Broad Agency Announcement

PReemptive Expression of Protective Alleles and Response Elements (PREPARE)

BIOLOGICAL TECHNOLOGIES OFFICE

HR001118S0037

June 6, 2018

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List of Abbreviations

ADME	Absorption, Distribution, Metabolism, and Excretion
ARS	Acute Radiation Syndrome
BuChE	Butyrylcholinesterase
CD	Capability Demonstration
CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
CRISPRa/i	CRISPR activator/inhibitor
CTI	Controlled Technical Information
CUI	Controlled Unclassified Information
DARPA/PRC	DARPA's Public Release Center
DEARE	Delayed Effects of Acute Radiation Exposure
DoD	Department of Defense
ELSI	Ethical, Legal, and Societal Implications
EUA	Emergency Use Authorization
FDA	Food and Drug Administration
G-CSF	Granulocyte-Colony Stimulating Factor
GM-CSF	Granulocyte-Macrophage Colony-Stimulating Factor
gRNA	guide ribonucleic acid
Gy	Gray (unit of ionizing radiation dose)
IND	Investigational New Drug
MCM	Medical Countermeasure
MoPs	Mechanisms of Protection
OP	Organophosphate
PGM	Programmable Gene Modulator
PGM-MCM	Programmable Gene Modulator – Medical Countermeasure
PI	Principal Investigator
PM	Program Manager
POC	Proof of Concept
SoA	State of the Art
ssRNA	Single-stranded ribonucleic acid
TA	Technical Area
TPP	Target Product Profile

PART I: OVERVIEW INFORMATION

- **Federal Agency Name** – Defense Advanced Research Projects Agency (DARPA), Biological Technologies Office
- **Funding Opportunity Title –** PReemptive Expression of Protective Alleles and Response Elements (PREPARE)
- **Announcement Type –** Initial announcement
- **Funding Opportunity Number –** HR001118S0037
- **Catalog of Federal Domestic Assistance Numbers (CFDA) – 12.910 Research and Technology Development**
- **Dates**
    - Posting Date: **June 6, 2018**
    - Proposal Abstract Due Date: **July 12, 2018**
    - Proposal Due Date: **August 27, 2018**
    - Any other relevant date(s) - **Proposers Day, June 13, 2018**

    https://www.fbo.gov/spg/ODA/DARPA/CMO/DARPA-SN-18-45/listing.html

- **Concise description of the funding opportunity:** The PREPARE program aims to develop programmable gene modulators for humans that can provide specific, effective, safe, and transient medical countermeasures and prophylaxes to combat biological, chemical, and/or radiological threats to public health and national security.
- **Anticipated individual awards** - Multiple awards are anticipated.
- **Types of instruments that may be awarded** - Procurement contract, cooperative agreement or Other Transactions.
- **Agency contact**
    - Points of Contact
      The BAA Coordinator for this effort may be reached at:
      PREPARE@darpa.mil
      DARPA/BTO
      ATTN: HR001118S0037
      675 North Randolph Street
      Arlington, VA 22203-2114

PART II: FULL TEXT OF ANNOUNCEMENT

1. Funding Opportunity Description

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

The Defense Advanced Research Projects Agency (DARPA) is soliciting innovative proposals to develop a platform capability for the production of Medical Countermeasures (MCMs) that bolster natural genetically-encoded defenses against biological, chemical, and/or radiological threats to public health and national security. Proposed research should investigate disruptive approaches for the identification of gene targets that, when modulated, confer protection or resistance against these threats; the development of novel tools to modulate the activity of target gene(s); and the generation of clinical formulations that enable delivery to the appropriate cells and tissues in vivo. The integration of these approaches into a platform that can produce novel MCMs should enable a specific, potent, safe, and transient approach for directly modulating the activity of target genes to limit the damaging and potentially fatal consequences of a broad range of threats to warfighters, first responders, and civilian populations.

1.1. BACKGROUND AND PROGRAM OVERVIEW

Influenza pandemics, organophosphate poisoning, opioid overdose, and exposure to ionizing radiation are representative of the broad spectrum of biological, chemical, and radiological threats that can significantly impact public health and national security. These seemingly disparate threats share a common challenge: despite decades of laboratory experimentation and significant research investment, broad-acting, longer-lived, and effective MCMs remain elusive. While current pharmaceutical and biologic MCMs confer some protection for these categories of threats, strategies to rapidly and flexibly discover, design, manufacture, scale, and administer these solutions remain inadequate for public health emergencies, pandemic preparedness, and force protection. The current one threat/one MCM paradigm is not sufficient to address the diverse and rapidly evolving threat space.

The human genome encodes a number of genes whose products can confer some protection against these threats, however, the time between threat exposure and expression of protective genes is often too long, leading to severe symptoms or even death. DARPA's PReemptive Expression of Protective Alleles and Response Elements (PREPARE) program expands upon recent advances in genome engineering, insights into host/threat response, and *in vivo* delivery to implement a novel paradigm for the development of a common molecular architecture for MCMs that bolster innate host defenses to combat an array of national security and public health threats. PREPARE is anticipated to deliver a capability to generate programmable gene modulator MCMs (PGM-MCMs) to enable safe, transient, and preemptive activation of intrinsic host defenses against a variety of threats to health, as well provide novel solutions for the direct neutralization of pathogenic viral genomes.

Importantly, transient and clinically relevant PREPARE PGM-MCM interventions may also provide an alternative to permanent somatic cell genome editing approaches that permanently alter host primary DNA sequences (e.g., CRISPR-Cas9). PGM-MCMs may act at the level of the transcriptome, the epigenome, and the epitranscriptome. PGM-MCMs should consist of noncanonical and non-permanent genome editors, defined as transient and programmable modulators of endogenous gene targets, transcripts, and pathways that do not alter primary DNA sequence, cause life-long gene expression changes in the host, or create DNA lesions in a host genome in any way[1].

PGM-MCMs should be designed in a manner that enables somatic interventions at common pathway nodes to enhance protective host responses across multiple threats, promote universal neutralization of viral threats, and be easily re-targeted and re-configured for rapid adaptation and response to new and emergent threats. This architecture should be compatible with the potential for stockpiling common MCM reagents (e.g., an RNA editor) and time-of-need manufacture of PGM-MCM reagents (e.g., guide RNAs) to enable the most agile, timely, and robust response to known and emergent public health and national security threats.

Specific proofs of concept demonstrated under the PREPARE program will focus on measurable progress towards the development and testing of PGM-MCMs to address four primary threats that represent a range of threats to public health and national security that may be encountered. The four primary threats that PREPARE will address are:

- Influenza viral infection
- Opioid overdose
- Organophosphate (OP) poisoning
- Exposure to gamma radiation

MCM development for influenza poses unique challenges due to strain variation and the ability to rapidly mutate and resist existing MCMs or evade the immune system. Highly conserved components of the influenza virus have provided insights into possible universal treatment or prophylaxis options, but these have proved elusive thus far. In addition, the demonstrated ability to synthesize and engineer biological threats *de novo* (e.g., 1918 influenza) further emphasizes the need for agnostic MCM platforms that are easily re-configurable and compatible with simple and rapid manufacture. Direct neutralization of viral genomes in highly conserved regions may afford near-universal protection for the host and reduce the likelihood of developing viral resistance. Approaches that modulate host defenses against viruses, or bolster immune responses, may further amplify protection. For example, recent studies have identified host gene targets that, when modulated, confer protection against influenza infection in experimental systems[2,3].

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[1] Wegrzyn *et al*., Genome Editing: Insights from Chemical Biology to Support Safe and Transformative Therapeutic Applications. *ACS Chem Biol*. 2018 Feb 16;13(2):333-342.

[2] Han *et al*., Genome-wide CRISPR/Cas9 Screen Identifies Host Factors Essential for Influenza Virus Replication. *Cell Rep.* 2018 Apr 10;23(2):596-607.

[3] Heaton *et al*., A CRISPR activation screen identifies a pan-avian influenza virus inhibitory host factor. *Cell Rep.* 2017 Aug 15; 20(7): 1503–1512.

MCMs against opioid overdose or organophosphate pesticides require rapid intervention to improve patient prognosis. Currently, the state of the art (SoA) for mitigation of opioid (e.g., fentanyl) or organophosphate (e.g., pesticides) poisoning are small molecules such as naloxone or atropine/pralidoxime, respectively. While effective, these small molecule MCMs require immediate administration to reverse effects of poisoning and require repeat dosing due to short half-lives. SoA biologics such as human-derived butyrylcholinesterase (BuChE) for the stoichiometric neutralization of OPs need to be recombinantly produced or purified from human plasma, then intravenously administered as a prophylaxis against organophosphate exposure, which is costly, not scalable, and requires frequent re-administration.

For treatment of acute radiation syndrome (ARS) that may result from radiation therapy or occupational exposures, FDA-approved treatments are limited to recombinant human proteins G-CSF (Neupogen® and its PEGylated form Neulasta®) and GM-CSF (Leukine®), administered to stimulate hematopoietic response. These MCMs do not address the full range of ARS symptoms and require frequent re-administration and close monitoring of patient health.

In order to bridge the gap between experimental proof of concept and clinical translation of PGM-MCMs to solve these public health and national security challenges, development of the PREPARE capability will require innovation across several key component areas to generate a platform that can be applied in an agnostic manner for any threat category. This platform should be designed to determine: which genes exhibit intrinsic protections against the threat; which programmable gene modulation tools are most appropriate to modulate the activity of those genes for a given threat; and how and where the PGM-MCMs should be delivered *in vivo* for greatest protective effect against a threat (**Figure 1**). The integrated PREPARE platform components and resulting PGM-MCMs should be iteratively tested and optimized *in vivo* against various threat challenges with increasing complexity and performance requirements on a path towards clinical translation and regulatory application submission; for example, Food and Drug Administration (FDA) Investigational New Drug (IND) or Emergency Use Authorization (EUA).

