detailed (e.g., excitotoxicity, inflammatory, etc.) for a minimum of six hours post-administration. Success will be determined by a consistent > 90% reduction of relevant downstream molecular injury signaling across successive time points (e.g., minutes-hours post injury). Additionally, successful countermeasures will have, at a minimum, demonstrated > 90% reduction in histological markers of neuropathology and neuroinflammation relative to blast-exposed control animals. Performers should include vehicle treatments and SOA comparisons (e.g., barrier provisions such as helmets etc.).

Test 5 (36 months) – TA1: Countermeasure Intervention II

Performers will demonstrate countermeasures result in a therapeutic reduction of behavioral and cognitive deficits upon blast exposure. Up to three countermeasures may be assessed in a minimum of two genetically divergent, blast appropriate, TBI animal models. Assessment will consist of prophylactic administration of countermeasures by drug delivery system or invasive approaches (i.e., IV infusion, lumbar puncture). Following administration, animals will undergo blast injury, and time resolved behavioral and cognitive assessments. No less than four total cognitive and behavioral assessments must be detailed (e.g., learning, memory, vestibular, etc.). All cognitive and behavioral assessments must have baseline, and acute measurements (e.g., before, and immediately after sustaining blast injury). Success will be determined by a consistent > 90% reduction of behavioral and cognitive impairment across successive time points (e.g., minutes-hours-days post injury) relative to blast exposed control animals. Performers should include vehicle treatments, and SOA comparisons (e.g., barrier provisions such as helmets, etc.).

Test 6 (42 months) – Integrated Countermeasure I

IV&V will assess Integrated Countermeasures for temporal and spatial release after a single administration and two-day residence time. One Integrated Countermeasure will be assessed in a minimum of two genetically divergent, blast appropriate, TBI animal models. Assessment will consist of prophylactic administration of the Integrated Countermeasure by minimally invasive (e.g., patch, eye-drop) or invasive (e.g., IV infusion, subcutaneous injection) means. Animals will undergo blast injury no sooner than one day, and no later than two days post administration.

Performers will be required to demonstrate the absence of toxicity as characterized by molecular, behavioral, and cognitive baselines from therapeutic payloads whether they are activated or not activated. In the inactive and activated state (even if activated without blast exposure), it needs to be shown that there is no toxic effect upon activation no sooner than one day, and no later than two days post administration in a minimum of two genetically divergent animal models. Preliminary efficacy and safety data may be gleaned.

Performers will be required to provide time resolved data collection, along with cell-type, and region-resolved selective targeting/bioactivity, compared to non-temporal and non-spatially targeted delivery of the same therapeutic payload for models of blast exposure, and false pretense exposure. Success will be considered > 90% therapeutic bioactivity at the targeted loci within five seconds of blast injury, and no molecular, cognitive, or behavioral anomalies associated with exposure to false pretenses.

Test 7 (46 months) – Integrated Countermeasure II

IV&V will assess Integrated Countermeasures for protection against blast injury after a single administration and three-day residence time. One Integrated Countermeasure may be assessed in a minimum of two genetically divergent, blast appropriate, TBI animal models. Assessment will consist of prophylactic administration of the Integrated Countermeasure by minimally invasive means (i.e., oral, microneedle patch, eye-drop, etc.). Animals will undergo blast injury no sooner than one day, and no later than three days post administration.

IV&V assessments will include no less than one false pretense concurrent with the three-day window of treatment and blast exposure (i.e., administration, false pretense, and blast exposure, within three-days).

Performers will be required to demonstrate no less than four total cognitive and behavioral measurements (e.g., learning, memory, vestibular, etc.). Cognitive and behavioral measures must assess prophylactic use (e.g., absence of kinetic injury), acute (e.g., within minutes of blast exposure), and chronic (hours-days) after kinetic injury. Success will be determined by (1) zero cognitive or behavioral anomalies during prophylactic use, (2) a consistent > 90% reduction of cognitive and behavioral impairment post blast, across successive time points relative to control animals. Performers should include delivery vehicle treatments and SOA comparisons (e.g., barrier provisions such as helmets, etc.).