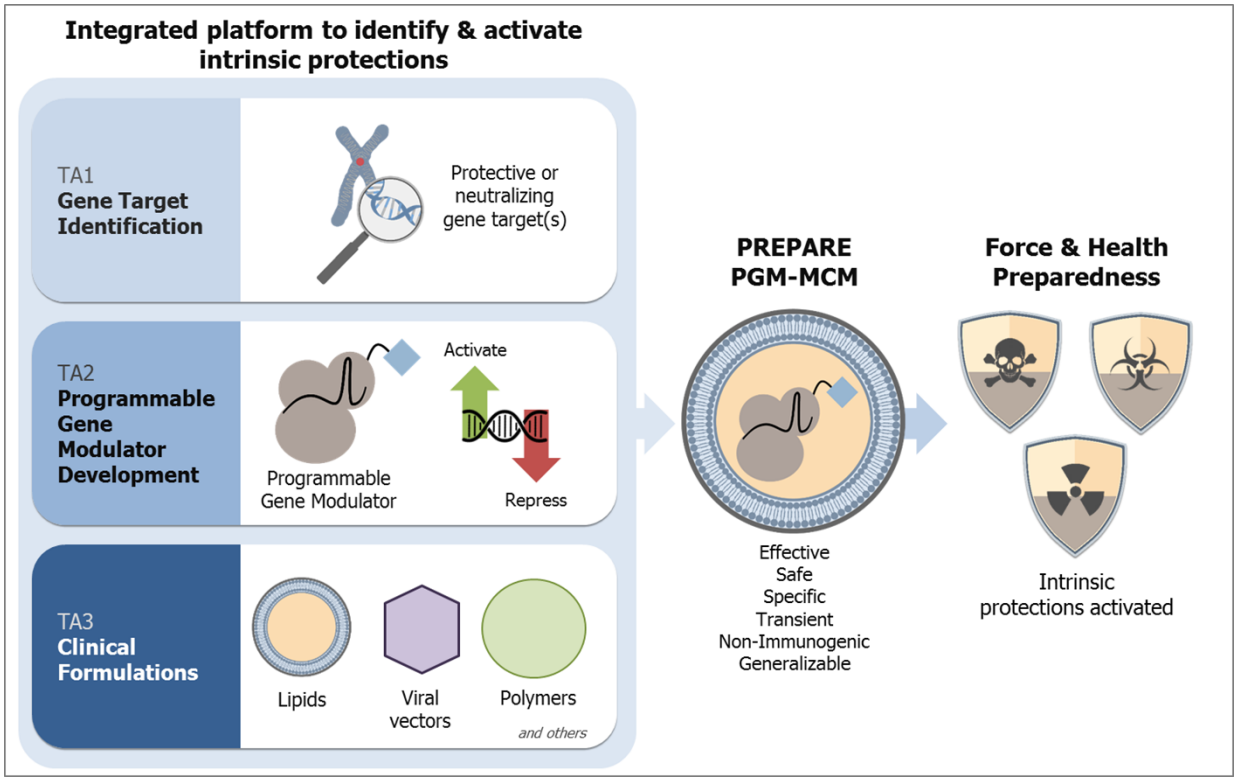

Figure 1 *Schematic of PREPARE program objectives.*

1.2. PROGRAM STRUCTURE

PREPARE is structured into a four (4) year effort consisting of two (2) phases for two (2) years each (**Figure 2**).

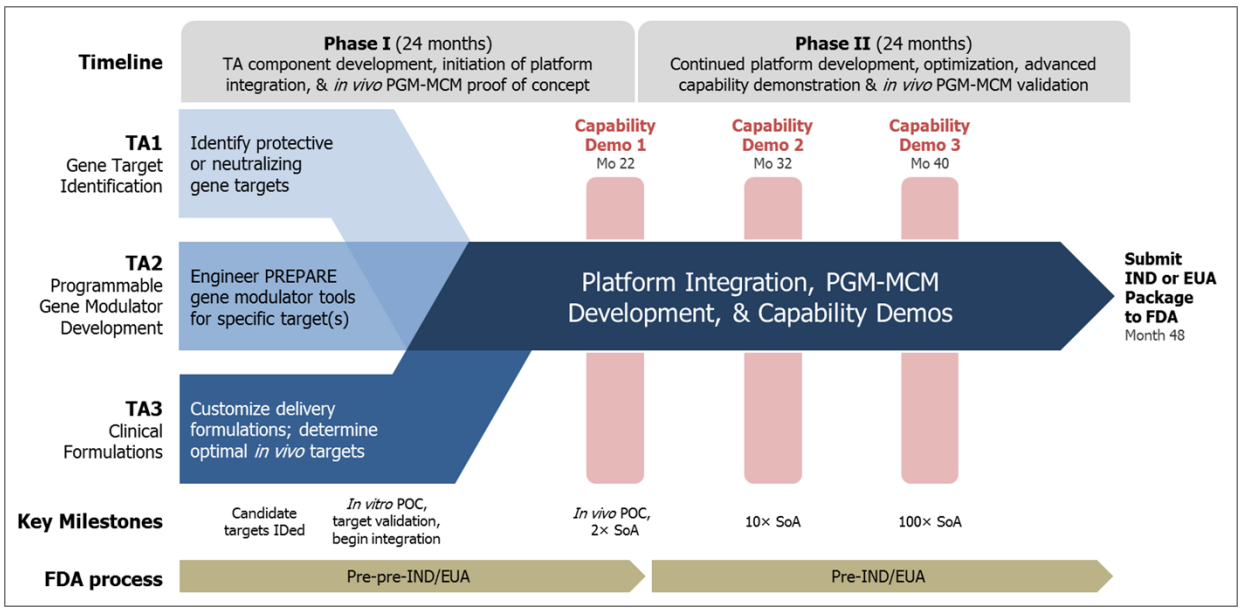

Figure 2 *PREPARE Program Structure & Timeline.*

Phase I

Technical Area Component Development
Proposers must indicate their primary selection of the relevant threats that they intend to pursue under the PREPARE program from the following: influenza, opioids, organophosphates, or gamma radiation. In Phase I, proposers should concurrently develop and integrate component innovations spanning three Technical Areas (TAs):

- TA1: Gene Target Identification
- TA2: Programmable Gene Modulator Development
- TA3: Clinical Formulations

During Months 1 to 12 of Phase I, proposer teams should generate foundational capabilities to identify targets within genomes that can counter the health risks posed by influenza, opioids, organophosphates, or gamma radiation (TA1); develop libraries of programmable gene modulators to control protective gene activity (TA2); and develop formulations to deliver the programmable gene modulators to the cells and tissues where their activity is required (TA3), and should establish proof-of-concept that these capabilities can be applied to reduce the effects of the selected threats in *in vitro* systems.

Platform Integration and Capability Demonstration 1
Beginning in Month 13, proposers are required to functionally integrate TA1, TA2, and TA3 components into a platform that enables the production of PGM-MCMs for testing against the selected threat(s) *in vivo*. Phase 1 should culminate with a proof-of-concept Capability Demonstration 1 (CD1) to test the performance of PGM-MCMs against SoA MCMs in a relevant *in vivo* animal model against the proposer-selected threat. By the end of Phase I, proposers must also demonstrate multiplex capability (i.e., >1 target modulated, such as multiple protective genes modulated or multiple sites within a viral genome neutralized) and/or generalizability (i.e., >1 threat protected against, such as multiple influenza strains) of PGM-MCMs for a variety of genomic targets and threats *in vitro* and/or *in vivo*. CD1 must be completed by Month 22. During Phase I, proposers must also draft a Target Product Profile (TPP) and engage with the appropriate regulatory bodies (e.g., FDA pre-pre-IND and/or EUA discussions) to inform PGM-MCM development and strategy for eventual clinical translation.

Phase II

PGM-MCM Development and Capability Demonstrations 2 and 3
Phase II will focus on optimizing and expanding the capabilities of the integrated PGM-MCM discovery and production platform. Proposers should continue to refine the integrated platform so that it may develop into a robust platform that can be readily tested to generate relevant PGM-MCMs to reduce host risk against a broad range of novel or emerging public health and national security threats. In order to demonstrate measurable progress against PREPARE program goals, proposers should conduct increasingly more challenging Capability Demonstrations – CD2 to be completed by Month 32 and CD3 to be completed by Month 40 – to demonstrate greater *in vivo* protection; increased formulation versatility; greater understanding of the mechanisms of

protection (MoPs) and failure; and thorough *in vivo* characterizations of PGM-MCM activity to include absorption, distribution, metabolism, and excretion (ADME), immunogenicity, and toxicity studies.

Regulatory Submission

Phase II should culminate in an IND or EUA submission to the FDA. Pre-IND or equivalent EUA interactions are anticipated during Phase II to inform PGM-MCM development and eventual clinical translation. Prior to the end of the program (Months 41 to 48), proposers should finalize all necessary IND/EUA submission requirements, data analysis, platform optimization, and plans for technology transition. Although pre-EUA activities may be pursued, they should not replace efforts to develop PGM-MCM products for FDA approval through IND pathways and, where possible, IND and EUA activities should proceed in parallel. Successful teams should advance their most promising final PGM-MCM products for a given threat(s) indication for IND and/or EUA submission to the FDA by the end of the program.

1.3. TECHNICAL AREAS, PLATFORM INTEGRATION, AND CAPABILITY DEMONSTRATIONS

TA1: GENE TARGET IDENTIFICATION

TA1 is focused on the identification and validation of: (a) endogenous host genes or druggable targets that, when modulated (e.g., up- or down-regulated), confer protection against the selected threats; and/or (b) viral genome targets for neutralization. Proposers must develop agnostic, genome-wide approaches (e.g., CRISPRa/i, etc.) to characterize host genomic, transcriptomic, epigenomic, and/or epitranscriptomic drivers of protection against the selected threats using high-throughput molecular and bioinformatic methodologies. Proposers must also provide insight into the dynamic range and minimum gene expression thresholds that must be achieved to confer host protection against threat(s). If relevant, proposers must also determine the gene regulatory elements that will enable gene modulation (e.g., promoters, enhancers). In the case of viral threats like influenza, it is anticipated that direct modulation and neutralization of the viral genome at one or more target sites may serve to further protect the host from this category of threat and reduce the likelihood of development of resistances or evolutionary escape. Similarly, exposure to health threats may result in a polygenic host protective response where ultimately the modulation of multiple gene targets (i.e., multiplex) may provide optimal protective response. Modulation of gene targets identified in TA1 should significantly improve physiological outcomes, including survival and reduction of pathologies following exposure to a threat. In addition to *de novo* data collection during TA1, proposers are encouraged to leverage and expand upon pre-existing human datasets and/or archived patient samples relevant to the pursued threat.

TA1 development should yield foundational data and should be staged such that preliminary screening and target validation may involve, but not require, *in vitro* experimentation prior to *in vivo* work in an appropriate animal model. To identify protective gene targets and optimal cell and tissue types, screening and validation against selected threat(s) may be performed: (a) *in vitro* in relevant organoid and/or microtissue/microphysiological culture systems that best approximate human physiology; and/or (b) *in vivo* in a threat-relevant healthy animal model. Use of cell cultures that are not representative of healthy cellular biology and physiology will require additional justification; proposals exclusively employing cancer cell lines for gene target discovery will be considered out of scope. Proposers must clearly indicate the approach to

determine baseline healthy gene expression states and protective gene expression ranges in a given *in vitro* or *in vivo* model, and methods to quantify perturbations to those states. It is critical that proposers ensure that protection from threats through modulation of the identified protective genes can be conferred while avoiding any toxic, immunogenic, carcinogenic, or otherwise adverse effects in healthy organisms.

Successful completion of TA1 activities should yield a component capability that can be used to scan genomes to identify genes that, when modulated, should protect a host against a given threat. By the end of month 12, proposers are expected to use the TA1 component capability to generate a prioritized list of protective candidate genes, relevant regulatory regions, target cell and tissue types, and gene target threshold and range of expression that must be reached in order to confer protection against the proposer-selected threat(s) to be tested in subsequent CDs. These key TA1 deliverables define the gene target(s) specifications that inform the draft TPP and integration with innovations from TA2 and TA3 in a synergistic manner and help refine performance metrics for PGM-MCMs *in vivo* beginning in Month 13.

TA2: PROGRAMMABLE GENE MODULATOR DEVELOPMENT

TA2 is focused on the design and development of PGMs that can be used preemptively or post-exposure to alter gene expression levels of target alleles to confer protection against (or directly neutralize) selected threat(s) *in vivo* in a manner that leaves primary DNA sequence intact and avoids life-long alteration of transcripts or gene expression patterns. As such, PGMs may include, *but are not limited to*: targeted DNA-binding protein scaffolds linked to transcriptional activators, repressors, and epigenetic modifiers; targeted RNA-nucleases; and RNA base editors. PGMs may also transiently alter the abundance or half-life of gene products or transcripts or the primary RNA sequence of a transcript itself for the desired effect.

Proposers must establish candidate PGM libraries of component parts and perform high-throughput, combinatorial screens to test PGMs in *in vitro* cell, organoid, and/or *in vivo* systems to determine optimal designs for programmable and controllable modulation of target genes across a broad dynamic range of expression (e.g., 2-fold to 10,000-fold) and duration of effect (e.g., hours to months). Proposers must validate PGM performance *in vivo.* Given that there are multiple ways in which optimal level and duration of gene modulation may be achieved (e.g., epigenetically, at the transcript level, through delivery formulation (see TA3 below), or combinations therein), proposers must clearly indicate how their PGM testing approach will enable the selection of the best and most robust approach among them to address both gene modulation level and duration challenges. Proposers are expected to leverage bioinformatic tools and models to expedite PGM design, development, and performance prediction. Proposers must clearly indicate how their selected PGM methodologies will address: gene target specificity; mitigation of risk for off-target effects; tunable control of gene modulation level and duration; ease of manufacture and scale-up; adaptation to new gene targets; and multiplexability and generalizability. Proposers must also assess and mitigate risk for intended downstream *in vivo* applications, including potential for pre-existing immunities and/or *de novo* immune response.

Successful completion of TA2 should yield a component capability that can be tested to determine the most appropriate molecular tools to modulate protective gene targets. By the end of month 12, proposers are expected to use the TA2 component capability to generate a

prioritized list of top candidate PGMs (sequence, format, etc.); an understanding of the mechanism of gene modulation (e.g., epigenetic, transcriptomic, etc.); and key PGM features including range and duration of gene modulation to enable effective, safe, transient, specific, and multiplexable modulation of target genes to confer protection against the selected threats to be tested in CD1. These key TA2 deliverables define the PGM specifications that inform the draft TPP and integration with innovations from TA1 and TA3 in a synergistic manner and help refine performance metrics for PGM-MCMs *in vivo* beginning in Month 13.

TA3: CLINICAL FORMULATIONS

TA3 is focused on developing novel clinical formulations to enable cell-, tissue-, and/or organ-specific delivery of PGMs to access gene targets that are protective against the selected threats. Proposers may pursue any delivery formulation including, *but not limited to*, viral vectors, lipid nanoparticles, polymer-based systems, mRNA, or completely novel formulations.

Proposers should generate high-throughput, combinatorial screens of delivery formulations for PGMs. Proposers are encouraged to either explore delivery in organoid, microtissue, 3D cell culture, or similar systems that may be more predictive of *in vivo* success while maintaining sufficient throughput for iterative optimization of a chosen clinical formulation or initiate studies directly *in vivo*. It is important to note that the cell and tissue context within which intrinsic gene-encoded host protections are activated may be as critical to the protective response as the genes themselves. Similarly, the "normal" spatial expression pattern of an endogenous threat-protective gene may not always correspond to the most optimal target for induction of preemptive or post-exposure protection. Therefore, proposers must describe the methods that will be employed to determine the optimal cell/tissue/organ targets for robust protective response. Proposers must validate delivery formulation performance *in vivo*, and are expected to leverage bioinformatic tools and models to expedite delivery formulation design and testing.

Proposers must clearly indicate how their selected delivery formulation approach will address, and mitigate risk for potential failure modes, such as immunogenicity (adaptive and pre-existing) that would interfere with re-administration/multi-dosing treatment regimens, endosomal escape, toxicity, lack of cell tropism diversity, suboptimal ADME kinetics, cargo size limitations, off-tissue effects, and ease of manufacture and scale-up.

Successful completion of TA3 should yield a component capability that can be tested to determine the most appropriate delivery formulations to access target cells and tissues for a given threat. By the end of month 12, proposers are expected to use the TA3 component capability to generate a prioritized list of top candidate delivery formulations to enable highly-specific PGM cargo delivery *in vivo* and optimal cell types, tissues, and organs for maximal threat protection through target gene modulation to be tested in CD1. These key TA3 deliverables define the delivery formulation specifications that inform the draft TPP and integration with innovations from TA1 and TA2 in a synergistic manner and help refine performance metrics for PGM-MCMs *in vivo*.

PLATFORM INTEGRATION AND CAPABILITY DEMONSTRATIONS

Beginning in Month 13, proposers are expected to address the topics below (in order of occurrence):

1. *Target Product Profile*: submit to DARPA a draft TPP for PGM-MCMs in development.
2. *Platform Integration*: integrate innovations from TA1, TA2, and TA3 components into a platform capability.
3. *Capability Demonstrations*: test integrated PGM-MCMs to protect against selected threats in 3 increasingly difficult CDs.
4. *PGM-MCM Characterization*: comprehensively evaluate and characterize PGM-MCM activity *in vivo* after each CD.

Target Product Profile:
PGM-MCM use cases should be specified in a draft TPP that states the overall intent, development process, and end specifications of the PGM-MCM. The draft TPP should include foundational knowledge established in Year 1 including gene target(s) specifications (TA1), PGM specifications (TA2), and delivery formulation specifications (TA3). Advantages of using a TPP early in the development process can facilitate the efficiency of FDA interactions and communications. A TPP helps focus the development of a product and can help address issues early on in the development process thereby preventing late-stage development failures and decreasing the total time involved with development. Early TPPs can be brief depending on the status of the development process.

Platform Integration:
Proposals must address how platform integration and optimization are expected to proceed from Months 13 through 48, including optimization steps, expected risks, and risk mitigation strategies. The component capabilities from TAs 1-3 should work as an integrated whole to generate PGM-MCMs. However, it is anticipated that various component development strategies may be re-visited at varying times throughout the program (e.g., following each Capability Demonstration) to optimize PGM-MCM performance and refine platform functionality. For example, following a given *in vivo* test, if a given PGM-MCM provides encouraging results, but does not reach performance targets for level of gene expression, proposers may revisit the TA2 programmable gene modulator component to identify PGM tools with an improved dynamic range of expression control and/or TA1 gene target identification component to identify improved target sequences (e.g., regulatory elements) that are supportive of higher levels of expression.

Capability Demonstrations:
PGM-MCM safety, efficacy, specificity, and transience ***must*** be tested *in vivo* in CDs. While proposers are encouraged to test PGM-MCM multiplexability (e.g., multiple targets) and generalizability (e.g., multiple threats) *in vivo* prior to the end of Phase I, *in vitro* proof-of-concept for these two criteria will fulfill program requirements during this period.

A series of three sequential CDs of increasing difficulty should be designed to test the ability of integrated PGM-MCMs to protect against selected threats prophylactically (pre-exposure or immediate post-exposure administration) and/or therapeutically (post-exposure administration) in healthy threat-relevant model organisms (**Figure 3**). It is intended that CDs follow design-test-learn-iterate principles where experimental outcomes and regulatory feedback from CD1 should inform design and implementation of CD2, and so on, to facilitate eventual clinical translation of

PGM-MCMs. Specific investigations of the mechanisms of protection (MoPs), failure modes, and a thorough *in vivo* characterization of PGM-MCMs and outcomes should be included at each CD in order to inform subsequent designs. CDs can begin at any time but must be completed by Month 22 (CD1), Month 32 (CD2), and Month 40 (CD3).