<u>Phase III (Option Two)</u>
Prior to the end of Phase II (month 46), performers will be required to have engaged with the FDA. Performers should have a clear understanding of all necessary IND/EUA application

submission requirements, safety and toxicity data requirements, efficacy demonstrations, Integrated Countermeasure formulations, and plans for technology transition. This phase (Phase III, Months 48-60) will focus on collecting any remaining data, responding to regulatory feedback, and submission of regulatory application(s). For example, submission of package to support FDA IND application, including previous safety and efficacy data from Phases I and II, large animal (e.g., non-human primates) pharmacological and toxicological safety data demonstrating the products are reasonably safe for human testing, and documentation demonstrating capability for good manufacturing practice (GMP) of sufficient quantities of product for clinical testing. Pre-EUA activities are not required but may proceed in parallel to the required FDA approval through IND pathways.

Milestones & Metrics

In order for the Government to evaluate the effectiveness of Cornerstone technologies in achieving the stated program objectives, proposers should note that the Government hereby promulgates the following program metrics that may serve as the basis for determining whether satisfactory progress is being made to warrant continued funding of the program. Although the following program metrics are specified, proposers should note that the Government has identified these goals with the intention of bounding the scope of effort, while affording the maximum flexibility, creativity, and innovation in proposing solutions to the stated problem.

Quantitative metrics are expected to vary for each proposer-approach and system. **Some exemplary milestones and metrics are included below for proposers to consider, but proposers should adjust accordingly for their given countermeasure and system.** Final metrics are to be determined at the 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 (i.e., assessment).

In addition to the tests and system demonstration milestones, performers will be required to participate in program review meetings every six months. All performers will attend these Technical Interchange Meetings (TIMs) to brief their latest results and progress toward program goals. The meetings will include Government participation from interagency stake holders and end-users. Government sidebars will be held to provide individual feedback to the performers and to ensure they are developing relevant technologies. Teleconferences will be held with each team at monthly intervals. Site visits will be conducted at the Program Manager's discretion. Table 2 is a summary of the milestones and metrics for each team throughout the Cornerstone program.

Table 2: CORNERSTONE PROGRAM MILESTONES AND METRICS

PHASE			TA1 Identify, Optimize and Validate Prophylactic Countermeasure	TA2 Develop Spatial and Temporal Delivery
PHASE	1	3 MO	Identify structures for top first responder target receptors	
		6 MO	Complete target receptor druggability prediction	Payload temporal release *in vitro* (<seconds)
		9 MO	Docking and structure-based virtual screening Preliminary toxicity (ADME) predictions delivered for top ranking countermeasures	
			Test 1: Demonstrate (1) target causality, (2) spatial relevance, (3) temporal relevance *in vivo*	
		12 MO	Top ranking countermeasures filtered against annotated off-target receptors Deliverable: Draft list of countermeasures Begin de novo synthesis (if needed)	Region- or cell-type specific delivery and or bioactivity *in vitro* or *ex vivo*
		18 MO	Confirm target-engagement specificity *in vitro* (i.e., in excess of 10-fold vs off-target binding)	**Test 2:** Demonstrate *in vivo* >80% payload bioactivity or temporal specific delivery <5 seconds post kinetic exposure
		22 MO	Finalized list of first in class countermeasures with (1) target-specific activity, (2) off-target specific activity, and (3) data supporting plausible inhibition of downstream injury cascades Complete countermeasure synthesis (if needed) Countermeasure inhibits downstream injury pathway activation *in vitro/ex vivo* Complete high throughput assessments (safety, toxicity) for top candidate countermeasures	No overt toxicity of the delivery system *in vitro* or *ex vivo* in multiple organ systems No overt toxicity of the delivery system *in vivo* over 3-days **Test 3:** Demonstrate *in vivo* spatial and temporal specific delivery or bioactivity (e.g., PNS, CNS, Hippocampal, Cortex, Otolith)
			Milestone: Demonstrate target causality. Finalized Countermeasure List. Top Candidate Countermeasures block target activity *in vitro*.	
	2	30 MO	Demonstrate 2-day residence time of delivery system *in vivo* Integrated Countermeasure: *in vitro* temporal & spatial release of countermeasure **Test 4:** Reduction of molecular injury pathway activation and histopathology (90% vs control) in 2+ *in vivo* models	
		36 MO	**Test 5:** Reduction of cognitive and behavioral deficits (90% vs control) in 2+ *in vivo* models	
		42 MO	**Test 6:** Integrated Countermeasure: *in vivo* temporal & spatial release of countermeasure after a single dose (2-day residence time)	
		46 MO	**Test 7:** Integrated Countermeasure: Reduction of cognitive, behavioral, and molecular injury in NHPs, or appropriate large animal models (>95% vs uninjured prophylactic treated controls). Demonstrate single dose 3-day residence time maintains no overt toxicity	
	3	60 MO	Regulatory engagements and submissions	

Phase I (Base): Development and Initial Demonstration

- Month 1: Virtual program/Phase I kickoff.
- Month 3: Institutional Animal Care and Use Committee (IACUC) and Animal Care and Use Review Office (ACURO) approvals.
- Month 9: Performers assess (1) target causality, (2) spatial relevance, and (3) temporal relevance in injury models (Test 1).
- Month 10: Critical design review of Test 1 experimental setup, resulting data sets, analysis.
- Month 12: Demonstrate cell- or region-specific payload presence and/or bioactivity relative to non-targeted approaches *in vitro/ex vivo* models.
- Month 18: Demonstrate temporal specific payload delivery (less than 5 seconds) relative to non-targeted approaches *in vivo* (Test 2).
- Month 20: Demonstrate spatial specific payload delivery (cell- or region-specific) relative to non-targeted approaches *in vivo* (Test 3).
- Month 22: Deliver Tests 2 and 3 reports.

Phase II (Option): Integrated Countermeasure, Optimization and Efficacy

- Month 25: Phase II Kick-off meeting.
- Month 30: Demonstrate diminished pathological molecular and histopathological responses to kinetic injury (90% vs control) in two or more in vivo models (Test 4).
- Month 32: Deliver report for Test 4.
- Month 36: Demonstrate reduced cognitive and behavioral deficits (90% vs control) in two or more in vivo models of kinetic injury (Test 5).
- Month 38: Deliver report for Test 5.

- Month 42: Demonstrate temporal and spatial release of Countermeasure in response to injury after two-day residence time (Test 6).
- Month 44: Deliver report for Test 5. Deliver final plan for Phase III studies and documentation.
- Month 46: Final demonstration of safety and functionality with protection against molecular, cognitive, and behavioral injury in two or more large animal models (>95% vs uninjured prophylactic treated controls). Demonstration includes a single dose three-day residence time with no safety anomalies.
- Month 48: Deliver report for End of Phase Demonstration.

Phase III Option: IND Submission

- Month 49: Initiate NHP pre-clinical studies. Initiate demonstration of GMP capability.
- Month 55: Deliver mid-phase progress report.
- Month 59: Submission of package to support FDA IND application, including previous safety and efficacy data from Phases I and II, large animal (e.g., NHP) pharmacological and toxicological safety data demonstrating the products are reasonably safe for human testing, and documentation demonstrating capability for GMP manufacturing of sufficient quantities of product for clinical testing.
- Month 60: Deliver Program Final report.