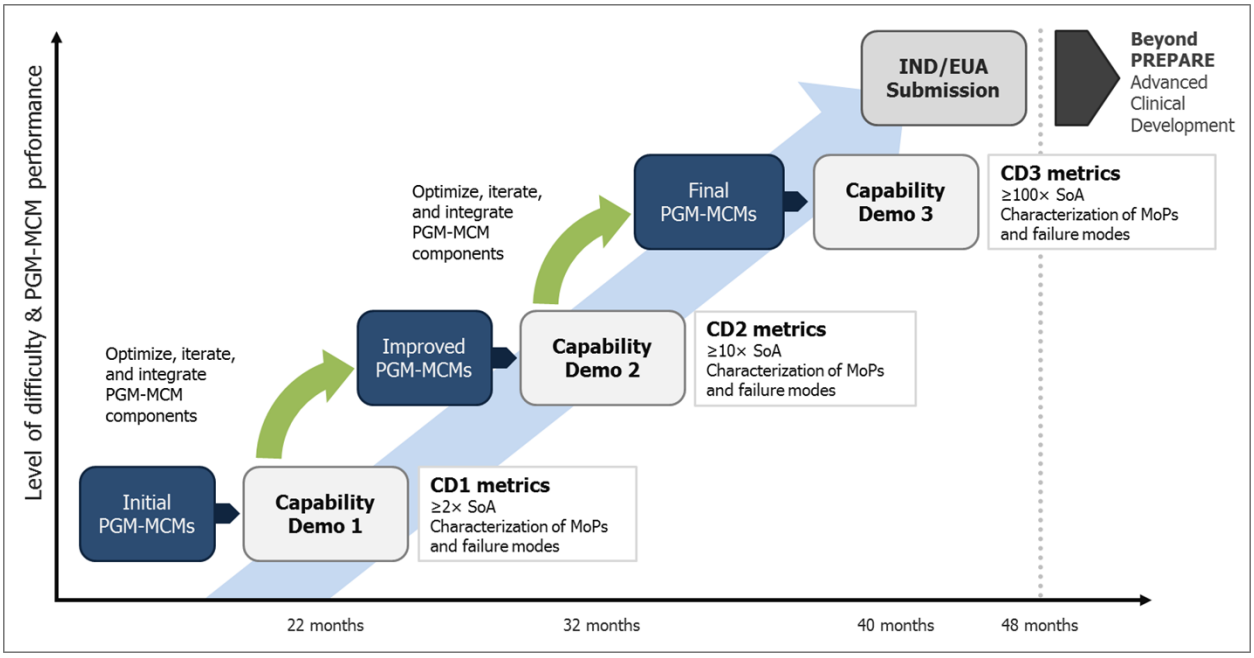

Figure 3 *PREPARE Capability Demonstrations*

For each CD, proposers must compare the performance of PGM-MCMs head-to-head against SoA MCMs for a given threat and must demonstrate improved performance compared to SoA MCMs (≥2× SoA for CD1; ≥10× SoA for CD2; ≥100× SoA for CD3) where improvement over SoA should focus on improvements in host functionality and survival, including, *but not limited to,* improved level of protection (e.g., survival rate), time to protection, breadth of threats covered (e.g., broad activity against multiple strains/universality), and/or duration of protection (e.g., months). For additional details regarding metrics, please see Section 1.4 PROGRAM METRICS.

For each successive CD of increasing difficulty, proposers are expected to demonstrate further utility of PGM-MCMs, which may include, but not be limited to:

- Increasing threat exposure dose while maintaining or improving protection and/or duration of protection
- Increasing number of PGM-MCM targets (e.g., multiple host genes, or host gene plus direct viral genome neutralization targets) for increased protection
- Expanding from one threat category (e.g., chemical) to multiple (e.g., chemical and radiological)

- Expanding from one threat to multiple threats within the same category (e.g., protection against multiple viral flu subtypes (e.g., A and B) or strains (e.g., H1N1, H3N2, H7N9, and H5N1) simultaneously)
- Increasing efficacy of existing MCMs, when used in combination with PGM-MCMs

PGM-MCM Characterization:
Throughout the Integration and Capability Demonstration activities that are anticipated during Months 13-48, in addition to assessment of survivability and duration of protection outlined above, proposers should pursue a comprehensive characterization of PGM-MCM activity *in vivo*. Proposers must demonstrate progress against intermediate performance and characterization goals and develop an increased understanding of the mechanisms, and potential failure modes, that underlie PGM-MCM activity *in vivo*. These intermediate assessments are expected to occur in parallel with the CDs and must increase in complexity and comprehensiveness with each subsequent program Phase and CD, including (but not be limited to) an understanding of the mechanisms of protection, failure modes, impact on symptomatology and pathology, measurement of ADME properties, toxicity, on- and off-target activity in host transcriptome, on- and off-tissue activity, immune response (pre-existing and adaptive). More specific examples include:

- Months 13 – 24/CD1: Characterization in Months 13-24 is focused on acute responses (minutes to hours). Proposers must further refine the kinetics of PGM-MCM modulation of protective host targets and establish a quantitative representation of system kinetics to include:
  - temporal requirements for modulation (ramp up and ramp down) and magnitude of activation/repression response;
  - measurement of on/off-target activity or toxicities at the level of the genome, transcriptome, and epigenome as well as the cell, tissue, and organ level;
  - ADME measurements over a minimum 24-hour period to understand system kinetics;
  - physiological responses, including immune responses (i.e., immune cell activation, inflammatory response, and cytokine release);
  - standard toxicology studies;
  - molecular and histological analyses of cellular targets and tissues;
  - behavioral responses to include waking, sleeping, feeding, grooming, etc.

  Proposers must assess, beyond survival/death, the impact of the PGM-MCM on all of the subcategories described above and syndromes relevant to the specific threat (s) investigated.
- Months 25 – 36/CD2: Characterization as above for Months 13 – 24 (acute responses), and additionally:
  - persistent responses (days – weeks);
  - route of administration;
  - dosage;
  - any requirements introduced through regulatory engagement.
- Months 37 – 40/CD3: Characterization as above for Months 13 – 36, and additionally chronic responses (months) and extensive longer-term toxicology studies, including:
  - genetic toxicology;
  - carcinogenicity;

- reproductive and developmental toxicity;
- any requirements introduced through regulatory engagement.

Data generated during intermediate characterizations and assessments should provide the basis for optimization and improvement in subsequent iterations of PGM-MCM design and implementation. Proposers must also not only quantitatively define and describe a method to measure duration and magnitude of protective response *in vivo*, but also demonstrate the transient nature of PGM-MCMs either passively through basal cellular processes or actively through self-contained timed reversal to return the system to a baseline state. Proposers may consider exogenous application of gene targets (i.e., gene-encoded or as biologics) to assist with determination of dosing regimens, etc.

FURTHER RECOMMENDATIONS FOR CBRN and PGM-MCM TESTING

Proposers ***must*** select a threat (influenza, opioid overdose/poisoning, organophosphate poisoning, or gamma radiation) that should remain consistent throughout their proposal to ensure the most cohesive and impactful program outcome. Additional national security or public health relevant threats may be explored in a limited manner in Phase I (e.g., *in vitro* demonstration only) to demonstrate the feasibility of generalizability and multiplexability of the PGM-MCM approach. If additional threats are proposed for investigation in a limited manner, appropriate technical justification, such as overlap in MoPs or simulation of real-world scenarios, must be included. Additional threat-specific recommendations are included below.

Influenza viruses:
Proposers pursuing the influenza viral threats ***must*** investigate the ability of PGM-MCMs to neutralize multiple influenza strains and sub-types to meet generalizability requirements for Phase I, but proposers may also pursue limited investigation (e.g., *in vitro* demonstration) of the ability to neutralize additional ssRNA viruses with clear national security relevance for additional demonstration of PGM-MCM platform capability. *De novo* synthesis or re-creation of eradicated viral threats or genesis of novel pathogens, or pathogens with increased transmission or pathogenicity, are not permissible under the PREPARE program. To identify improvements in the symptomatology, pathology, and understanding of mechanisms of protection (or failure), proposers should utilize assays, methods, and animal models appropriate to the investigation of influenza to quantify relevant exposure phenomena such as viremia, anti-viral cytokine profiles, host transcriptomic responses, transmission, etc.

Opioids and organophosphates:
If opioids are selected as a threat target, proposers should focus on mitigating the toxic effects of opioids (e.g., respiratory depression, increasing metabolic turnover) or developing non-opioid approaches to pain management. Development of non-addictive pain solutions in general or treatments for addiction is considered out of scope for the PREPARE program. To identify improvements in the symptomatology, pathology, and understanding of mechanisms of protection (or failure), proposers should utilize assays and methods appropriate to the threat(s) chosen to quantify relevant exposure phenomena such as serum levels of metabolites or enzymatic activity, respiratory rate, opioid receptor occupancy, etc.

Gamma radiation:

It is highly encouraged that proposers assess increasing doses of total body irradiation (e.g., 0.5 to 10 Gy) to identify gene targets that may confer radiation protection using a proposer-chosen radiation source that can recapitulate radiation exposure relevant for therapeutic radiation uses or occupational exposures. Proposers should quantitatively define and provide technical justification for the screening doses and timing of PGM-MCM intervention, and indicate how the selected approach relates to public health and national security need. To identify improvements in the symptomatology, pathology, and understanding of mechanisms of protection (or failure), proposers should utilize assays and methods appropriate to the radiological exposure chosen to quantify physiological phenomena such as, measurement of hematopoietic response, DNA damage, cell death, cognitive impairment, and other physiological changes associated with Acute Radiation Sickness (ARS) subsyndromes (gastrointestinal, hematopoietic, and neurovascular syndromes) or Delayed Effects of Acute Radiation Exposure (DEARE).

Animal models:
For each threat type, proposers must identify an animal model used in each CD, and relevance to downstream human clinical translation. Proposers must provide technical justification as to why the model is appropriate for the chosen threat type (e.g., mode and magnitude of exposure, citation of literature supporting MCM development for specified threat using the model with physiological and molecular responses relevant to human exposure). Furthermore, it is expected that animal models used in the CDs are healthy, wildtype organisms. Proposers may use transgenic organisms, such as reporter lines, but must clearly articulate how the transgenic features do not interfere or bias results or responses to the selected threat.

1.4. **PROGRAM METRICS**

In order for the Government to evaluate the effectiveness of a proposed solution 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. Note that individual metrics for TA1, TA2, and TA3 must be met by Month 13, while all other metrics refer to the remainder of the program.

Quantitative performance metrics are expected to vary for each proposer-selected threat area and system. Proposers to the PREPARE program are required to define ambitious, specific, and quantitative metrics in support of program goals, including intermediate metrics (e.g., every six months or sooner) to help further evaluate progress. Some exemplary milestones and metrics are included below for proposers to consider, but proposers should adjust accordingly for their given threat and system. Final metrics are to be determined at time of award negotiation and are subject to DARPA approval. Proposers should note that program metrics may serve as the basis for determining whether satisfactory progress is being made to warrant continued funding of the program.