1.5. GENERAL REQUIREMENTS

Teaming

Proposers are responsible for assembling a complete team that has technical expertise, capabilities, and facilities to address all objectives of the program. Proposers must address both TAs which should run in parallel. A complete proposer team should, therefore, not only have the ability to meet the technical challenges of each TA and create an integrated countermeasure, but also have the ability to demonstrate protection against blast and non-lethal false pretenses in relevant preclinical models at appropriate containment levels. It is also encouraged that proposer teams include members that have industrial and commercial experience to aid in focusing on technology research and development strategy for eventual clinical translation. This could include, for example, expertise in medical product development and Good Laboratory Practice (GLP) or GMP manufacturing of medical countermeasures for use in preclinical and clinical settings to effectively navigate the preparatory process for IND/EUA, or equivalent, submission during the program effort. Describe any formal teaming agreements that are required to execute this program. All teams are encouraged to identify a Project Manager to serve as the primary point of contact to communicate with the DARPA Program Manager and Contracting Officer Representative, coordinate effort across performer teams, organize regular performer meetings or discussions, facilitate data sharing, and ensure timely completion of milestones and deliverables. For teams that are not physically co-located, proposers must articulate how logistical challenges will be overcome to ensure smooth collaboration and an integrated work product.

Animal Subject Research

It is anticipated that Animal Subjects Research (ASR) will occur under this effort. As such, proposals should address experience authoring and executing successful ASR protocols. Furthermore, full proposals must include detailed plans for how the performer intends to acquire

all required approvals in a timely manner to meet specified milestones, including local Institutional Animal Care and Use Committee (IACUC) and DoD Animal Care and Use Review Office (ACURO) approvals. Proposers are requested to include a draft IACUC protocol package which **will not count toward page limits**. Proposers are requested to separate ASR tasks from those that do not require animal subjects research within their Statements of Work.

Ethical, Legal, and Societal Implications (ELSI)
DARPA maintains its commitment to ensuring that efforts funded under this BAA adhere to ethical and legal regulations currently in place for Federal and DoD-funded research. Program developments will be discussed with a panel of expert external advisors with expertise in bioethical issues that may emerge as a consequence of advances in biomedical science and technology, including human gene modulation. Proposers to this BAA should address potential ethical, legal, and societal implications of the proposed technology, with a special emphasis on strategies to enable safe, transient, non-permanent Cornerstone technologies.

Deliverables
All products, material and otherwise, that will be provided to the government as outcomes from conducted research should be defined as part of the proposal. Performers need to reserve time and budget to fulfill obligations for travel to review meetings and the transmission of report documentation. In addition to the milestones and metrics listed above:

- End of Phase reports: At the end of Phase 1 and Phase 2, prior to the initiation of the subsequent phase 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 reasonably conveyed.
- Monthly financial reports: Performers are required to provide financial status updates. These reports should be in the form of an editable MS Excel file, and should provide financial data including, but not limited to, the following: program spend plan by phase and task, incurred program expenditures to date by phase and task, and invoiced program expenditures to date by phase and task. The prime performer is to include information for itself and all subawardees/subcontractors.
- Monthly technical progress reports: Each month (or as close to as scheduling permits), performers are required to provide research updates. These reports should be in the form of a standardized slide presentation given to DARPA and discussed with the program management team via teleconference. Length and detail level should be at the discretion of the Program Manager.
- Quarterly technical reports: Reports shall be prepared and submitted in accordance with the procedures contained in the award document.
- Semi-Annual 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, twice annually. 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, any ongoing technical or programmatic challenges that must be overcome to achieve the overarching goals of the program.

- Final Program Report: When the final funding phase closes out, performer teams will provide a final report that summarizes all research activities, outcomes, and molecular mechanisms discovered during the program.
- Any publications, research presentations, patent applications that result from the research pursued as part of the Cornerstone program shall be submitted to the DARPA Program Manager and DARPA for review prior to release.
- Any additional deliverables requested by the 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 6.2.3, "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. § 4003(f), the Government may award a follow-on production contract or Other Transaction (OT) for any OT awarded under this solicitation 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 solicitation, the Government expects that program goals as described herein either cannot be met by proposers intending to perform fundamental research or the proposed research is anticipated to present a high likelihood of disclosing performance characteristics of military systems or manufacturing technologies that are unique and critical to defense. Therefore, the Government anticipates restrictions on the resultant research that will require the awardee to seek DARPA permission before publishing any information or results relative to the program.

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 solicitation 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.§ 4892 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.

3.1.3. Applicants Considering Classified Submissions

Applicants shall ensure all industrial, personnel, and information system processing security requirements are in place and at the appropriate level (e.g., Facility Clearance (FCL), Personnel Security Clearance (PCL), certification and accreditation (C&A)) and any Foreign Ownership Control and Influence (FOCI) issues are mitigated prior to such submission or access. It is required that the facility has a laboratory space that has a safeguarding level of secret or higher

and a classified network accredited at secret or higher. Prime proposers without access to a currently accredited laboratory at the secret level or above and a classified network accredited at Secret or higher **will not be considered**. Additional information on these subjects can be found at http://www.dcsa.mil.

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 solicitation. 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 solicitation 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.

4.1.1. Addendum

A formal request for the HR001122S0022 Addendum including a Security Classification Guide may be submitted by filling out the Request Form (found in Appendix 2 to this BAA) and emailing the Request Form to Cornerstone@darpa.mil with the subject line titled "Request HR001122S0022 Addendum and Security Classification Guide." The attached Addendum Request Form is the only method of request that will be accepted. Additional security guidance via a DD Form 254, "DoD Contract Security Classification Specification" will be provided with the Addendum and SCG. Requests from uncleared facilities without a safeguarding level of secret or higher and an accredited IT system of secret of higher **will not be considered**.

Proposers should allow at least five (5) business days for processing requests for the addendum plus time for delivery. Requests for this information will not be accepted after August 4, 2022.

DARPA intends to use the Secure Internet Protocol Router Network (SIPRNet)\Joint Worldwide Intelligence Communications System (JWICS) and the FedEx shipping service in an effort to expedite receipt of the addendum. Please note that any requesting organizations that are unable to receive a secure electronic form of delivery may experience delays.

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. 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 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 14 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 **8** pages, including all figures, tables, and charts. All submissions must be written in English with type no smaller than 12-point font. 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; 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. 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?

C. Technical Plan: Outline and address all technical areas and challenges inherent in the approach and possible solutions for overcoming potential problems.

D. Capabilities: Provide a brief summary of expertise of the team, including subcontractors and key personnel. A principal investigator for the project must be identified, and a description of the team's organization. Include a description of the team's organization including roles and responsibilities. Describe the organizational experience in this area, existing intellectual property required to complete the project, and any specialized facilities. List Government-furnished materials or data assumed to

be available. If desired, include a brief bibliography with links to relevant papers, reports, or resumes of key performers.

E. Budget and Schedule: Cost and schedule estimate for the proposed research, including an estimate of (a) total cost, (b) cost for each task in each phase of the effort by prime and major subcontractors, and (c) any cost share (if applicable). Any anticipated government furnished equipment should be clearly identified.

F. Resumes (do not count towards page limit): Include no more than two (2) resumes, one of which must be from/for the Principal Investigator.

G. Bibliography (Optional, does not count towards page limit): If desired, include a brief bibliography with links to relevant papers and reports. The bibliography should not exceed two (2) pages.

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 1 is 30 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 TAs and follow the instructions herein may be rejected without further review.

a. Volume I, Technical and Management Proposal

Section I. Administrative (does not count towards page limit)

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

1. BAA number (HR001122S0022);
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, e-mail;
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, e-mail;
9. Award instrument requested: cost-plus-fixed-free (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 Slides: The slide template is provided as **Attachment 1** to the BAA posted at https://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, plan for achieving the milestones, and must include a simple process flow diagram of their final system concept. 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. Resumes count against the proposal page count. Identify a principal investigator (PI) for the project, and include an on-site program manager if the PI will contribute less than 50% time/effort to the project. Provide a clear description of the team's organization, including an organization chart that contains, as applicable: the programmatic relationship of team members, team members' unique capabilities/expertise, team members' task responsibilities, the teaming strategy among the team members, collaborators, subcontractors, etc., 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, etc., 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. Discuss any work in closely related research areas and previous accomplishments.

F. Statement of Work (SOW) NOT INCLUDED IN PAGE COUNT: The SOW should provide a detailed task breakdown, citing specific tasks and their connection to the interim milestones and program metrics. Each phase of the program should be separately

defined, and all tasks/subtasks should be identified by Technical Area. The SOW must not include proprietary information.