Throughout the course of the program, proposers must compare the performance of PGM-MCMs head-to-head against SoA MCMs for a given threat and must demonstrate improved performance

that increases over time with each subsequent Capability Demonstration: ≥2× SoA for CD1; ≥10× SoA for CD2; ≥100× SoA for CD3. Performance metrics should focus on improvements in host functionality and survival, including, *but not limited to,* the following categories:

- level of protection/survivability (e.g., survival rate)
- improved survivability at increased threat exposures/doses
- time to protection from MCM administration
- time window for effective treatment (i.e., time window between threat exposure and administration of MCM with maximal efficacy)
- breadth of threats covered at maximum protection (e.g., broad activity against multiple strains/universality)
- duration of protection (e.g., months)

Proposers must clearly indicate their target performance metrics for each CD. These metrics must describe the SoA MCM that will be used to benchmark performance, must define, in quantitative and qualitative terms, what is considered threat "protection" *in vivo*, and describe how it will be measured (e.g., target serum concentration of protective gene product detected for threat-relevant duration). **Successful completion of all CDs should yield a PGM-MCM with at least 100× improved performance *in vivo* over SoA for a given threat agent in at least one performance category.**

Table 1 below is exemplary of proposed performance metrics relative to SoA MCMs that must be provided by each proposer team. Additional program metrics appear in Tables 2-5. Proposers may select more than one performance category to exceed SoA MCMs, but must meet *at least* one performance category at ≥2× SoA for CD1; ≥10× SoA for CD2; ≥100× SoA for CD3. Teams that propose PGM-MCM solutions that exceed 2×, 10×, and 100× SoA for more than one performance category will be viewed more favorably. The category(s) selected should remain consistent throughout the course of the program, and may include, but are not limited to:

Table 1 – Performance Metrics Examples

			CD1 ≥2× SoA	**CD2** ≥10× SoA	**CD3** ≥100× SoA
Threat	**Performance Category**	**SoA MCM**	**Initial Therapeutic PGM-MCMs**	**Improved Therapeutic PGM-MCMs**	**Final Therapeutic PGM-MCMs**
Influenza example (Treatment)	Duration of Protection	Neuraminidase inhibitor/antiviral (e.g., oseltamivir)	20 hr serum half-life/duration of protection	100 hr serum half-life/duration of protection	1,000 hr serum half-life/duration of protection
		1 – 10 hr serum half-life			
Influenza example (Prophylaxis)	Breadth of Threats Covered	Seasonal Flu Vaccine	6 strains	30 strains	300 strains
		3 – 4 strains protection			

Opioid example (Treatment)	Duration of Protection	Competitive opioid receptor antagonist (e.g., naloxone) ~1 hr serum half-life	2 hr serum half-life/duration of protection	20 hr serum half-life/duration of protection	200 hr serum half-life/duration of protection
Organophosphate example (Treatment)	Duration of Protection	Muscarinic cholinergic receptor antagonist (e.g., atropine) 3 hr serum half-life	6 hr serum half-life/duration of protection	30 hr serum half-life /duration of protection	300 hr serum half-life/duration of protection
Gamma radiation example (Treatment)	Administration Efficacy Time Window	Hematopoietic colony-stimulating factor (e.g., G-CSF) <2 hr post-exposure	<4 hr post-exposure	<20 hr post-exposure	<200 hr post-exposure

Table 2 – TA1 metrics

TA1: Gene Target Identification (Months 1-12)	
Milestones and Deliverables	**Program Metrics**

• Perform high-throughput, agnostic screens to identify gene targets and regulatory elements that confer protection (or enable neutralization) against selected threat(s)
• Identify gene expression range of gene modulation required for each protective allele target(s) to confer protection against selected threat(s)
• Establish bioinformatics pipeline to receive and analyze omics data generated during threat screening and/or from pre-existing datasets
• Identify target cells/tissues and/or organs that confer optimal protection when gene targets are modulated
• *Key deliverables:*
  ○ Component ready for integration
  ○ Gene target specifications and performance metrics for *in vivo* PGM-MCM testing and validation in Years 2-4 for *in vivo* PGM-MCM testing and validation, to include: prioritized list of candidate protective gene targets and sequences and gene regulatory regions, target range of gene
	Proposers must define quantitative performance metrics for:
	• Criteria for selection and prioritization of protective gene targets, tissues, and modulation activity
	• Efficacy: e.g., level of protection and increased survival
	• Safety: e.g., non-toxic, non-carcinogenic when modulated
	• Specificity: e.g., no collateral off-target or off-tissue effects

expression that confers protection, and optimal cells and tissues for target modulation.	

Table 3 – TA2 metrics

TA2: Programmable Gene Modulator Development (Months 1-12)	
Milestones and Deliverables	**Program Metrics**

• Establish candidate PGM libraries of component parts that are modular, adaptable, multiplexable, and easily manufactured
• Perform high-throughput, combinatorial screens to test PGMs in *in vitro* cell, organoid, and/or *in vivo* systems
• Establish bioinformatics pipeline to receive and analyze omics data generated during PGM screening and development
• Plan describing the PGM component designs aligned with simple and rapid production and scale-up (e.g., tens to millions of doses in <1 week)
• *Key deliverables:*
  ○ Component ready for integration
  ○ PGM specifications and performance metrics for *in vivo* PGM-MCM testing and validation in Years 2-4, to include: prioritized PGM designs (sequence, format, etc.); mechanism of gene modulation, range of gene modulation control, duration of gene modulation control for targets
	Proposers must define quantitative performance metrics for:
	• Efficacy: e.g., dynamic range of gene modulation control (e.g., 2-fold to 10,000-fold) and duration (e.g., 30 days)
	• Safety: e.g., no toxicity or immunogenicity (pre-existing or adaptive)
	• Specificity: e.g., modulates only selected gene targets, active only in desired tissue type
	• Multiplexability & generalizability: e.g., modular design enables modulation new or multiple targets

Table 4 – TA3 metrics

TA3: Clinical Formulations (Months 1-12)	
Milestones and Deliverables	**Program Metrics**
• Perform high-throughput, combinatorial screens with delivery formulations *in vivo* or in an appropriate cell, organoid, or tissue system *in vitro* • Establish bioinformatics pipeline to receive and analyze omics data generated during clinical formulation screening • Demonstrate delivery formulations that deliver PGM cargo and target intended cell, tissue, organs *in vivo* • Plan describing the clinical formulation designs aligned with simple and rapid	Proposers must define quantitative performance metrics for: • Efficacy: e.g., delivers cargo at sufficient quantities and duration to facilitate modulation and confer protection • Capacity: e.g. capable of packaging PGMs (e.g., >10 kb, >200 kDa) • Safety: e.g., no toxicity or immunogenicity either pre-existing or induced by the clinical formulation; no effects on overall animal health • Specificity: e.g., no off-tissue delivery

production and scale-up (e.g., tens to millions of doses in <1 week)
• *Key deliverables:*
  o Component ready for integration
  o Delivery formulation specifications and performance metrics for *in vivo* PGM-MCM testing and validation in Years 2-4 for *in vivo* PGM-MCM testing and validation, to include: prioritized delivery formulations that efficiently, safely, and specifically deliver PGMs to target cells, tissues, and organs	

Table 5 – Demonstration metrics

Platform Integration & Capability Demonstrations (Months 13 - 48)	
Milestones and Deliverables	**Program Metrics**

• Generate draft Target Product Profile (Mo 13)
• Integrate TA1, TA2, and TA3 innovations (Mo 24)
• Demonstrate multiplexability (>1 target modulated) and generalizability (>1 threat protected against) of PGM-MCMs *in vitro* and/or *in vivo* (Mo 24)
• Engage regularly in informal pre-pre-IND/EUA (Mo 24) and formal pre-IND/EUA (Mo 36) discussion with the FDA in preparation for IND/EUA submission
• Demonstrate efficacy, safety, specificity, and transience of PGM-MCMs in CDs 1, 2, and 3
• Characterization of the mechanisms of protection and failure modes for each PGM-MCM *in vivo* for each CD
• Complete all pre-IND/EUA submission requirements and submit MCM IND/EUA to FDA (Mo 48)
• *Final program deliverables:*
  o PGM-MCM with 100× improvement over SoA MCM
  o Defined Target Product Profile and use case for an IND/EUA submission
  o IND/EUA or equivalent submission for corresponding PGM-MCM
	Proposers must define quantitative performance metrics for each metric category below for each Capability Demonstration (CD):
	• Efficacy: e.g., protection (i.e. survival) against increasingly more difficult threats delivered prophylactically (pre- or post-exposure prophylaxis) or therapeutically (post-exposure treatment) exceeding SoA MCMs for threat relevant duration
	  o CD1: ≥2× SoA MCM
	  o CD2: ≥10× SoA MCM
	  o CD3: ≥100× SoA MCM
	• Safety: e.g., no adverse effects in a healthy animal model, including toxicity, immunogenicity, overall health effects, etc.
	• Specificity: e.g., activity only at desired targets with no off-target or off-tissue effects
	• Transience: e.g., sustained *in vivo* protection before return to a wildtype state (i.e. no life-long modulation effect and ADME)
	• Manufacturability: e.g. PGM-MCM design and formulation compatible with simple and rapid production and scale-up (e.g., tens to millions of doses in less than 1 week)
	
	Characterization: Proposers must demonstrate that the specifications and metrics established at the end of Year 1 component development (i.e., draft TPP) should be demonstrated and achieved in Years 2-4 as part of a complete characterization and performance assessment of PGM-MCMs *in vivo*, including:
	
	• Gene Target(s): prioritized PGM designs (sequence, format, etc.); mechanism of gene

	modulation, range of gene modulation control, duration of gene modulation control for targets • Programmable Gene Modulator: prioritized PGM designs (sequence, format, etc.); mechanism of gene modulation, range of gene modulation control, duration of gene modulation control for targets • Clinical Formulations: prioritized delivery formulations that efficiently, safely, and specifically deliver PGMs to target cells, tissues and organs • Any other additional characterization or measurement as required by regulators

1.5. GENERAL REQUIREMENTS

In addition to the requirements above, proposers to the PREPARE program must address each of the following:

Teaming

Proposers are responsible for assembling a complete team that has technical expertise, capabilities, and facilities to address all requirements of the program. Proposers must address all three technical areas 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 platform for PGM-MCM production, but also have the ability to test PGM-MCMs in CDs with the selected threats in threat-relevant animal models at appropriate BSL/containment levels. It is also essential that proposer teams include members that have industrial and commercial experience to aid in focusing technology research and development strategy for eventual clinical translation. This could include, for example, expertise in medical product development and 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.

Informatics and Data Sharing

DARPA anticipates that a large amount of data will be generated under this program by each proposer, and the PREPARE program will require that information be shared with DARPA and US Government stakeholders. It is anticipated data analyses will be strengthened by compiling and integrating information across all teams, and while teams are encouraged to share their data with other PREPARE teams and the broader research community, it is not required. Proposers must include the description of a plan to provide data to DARPA, approximate timelines for release of data, types and formats of (meta)data, and total estimated data sizes. Academic

proposers considered to be conducting fundamental research on this program on campus may publish papers describing scientific or engineering advances that are general in nature and adhere to the above guidance. Should the character of the research change during award performance so that the research is no longer considered fundamental, the award will be modified to impose the restrictions on public release and dissemination of information that apply to those research efforts that are no longer considered fundamental research. For additional information on fundamental research, please see Section 2.2. Non-academic proposers shall submit any publications to DARPA's Public Release Center (DARPA/PRC) to process for pre-publication review. All proposers desiring to publish papers that may contain Controlled Unclassified Information (see below) shall submit them in advance in accordance with contractual requirements.