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.

G. Schedule and Milestones: Provide a detailed schedule (Gantt chart preferred) 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. If the Gantt chart cannot fit on a standard 8 ½ by 11" age, you are permitted to include it as an addendum/appendix.

H. Technology Transfer Plan: Proposers should provide a detailed plan, with milestones, showing how regulatory, safety, and transition aspects of the technology will be addressed. The plan should include descriptions of how potential DoD users will be engaged as well as paths for commercialization of the technology.

Section III. Additional Information

A brief bibliography of relevant technical papers and research notes (published and unpublished), which document the technical ideas upon which the proposal is based. Copies of not more than three (3) relevant papers can be included in the submission.

a. Volume II, Cost Management Proposal

Cover Sheet (LABELED "PROPOSAL: VOLUME II"):

1. BAA Number (HR001122S0022);
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-free (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 (as defined in Table 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. Unique Entity Identifier (UEI) (https://www.gsa.gov/about-us/organization/federal-acquisition-service/office-of-systems-management/integrated-award-environment-iae/iae-systems-information-kit/unique-entity-identifier-update);
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

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

The Government strongly encourages that proposers use the provided MS Excel™ DARPA Standard Cost Proposal Spreadsheet in the development of their cost proposals. A customized cost proposal spreadsheet may be an attachment to this solicitation. If not, the spreadsheet can be found on the DARPA website at http://www.darpa.mil/work-with-us/contract-management (under "Resources" on the right-hand side of the webpage). All tabs and tables in the cost proposal spreadsheet should be developed in an editable format with calculation formulas intact to allow traceability of the cost proposal. This cost proposal spreadsheet should be used by the prime organization and all subcontractors. In addition to using the cost proposal spreadsheet, the cost proposal still must include all other items required in this announcement that are not covered

by the editable spreadsheet. Subcontractor 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 solicitation. **Using the provided cost proposal spreadsheet will assist the Government in a rapid analysis of your proposed costs and, if your proposal is selected for a potential award, speed up the negotiation and award execution process**.

(1) Total program 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.
For Equipment and Materials associated with optional classified tasks, include a sanitized list.

iv. **Travel –** provide an itemized list of travel costs to include purpose of trips, departure and arrival destinations, projected airfare, rental car and per GSA approved 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, and explain how it is in the best interest of the project. **Plan for two (2) DARPA program review meetings per year.**

v. **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.

vi. **Other Direct Costs** – Consultants: provide executed Consultant Agreement that describes work scope, rate and hours.

vii. **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).

viii. **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).
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 half (1st 9-month period, and 2nd 9-month period), 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 another 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 which 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 (OT) Requests

All proposers requesting an OT must include a detailed list of milestones for each half of the program. 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.

Security Information

DARPA anticipates that submissions received under this BAA may be classified. Submission information can be found below and in Section 4.2.4.

Classified submissions shall use the outline and section numbering as directed by this document and the addendum. DARPA will provide specific security classification guidance via an SCG and DD Form 254, "DoD Contract Security Classification Specification."

Classified Proposal Markings

Classified submissions shall be transmitted and marked in accordance with the following guidance. If a submission contains Classified National Security Information or the suspicion of such, as defined by Executive Order 13526, the information must be appropriately and conspicuously marked with the proposed classification level and declassification date. Submissions requiring DARPA to make a final classification determination shall be marked as follows:

"CLASSIFICATION DETERMINATION PENDING.
Protect as though classified SECRET"

NOTE: Classified submissions must indicate the classification level of not only the submitted materials, but also the classification level of the anticipated award.

Classified Submission Requirements and Procedures

Proposers submitting classified information must have cognizant security agency approved facilities, information systems, and appropriately cleared/eligible personnel to perform at the classification level proposed. All proposer personnel performing Information Assurance (IA)/Cybersecurity related duties on classified Information Systems shall meet the requirements set forth in DoD Manual 8570.01-M (Information Assurance Workforce Improvement Program). Additional information on the subjects discussed in this section may be found at http://www.dcsa.mil.

Proposers choosing to submit non-DARPA classified information must ensure (1) they have permission from an authorized individual at the cognizant Government agency (e.g., Contracting Officer, Program Manager); (2) the proposal is marked in accordance with the source Security Classification Guide (SCG) from which the material is derived; and (3) the source SCG is submitted along with the proposal.

When submitting a hard copy of the classified proposal according to the instructions outlined below, proposers shall submit two (2) hard copies of the classified proposal and two (2) CD-ROMs containing the classified proposal broken into separate files containing:

(1) full proposal executive summary slides in MS PowerPoint,
(2) full proposal Volume I in searchable Adobe PDF,
(3) Statement of Work (SOW) in MS Word,
(4) full proposal Volume II in searchable Adobe PDF, and
(5) the unclassified DARPA cost proposal spreadsheet in Microsoft Excel.

Classified Information

Use transmission, classification, handling, and marking guidance provided by the solicitation SCG, the DoD Information Security Manual (DoDM 5200.01, Volumes 1 - 4), and the National

Industrial Security Program Operating Manual, including the Supplement Revision 1 (DoD 5220.22-M and DoD 5200.22-M Sup. 1), when submitting Confidential, Secret, and/or Top Secret classified information.

Secret classified information may be submitted via ONE of the two following methods to the mailing address listed in the contact information in Part I of this BAA:

- Hand-carried by an appropriately cleared and authorized courier to the DARPA Classified Document Registry (CDR). Prior to traveling, the courier shall contact the DARPA CDR at 703-526-4052 to coordinate arrival and delivery.

OR

- Mailed via U.S. Postal Service (USPS) Registered Mail, USPS Express Mail, or Federal Express (FedEx). All classified information will be enclosed in opaque inner and outer covers and double- wrapped. The inner envelope shall be sealed and plainly marked with the assigned classification and addresses of both sender and addressee. The inner envelope shall be addressed to Defense Advanced Research Projects Agency, ATTN: DARPA/BTO with a reference to the BAA number (HR001122S0022).

Each copy must be clearly labeled with BAA number HR001122S0022, proposer organization, technical point of contact, and unclassified proposal title (unclassified short title recommended). Senders should mail to the mailing address listed in the contact information herein.

Subcontractor proposals not submitted by the Prime should include the Prime organization name, proposal title (same as the Prime), and the Subcontractor contact information on the inner envelope.

The outer envelope shall be sealed with no identification as to the classification of its contents and addressed to Defense Advanced Research Projects Agency, Security & Intelligence Directorate, Attn: CDR.

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://nvlpubs.nist.gov/nistpubs/SpecialPublications/NIST.SP.800-171r2.pdf) and DoDI 8582.01 that are in effect at the time the solicitation 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) complaint 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.

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)

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 solicitation. 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/sys_attachment.do?sys_id=c08b64ab1b4434109ac5ddb6bc4bcbb8.

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 HR001122S0022. 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 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.

Unclassified Abstracts and Full Proposals
Submissions sent in response to HR001122S0022 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 the 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.

Classified Abstracts and Full Proposals
Proposers must submit two (2) hardcopies and two (2) electronic copies of the abstract or proposal in PDF (preferred) on a CD-ROM using the guidelines provided above in Section 4.2.3. Each copy must be clearly labeled with HR001122S0022, proposer organization, technical point of contact, and proposal title (short title recommended).

In addition to the hardcopies referenced above, unclassified cover sheets for proposal abstracts and unclassified cover sheets and cost volumes for full proposals sent in response to HR001122S0022 must be submitted via DARPA's BAA Website (https://baa.darpa.mil) in accordance with the guidance above.

To the maximum extent possible, prime contractor and subcontractor cost proposal documents (Volume II: Cost Volume Template and required supporting documentation) and completed DARPA cost proposal spreadsheets should be unclassified and submitted to DARPA via DARPA's BAA Website (https://baa.darpa.mil).