Controlled Unclassified Information (CUI)
To prevent the release of sensitive technical information, certain aspects of the proposed research may be considered CUI if they reveal host susceptibilities to threats or other vulnerabilities, and may require safeguarding or dissemination controls, pursuant to and consistent with applicable law, regulations, and government-wide policies. Proposals that anticipate the production of any such information must deliver a detailed risk mitigation plan to DARPA (see Section 4.2.2. Proposal Format Section II: I). Performers must partition potentially sensitive tasks from non-sensitive research efforts. All performers (prime contractor and subcontractor) desiring public release of project information that may contain CUI as defined above must submit a request for public release from DARPA/PRC in accordance with their contractual requirements.

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 genome modulation. Industry proposers that are considering the development of PGM-MCM solutions to address opioid challenges should additionally consider the following ethical considerations for industry partnerships in this space: https://acd.od.nih.gov/documents/presentations/032018_opioids-draft-report.pdf.

Regulatory Strategy
Proposers must present a detailed plan for early and continued engagement with regulators (e.g., FDA) throughout the program to discuss developing technologies and challenges in order to meet the program regulatory milestones (IND/EUA processes described above), to inform and improve the design of CDs during the program, and to facilitate the eventual translation of the tools generated for clinical use. Ideally, proposers will identify the applicant for the IND/EUA submission at the time of proposal submission. In addition, although pre-EUA activities may be pursued, they should not replace efforts to develop PGM-MCM products for FDA approval through IND pathways and, where possible, IND and EUA activities should proceed in parallel. It is anticipated that some of the biologics developed under this program may qualify for the FDA Animal Rule. IND/EUA submission must be for a threat-relevant indication.

Transition Strategy
Proposers must present a detailed plan for clinical translation and transition of the technologies developed under the program for advanced development. It is anticipated that the PREPARE platform and PGM-MCMs will be suitable for advanced development and licensing for many high impact applications in National Security, global health, and pharmaceutical development. It is critical that PREPARE platform technologies and PGM-MCMs be developed to combat threat(s) in a manner that positions them for clinical translation and generalizability by the end of the program to realize specific public health and national security benefit.

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.

- End of Phase reports: At the end of Phase 1 , 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 can be reasonably conveyed to academic reviewers.
- 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: The 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 PREPARE program.
- Any additional deliverables requested by the Contracting agent for this program (SPAWAR).

2. Award Information

2.1. GENERAL AWARD INFORMATION

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

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

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

Proposers looking for innovative, commercial-like contractual arrangements are encouraged to consider requesting Other Transactions. To understand the flexibility and options associated with Other Transactions, consult http://www.darpa.mil/work-with-us/contract-management#OtherTransactions.

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

2.2. FUNDAMENTAL RESEARCH

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

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

As of the date of publication of this BAA, the Government expects that program goals as described herein may be met by proposers intending to perform fundamental research and proposers not intending to perform fundamental research or the proposed research may present a high likelihood of disclosing performance characteristics of military systems or manufacturing technologies that are unique and critical to defense. Based on the nature of the performer and the nature of the work, the Government anticipates that some awards will include 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 select award instrument type and to negotiate all instrument terms and conditions with selectees. Appropriate clauses will be included in resultant awards for non-fundamental research to prescribe publication requirements and other restrictions, as appropriate. This clause 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 being performed by the awardee is restricted research, a subawardee may be conducting fundamental research. In those cases, it is the awardee's responsibility to explain in their proposal why its subawardee's effort is fundamental research

3. Eligibility Information

3.1. ELIGIBLE APPLICANTS

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

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

FFRDCs

FFRDCs are subject to applicable direct competition limitations and cannot propose to this BAA in any capacity unless they meet the following conditions: (1) FFRDCs must clearly

demonstrate that the proposed work is not otherwise available from the private sector. (2) FFRDCs must provide a letter on official letterhead from their sponsoring organization citing the specific authority establishing their eligibility to propose to Government solicitations and compete with industry, and their compliance with the associated FFRDC sponsor agreement's terms and conditions. This information is required 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.

Authority and Eligibility

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

3.1.2. Non-U.S. Organizations

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

3.2. ORGANIZATIONAL CONFLICTS OF INTEREST

FAR 9.5 Requirements

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

Agency Supplemental OCI Policy

In addition, DARPA has a supplemental OCI policy that prohibits contractors/performers from concurrently providing Scientific Engineering Technical Assistance (SETA), Advisory and Assistance Services (A&AS) or similar support services and being a technical performer. Therefore, as part of the FAR 9.5 disclosure requirement above, a proposer must affirm whether the proposer or *any* proposed team member (subawardee, consultant) is providing SETA, A&AS,

or similar support to any DARPA office(s) under: (a) a current award or subaward; or (b) a past award or subaward that ended within one calendar year prior to the proposal's submission date.

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

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

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

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

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

3.3. COST SHARING/MATCHING

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

For more information on potential cost sharing requirements for Other Transactions for Prototype, see http://www.darpa.mil/work-with-us/contract-management#OtherTransactions

3.4. OTHER ELIGIBILITY CRITERIA - COLLABORATIVE EFFORTS

It is anticipated that successful proposals will be comprised of multi-disciplinary teams, and that successful implementation will likely require academic and industrial collaborations. Teams may be led by industrial, academic, or non-profit entities, among others. It is expected that the proposed leadership team will include individuals with significant experience and expertise in directing operations and technology development, leading large and diverse teams with both academic and industrial partners, and have significant experience in the research and development of biologics for clinical use.

Proposers are expected to identify industrial and commercial partners to aid in focusing technology research and development strategy for eventual clinical translation. Proposed efforts

should be fully integrated and demonstrate that all components are necessary and inseparable. Disjointed efforts submitted under a single proposal will be considered nonresponsive. Proposers should provide justification for inclusion of any core team members that will not be co-located with the center (e.g., live threat agent testing facilities) and provide a clear plan for how they will be fully integrated into the project.

Successful proposals will tightly couple any proposed computational tool development with experimental work. Successful teams will include expertise in both theoretical and experimental science and technology, for example, in fields of biology relevant to the proposed threat(s), programmable gene modulator system(s), delivery system(s), model organism testing and evaluation systems, bioinformatics and modeling strategies, and regulatory strategy, among others.

DARPA will facilitate a Proposers Day (see Section 8.3 below) to encourage the formation of teams with the expertise necessary to meet the goals of the program and enable sharing of information among interested proposers through fbo.gov and the Proposers Day registration website.

DARPA requires that all teaming arrangements be resolved before proposal submission. Specific content, communications, networking, and team formation are the sole responsibility of the proposers. Teams/collaborative efforts must submit a single, integrated proposal led by a single Principal Investigator (PI) or prime contractor. Proposers may join any number of teams as a subcontractor and still submit a separate proposal as the PI (with or without subcontractors). In all cases, collaborating team members must submit a unified proposal.

4. Application and Submission Information

4.1. ADDRESS TO REQUEST APPLICATION PACKAGE

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

4.2. CONTENT AND FORM OF APPLICATION SUBMISSION

All submissions, including abstracts and proposals, must be written in English with type not smaller than 12-point font. Smaller font may be used for figures, tables, and charts. 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 highly 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 30 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. The cover sheet and (optional) submission letter is not included in the page count. All pages shall be formatted for printing on 8-1/2 by 11-inch paper with font size not smaller than 12-point. Smaller font sizes may be used for figures, tables, and charts.

Submissions must be written in English.

The page limit does NOT include:

1. Official transmittal letter (optional);
2. Cover sheet;
3. Executive summary slide;
4. Specific program plan;
5. Resumes; and
6. Bibliography (optional).

Abstracts must include the following components:

A. **Cover Sheet** (LABELED "ABSTRACT"):

1. BAA number (HR001118S0037);
2. Lead organization (prime contractor);
3. Other team members/subcontractors (if applicable);
4. Proposal Abstract title;
5. Technical point of contact (Program Manager or Principle Investigator) to include: salutation, last name, first name, street address, city, state, zip code, telephone, fax, email;
6. Administrative point of contract to include: salutation, last name, first name, street address, city, state, zip code, telephone, fax, e-mail;
7. Estimated cost; and
8. Estimated period of performance

B. **Executive Summary**: Clearly describe what is being proposed and what difference it will make (qualitatively and quantitatively), including brief answers to the following questions:
   1. What are you trying to 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 state of the art?
   4. Who will care and what will the impact be if you are successful?
   5. How much will it cost and how long will it take?

C. **Executive Summary Slide**: (does not count towards page limit): Provide a one-slide summary in PowerPoint that effectively and succinctly conveys the information requested in the slide template provided as **Attachment 1**. Use of this template is required.

D. **Specific Program Plan**: (does not count towards page limit): Provide a summary list of technical information as requested in **Attachment 2**. Use of this Excel template is required.

E. **Technical Plan**: Outline and address all technical challenges inherent in the approach and possible solutions for overcoming potential problems in each TA as well as Capability Demonstrations, and platform integration. This section should provide appropriate specific milestones (quantitative) at intermediate stages of the project to demonstrate progress and a brief plan for accomplishment of the milestones. In addition:

1. Describe and justify the choice of threat(s), PGM-MCM design, and experimental animal models, demonstrating relevance to public health and national security.
2. Describe and justify the experimental approach for each TA and for each Capability Demonstration, to include programmable gene modulators employed, threat(s) investigated, and relevant animal model(s) to be pursued.
3. Describe the methods for assaying threat protection mediated by PGM-MCMs *in vitro* and/or *in vivo*, and plan for comparison against SoA MCMs for a given threat.
4. Provide qualitative and quantitative metrics and milestones that will be used to measure progress against program goals, including a detailed strategy to integrate gene targets, programmable gene modulators, and delivery formulation into a platform capability to generate novel PGM-MCMs and quantitative metrics of how successful integration will be measured, including bioinformatics pipeline.
5. Outline a plan for FDA engagement, culminating in an IND or EUA submission by the end of the program.
6. Outline a plan for technology transition for continued advanced development during the program, and following completion of the program.

F. **Capabilities and Management**: Provide a brief summary of expertise of the team, including subcontractors and key personnel. It is expected that proposals will involve multidisciplinary teams that include expertise from multiple complementary disciplines, for example, synthetic biology, computational biology, bioinformatics, etc.

A principal investigator for the project must be identified, and a description of the team's organization for each TA. The team will be responsible for technology integration. 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. No more than two resumes should be included as part of the abstract.