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

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

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 HR001122S0022 summary. Submit your question(s) via e-mail to Cornerstone@darpa.mil. Any questions received after August 12, 2022 will likely not receive a response prior to the BAA closing date.

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; 5.1.3 Cost Realism; and 5.1.4 Realism of Proposed Schedule.

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. The timeline for achieving major milestones is aggressive but rationally supported with a clear description of the requirements and risks. The proposer's prior experience in similar efforts must clearly demonstrate an ability to deliver products that meet the proposed technical performance within the proposed budget and schedule. The proposed team has the expertise to manage the cost and schedule.

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.

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.

5.1.4. Realism of Proposed Schedule

The proposed schedule aggressively pursues performance metrics in the shortest timeframe and accurately accounts for that timeframe. The proposed schedule identifies and mitigates any potential schedule risk.

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 5.1. 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 solicitation; 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 non-disclosure 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. SUBMISSION STATUS NOTIFICATIONS

Proposal Abstracts and Full Proposals submitted in response to HR001122S0022 will be evaluated following the submission deadlines listed in Part 1. DARPA will respond as described below. These official notifications will be sent via e-mail to the Technical Point of Contact (POC) and/or Administrative POC identified on the submission coversheet.

6.1.1. Proposal Abstracts

DARPA will respond to abstracts with a statement as to whether DARPA is interested in the idea. If DARPA does not recommend the proposer submit a full proposal, DARPA will provide feedback to the proposer regarding the rationale for this decision. Regardless of DARPA's response to an abstract, proposers may submit a full proposal. DARPA will review all conforming full proposals using the published evaluation criteria and without regard to any comments resulting from the review of an abstract.

6.1.2. Full Proposals

As soon as the evaluation of all conforming 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 (likely virtual) and all key participants are required to attend. Performers should also anticipate one program-wide PI meeting in the Arlington, VA vicinity, and periodic site visits at the Program Manager's discretion. Proposers shall include, within the content of their proposal, 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.

6.2.1. Solicitation Provisions and Award Clauses, Terms and Conditions

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.

6.2.2. Controlled Unclassified Information (CUI) and Controlled Technical Information (CTI) 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.

6.2.3. 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, all proposers are required to submit for all award instrument types supplementary DARPA-specific representations and certifications at the time of proposal submission. See http://www.darpa.mil/work-with-us/reps-certs for further information on required representation and certification depending on your requested award instrument.

6.3. REPORTING

See "Deliverables" in Section 1.5.

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:
Cornerstone@darpa.mil
DARPA/BTO
ATTN: HR001122S0022
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

8.1. PROPOSERS DAY

DARPA will host a virtual Proposers Day in support of the Cornerstone program on **June 7, 2022**. The purpose is to provide potential proposers with information on the Cornerstone 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 to respond to the Cornerstone 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.

DARPA will not provide cost reimbursement for interested proposers in attendance. An online registration form and various other meeting details can be found at the registration website, https://events.sa-meetings.com/CornerstoneProposersDay.

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:
Cornerstone@darpa.mil
ATTN: DARPA-SN-22-29

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 HR001122S0022. 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 **HR001122S0022** 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)
   f○ **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:

10. APPENDIX 2 – Addendum Request Form

ADDENDUM REQUEST FORM	
	Date:
CAGE Code	
Facility Name	
Alias Type/Name	
Physical Location	
Classified Mailing Address	
Facility Clearance Status/Level	
Safeguarding Level	
Classified Laboratory Space (Identify classification level and accrediting authority)	
Classified Network (Identify classification level and accrediting authority)	
Facility Security Officer Name	
Facility Security Officer Phone	
Facility Security Officer E-mail	
DCSA Field Office	
DCSA Field Office Phone	
Technical Point of Contact Name	
Technical Point of Contact Phone	
Technical Point of Contact E-mail	
Preference for receiving classified materials (SIPRNet address, JWICS address, FedEx etc.)	
Share contact information with other addendum recipients for teaming purposes? (Y/N)	