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

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

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

H. **Resumes** (do not count towards page limit): Include (no more than 2) resumes of key team members.

I. **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 pages shall be printed on 8-1/2 by 11-inch paper with type not smaller than 12-point. Smaller font may be used for figures, tables, and charts. The page limitation for full proposals includes all figures, tables, and charts. 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.** A submission letter is optional and is not included in the page count. Volume I should include the following components:

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

a. Volume I, Technical and Management Proposal

Section I. Administrative

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

1. BAA number (HR001118S0037);
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 Principal 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 Grant 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, firm-fixed-price, cooperative agreement, Other Transaction, or other type (specify);
10. Place(s) and period(s) of performance;
11. Proposal validity period;
12. Total funds requested from DARPA, and the amount of cost share (if any); AND
13. Date proposal was submitted.

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

B. Official Transmittal Letter.

C. Executive Summary Slide: Provide a one-slide summary in PowerPoint that effectively and succinctly conveys the main objective, key innovations, expected impact, and other unique aspects of the proposed project. The slide template is provided as **Attachment 1**. Use of this template is required.

D. Specific Program Plan: (does not count towards page limit): Provide a summary list of technical information as requested in **Attachment 2**. Use of this Excel template is required.

Section II. Detailed Proposal Information

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

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

B. Goals and Impact: Clearly describe what the team is trying to achieve and the difference it will make (qualitatively and quantitatively) if successful. Describe the innovative aspects of the project in the context of existing capabilities and approaches, clearly delineating the uniqueness and benefits of this project in the context of the state of the art, alternative approaches, and other projects from the past and present. Describe how the proposed project is revolutionary and how it significantly rises above the current state of the art. Describe the deliverables associated with the proposed project and any plans to commercialize the technology, transition it to a customer, or further the work.

C. Technical Plan: Outline and address technical challenges inherent in the approach and possible solutions for overcoming potential problems. This section should provide appropriate measurable milestones (quantitative if possible) at intermediate stages of the program to demonstrate progress and a plan for achieving the milestones. The technical plan should demonstrate a deep understanding of the technical challenges and present a credible (even if risky) plan to achieve the program goal. Discuss mitigation of technical risk.

D. CUI Risk Mitigation Plan: (Required for proposers who anticipate generating work that may be considered CUI in accordance with "Controlled Unclassified Information" in Section 1.5): Provide a detailed plan for how the organization and its subcontractors will meet CUI safeguarding requirements. The plan should provide a detailed strategy to protect CUI without unnecessarily compartmentalizing information flow within or among performer teams. This plan must describe safeguard procedures for generating sensitive program deliverables (e.g., identified host genes and methodologies that yield insights into host resistance or susceptibilities to threats).

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

F. Capabilities: Provide a brief summary of expertise of the team, including subcontractors and key personnel. It is expected that proposals will involve multidisciplinary teams that include expertise from multiple complementary disciplines, for example, gene editing, chemistry, physiology, computational biology, bioinformatics, regulatory experience, etc.

A principal investigator for the project must be identified, and a description of the team's organization for each TA. The team will be responsible for technology integration. 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.

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

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

G. Statement of Work (SOW): 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. The SOW must not include proprietary information. The task structure must be consistent with that in Section G. Schedule and Milestones and Volume II Cost Proposal summary of program costs by phase, TA and task. The Government encourages proposers to complete an editable MS Word document, and this template document is provided as **Attachment 3** to this BAA. If you choose to use Attachment 3, submit the MS Word document template in addition to Volume I and II of your proposal.

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 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.

It is recommended that the SOW be developed so that each Technical Area and Phase of the program is separately defined.

Do not include any proprietary information in the SOW.

H. Schedule and Milestones: Provide a detailed schedule showing tasks (task name, duration, work breakdown structure element as applicable, performing organization), milestones, and the interrelationships among tasks. The task structure must be consistent with that in the SOW. Measurable milestones should be clearly articulated and defined in time relative to the start of the project.

I. Technology Transfer Plan: Proposers must present a detailed plan for clinical translation and transition of the technologies developed under the program for advanced

development. The PREPARE platform and PGM-MCMs will be suitable for advanced development and licensing for many high impact applications in National Security, global health, and pharmaceutical development. It is critical that PREPARE platform technologies and PGM-MCMs be developed to combat threat(s) in a manner that positions them for clinical translation and generalizability by the end of the program to realize specific public health and national security benefit.

Section III. Additional Information (Note: Does not count towards page limit)

A resume or biosketch is required for key personnel.

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") with Appendix I:

1. BAA number (HR001118S0037);
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 Grant 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) and period(s) of performance;
11. Total proposed cost separated by basic award and option(s) (if any);
12. Name, address, and telephone number of the proposer's cognizant Defense Contract Management Agency (DCMA) administration office (*if known)*;

13. Name, address, and telephone number of the proposer's cognizant Defense Contract Audit Agency (DCAA) audit office (*if known*);
14. Date proposal was prepared;
15. DUNS number (http://www.dnb.com/get-a-duns-number.html);
16. Taxpayer ID number (https://www.irs.gov/Individuals/International-Taxpayers/Taxpayer-Identification-Numbers-TIN);
17. CAGE code (https://cage.dla.mil/Home/UsageAgree); and
18. Proposal validity period.

Note that nonconforming proposals may be rejected without review.

Proposers that do not have a Cost Accounting Standards (CAS) compliant accounting system considered adequate for determining accurate costs that are negotiating a cost- type procurement contract must complete an SF 1408. For more information on CAS compliance, see http://www.dcaa.mil/cas.html. To facilitate this process, proposers should complete the SF 1408 found at http://www.gsa.gov/portal/forms/download/115778 and submit the completed form with the proposal. To complete the form, check the boxes on the second page, then provide a narrative explanation of your accounting system to supplement the checklist on page one. For more information, see (http://www.dcaa.mil/Home/Preaward).

The Government encourages proposers to complete an editable MS excel budget template that covers items 1.a, 1.d, 3, 4, 5, and 6 discussed below. This template document is provided as Attachment 4 to this BAA. If you choose to use **Attachment 4**, submit the MS Excel template in addition to Volume I and II of your proposal. Volume II must include all other items discussed below that are not covered by the editable MS excel budget template. Proposers are welcome to utilize an alternative format, provided the information requested below is clearly and effectively communicated.

(1) Total program cost broken down by major cost items to include:
   i. Direct Labor – Including individual labor categories with associated labor hours and direct labor rates. If selected for award, be prepared to submit supporting documentation to justify labor rates. (i.e., screenshots of HR databases, comparison to NIH or other web-based salary database);
   ii. Consultants – If consultants are to be used, proposer must provide a copy of the consultant's proposed SOW as well as a signed consultant agreement or other document which verifies the proposed loaded daily / hourly rate, hours and any other proposed consultant costs (e.g., travel);
   iii. Indirect Costs – Including Fringe Benefits, Overhead, General and Administrative Expense, Cost of Money, Fee, etc. (must show base amount and rate), if available, provide current Forward Pricing Rate Agreement or Forward Pricing Rate Proposal. If not available, provide 2 years historical data to include pool and expense costs used to generate the rates. For academia, provide DHHS or ONR negotiated rate package or, if calculated by other than a rate, provide University documentation identifying G&A and fringe costs by position;
   iv. Travel – Provide the purpose of the trip, number of trips, number of days per trip, departure and arrival destinations, number of people, estimated rental car and

airfare costs, and prevailing per diem rates as determined by gsa.gov, etc.; Quotes must be supported by screenshots from travel websites;

v. Other Direct Costs – Itemized with costs including tuition remission, animal per diem rates, health insurance/fee; back-up documentation is to be submitted to support proposed costs;

vi. Equipment Purchases – Itemization with individual and total costs, including quantities, unit prices, proposed vendors (if known), and the basis of estimate (e.g., quotes, prior purchases, catalog price lists, etc.); any item that exceeds $5,000 must be supported with back-up documentation such as a copy of catalog price lists or quotes prior to purchase (NOTE: For equipment purchases, include a letter stating why the proposer cannot provide the requested resources from its own funding), and;

vii. Materials – Itemization with costs, including quantities, unit prices, proposed vendors (if known), and the basis of estimate (e.g., quotes, prior purchases, catalog price lists, etc.); any item that exceeds $5,000 must be supported with back-up documentation such as a copy of catalog price lists or quotes prior to purchase.

(2) A summary of major program tasks by Government Fiscal Year (GFY = Oct 1 – Sep 30)
(3) A summary of total program costs by phase, TA and task;
(4) A summary of projected funding requirements by month;
(5) 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;
(6) An itemization of Subcontracts. All subcontractor cost proposal documentation must be prepared at the same level of detail as that required of the prime. Details may be submitted in the format of the editable MS excel spreadsheet in Attachment 4. 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);
(7) The source, nature, and amount of any industry cost-sharing. 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;
(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); and
(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.

4.2.3. Additional Proposal Information

Proprietary Markings

Proposers are responsible for clearly identifying proprietary information. Submissions containing proprietary information must have the cover page and each page containing such information clearly marked with a label such as “Proprietary” or “Company Proprietary.” NOTE: “Confidential” is a classification marking used to control the dissemination of U.S. Government

National Security Information as dictated in Executive Order 13526 and should not be used to identify proprietary business information.

Unclassified Submissions

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

Human Research Subjects/Animal Use

Proposers that anticipate involving Human Research Subjects or Animal Use must comply with the approval procedures detailed at http://www.darpa.mil/work-with-us/additional-baa.

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 Transactions for Prototypes shall follow the applicable rules and

regulations governing these various award instruments, but, in all cases, should appropriately identify any potential restrictions on the Government's use of any Intellectual Property contemplated under the award instrument in question. This includes both Noncommercial Items and Commercial Items. Proposers are encouraged to use a format similar to that described in the section above. If no restrictions are intended, then the proposer should state "NONE."

System for Award Management (SAM) and Universal Identifier Requirements

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

International entities can register in SAM by following the instructions in this link: https://www.fsd.gov/fsd-gov/answer.do?sysparm_kbid=dbf8053adb119344d71272131f961946&sysparm_search=KB0013221.

4.2.4. Submission Information

DARPA will acknowledge receipt of all submissions and assign an identifying control number that should be used in all further correspondence regarding the submission. DARPA intends to use electronic mail correspondence regarding HR001118S0037. Submissions may not be submitted by fax or e-mail; any so sent will be disregarded.

Submissions will not be returned. An electronic copy of each submission received will be retained at DARPA and all other non-required copies destroyed. A certification of destruction may be requested, provided the formal request is received by DARPA within five 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.

For Proposers Submitting Proposal Abstracts or Full Proposals as Hard Copies/On CD-ROM:

Proposers must submit an original hardcopy and one (1) electronic copy of the abstract or proposal in PDF (preferred) on a CD-ROM to the mailing address listed in Part I. Each copy must be clearly labeled with HR001118S0037, proposer organization, technical point of contact, and proposal title (short title recommended).

Please note that submitters via hardcopy/CD-ROM will still need to visit https://baa.darpa.mil to register their organization concurrently to ensure the BAA office can verify and finalize their submission.

For Proposers Submitting Proposal Abstracts, or Full Proposals Requesting Procurement Contracts or OTs through DARPA's BAA Submission Portal:

Abstracts and Full Proposals sent in response to HR001118S0037 may be submitted via DARPA's BAA Website (https://baa.darpa.mil). Visit the website to complete the two-step registration process. Submitters will need to register for an Extranet account (via the form at the URL listed above) and wait for two separate e-mails containing a username and temporary password. After accessing the Extranet, submitters may then create an account for the DARPA BAA website (via the "Register your Organization" link along the left side of the homepage), view submission instructions, and upload/finalize the abstract. Proposers using the DARPA BAA Website may encounter heavy traffic on the submission deadline date; it is highly advised that submission process be started as early as possible.

All unclassified concepts submitted electronically through DARPA's BAA Website must be uploaded as zip files (.zip or .zipx extension). The final zip file should be no greater than 50 MB in size. Only one zip file will be accepted per submission. Classified submissions and proposals requesting assistance instruments (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 submission process be started as early as possible.

For Full Proposals Requesting Cooperative Agreements only:

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

Submissions: Proposers must submit the three forms listed below.

> SF 424 Research and Related (R&R) Application for Federal Assistance, available on the Grants.gov website at https://apply07.grants.gov/apply/forms/sample/RR_SF424_2_0-V2.0.pdf. *This form must be completed and submitted.*
>
> To evaluate compliance with Title IX of the Education Amendments of 1972 (20 U.S.C. A§ 1681 Et. Seq.), the Department of Defense is using the two forms below to collect

certain demographic and career information to be able to assess the success rates of women who are proposed for key roles in applications in science, technology, engineering, or mathematics disciplines. Detailed instructions for each form are available on Grants.gov.

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

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

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

Hard-copy Submissions: Proposers electing to submit cooperative agreement proposals as hard copies must complete the SF 424 R&R form (Application for Federal Assistance,) available on the Grants.gov website http://apply07.grants.gov/apply/forms/sample/RR_SF424_2_0-V2.0.pdf.

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.

4.2.5. Disclosure of Information and Compliance with Safeguarding Covered Defense Information Controls

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

DFARS 252.204-7000, "Disclosure of Information"
DFARS 252.204-7008, "Compliance with Safeguarding Covered Defense Information Controls"
DFARS 252.204-7012, "Safeguarding Covered Defense Information and Cyber Incident Reporting"

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

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

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

4.3. FUNDING RESTRICTIONS

Not applicable.

4.4. OTHER SUBMISSION REQUIREMENTS

Not applicable.

5. Application Review Information

5.1. EVALUATION CRITERIA

Proposals will be evaluated using the following criteria, listed in descending order of importance: 5.1.1 Overall Scientific and Technical Merit; 5.1.2 Potential Contribution and Relevance to the DARPA Mission; and 5.1.3 Cost Realism.

5.1.1. Overall Scientific and Technical Merit

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

The proposed technical team has the expertise and experience to accomplish the proposed tasks. Task descriptions and associated technical elements provided are complete and in a logical sequence with all proposed deliverables clearly defined such that a final outcome that achieves the goal can be expected as a result of award. The proposal identifies major technical risks, and planned mitigation efforts are clearly defined and feasible. If applicable, the CUI risk mitigation plan effectively presents a strategy for safeguarding controlled unclassified information.

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. Due to the likelihood of commercial application, appropriate direct cost sharing may be a positive factor in the evaluation. DARPA recognizes that undue emphasis on cost may motivate proposers to offer low-risk ideas with minimum uncertainty and to staff the effort with junior personnel in order to be in a more competitive posture. DARPA discourages such cost strategies.

5.2. REVIEW OF PROPOSALS

Review Process

It is the policy of DARPA to ensure impartial, equitable, comprehensive proposal evaluations based on the evaluation criteria listed in Section 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 BAA; proposals that fail to do so may be deemed non-conforming and may be removed from consideration. Proposals will not be evaluated against each other since they are not submitted in accordance with a common work statement. DARPA's intent is to review proposals as soon as possible after they arrive; however, proposals may be reviewed periodically for administrative reasons.

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

Handling of Source Selection Information

DARPA policy is to treat all submissions as source selection information (see FAR 2.101 and 3.104) and to disclose their contents only for the purpose of evaluation. Restrictive notices notwithstanding, during the evaluation process, submissions may be handled by support contractors for administrative purposes and/or to assist with technical evaluation. All DARPA support contractors performing this role are expressly prohibited from performing DARPA-sponsored technical research and are bound by appropriate nondisclosure agreements. Subject to the restrictions set forth in FAR 37.203(d), input on technical aspects of the proposals may be solicited by DARPA from non-Government consultants/experts who are strictly bound by the appropriate 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. SELECTION NOTICES

As soon as the evaluation of a proposal is complete, the proposers will be notified that: (1) the proposal has been selected for funding pending contract negotiations, or (2) the proposal has not been selected. These official notifications will be sent via email to the Technical POC identified on the proposal 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 full proposals submitted 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 a proposal 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/or 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 and semi-annual program-wide meetings in a location central to the performer teams (assume alternating U.S. coasts for budgeting purposes), that all key participants are required to attend. 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. Performers should anticipate at monthly or quarterly meetings, including teleconference calls, in-person program reviews, and site visits by DARPA Program Manager and/or Government team.

6.2.1. FAR and DFARS Clauses

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

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

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

6.2.3. Representations and Certifications

If a procurement contract is contemplated, prospective awardees will need to be registered in the SAM database prior to award and complete electronic annual representations and certifications consistent with FAR guidance at 4.1102 and 4.1201; the representations and certifications can be found at www.sam.gov. Supplementary representations and certifications can be found at http://www.darpa.mil/work-with-us/additional-baa.

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6.2.4. Terms and Conditions

A link to the DoD General Research Terms and Conditions for Grants and Cooperative Agreements and supplemental agency terms and conditions can be found at http://www.darpa.mil/work-with-us/contract-management#GrantsCooperativeAgreements.

6.3. REPORTING

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

6.4. ELECTRONIC SYSTEMS

6.4.1. Wide Area Work Flow (WAWF)

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

6.4.2. i-EDISON

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

7. Agency Contacts

Administrative, technical or contractual questions should be sent via e-mail to PREPARE@darpa.mil.

Points of Contact
The BAA Coordinator for this effort may be reached at:
PREPARE@darpa.mil

DARPA/BTO
ATTN: HR001118S0037
675 North Randolph Street
Arlington, VA 22203-2114

8. Other Information

8.1. FREQUENTLY ASKED QUESTIONS (FAQ)

All administrative, technical, and contractual questions should be emailed to PREPARE@darpa.mil. All questions must be in English and must include the name, e-mail address, and the telephone number of a point of contact.

DARPA will attempt to answer questions in a timely manner; however, questions submitted within seven (7) days of the proposal due date may not be answered. DARPA will post an FAQ list at http://www.darpa.mil/work-with-us/opportunities. The list will be updated on an ongoing basis until the full proposal deadline as stated above in Part I.

8.2. AGENCY LEVEL PROTESTS

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

8.3. PROPOSERS DAY

DARPA will host a Proposers Day in support of the PREPARE program on **Wednesday, June 13, 2018.** The purpose is to provide potential proposers with information on the PREPARE program, promote additional discussion on this topic, address questions, provide a forum to present their capabilities, and to encourage team formation.

Interested proposers are not required to attend to respond to the PREPARE 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 FBO.gov website.

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/PREPAREProposersDay.

To encourage team formation, interested proposers are encouraged to submit information to be shared with all potential proposers through the DARPA Opportunities Page. This information may include contact information, relevant publications, and a slide or poster to summarize the proposer's interests.

Participants are required to register no later than **Wednesday, June 6, 2018**. 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.

Registrations will be accepted on a first come first serve basis, subject to room restrictions.

All foreign nationals, including permanent residents, must complete and submit a DARPA Form 60 “Foreign National Visit Request,” which will be provided in the registration confirmation email.

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 beginning on Page 33 of HR001118S0037. 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 **HR001118S0037** included on your Cost Proposal cover sheet?
   ○ **YES** ○ **NO** **Appears on Page(s)** [Type text]
   If reply is "No", please explain:

2. Does your Cost Proposal include (1) a summary cost buildup by Phase, (2) a summary cost buildup by Year, and (3) a detailed cost buildup of for each Phase that breaks out each task and shows the cost per month?
   ○ **YES** ○ **NO** **Appears on Page(s)** [Type text]

   If reply is "No", please explain:

3. Does your cost proposal (detailed cost buildup #3 above in item 2) show a breakdown of the major cost items listed below:
   Direct Labor (Labor Categories, Hours, Rates)
   ○ **YES** ○ **NO** **Appears on Page(s)** [Type text]

   Indirect Costs/Rates (i.e., overhead charges, fringe benefits, G&A)
   ○ **YES** ○ **NO** **Appears on Page(s)** [Type text]

   Materials and/or Equipment
   ○ **YES** ○ **NO** **Appears on Page(s)** [Type text]

   Subcontracts/Consultants
   ○ **YES** ○ **NO** **Appears on Page(s)** [Type text]

   Other Direct Costs
   ○ **YES** ○ **NO** **Appears on Page(s)** [Type text]

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

   If reply is "No", please explain:

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

If reply is "No", please explain:

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

   If reply is "No", please explain:

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

   If reply is "No", please explain:

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

   If reply is "No", please explain:

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

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

   If reply is "No", please explain:

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

    If reply is "No", please explain:

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

    If reply is "No", please explain:

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

    If reply is "No", please explain:

13. Have all team members (prime and subcontractors) who are considered a Federally Funded Research & Development Center (FFRDC), included documentation that clearly demonstrates work is not otherwise available from the private sector AND provided a letter on letterhead from the sponsoring organization citing the specific authority establishing their eligibility to propose to government solicitations and compete with industry, and compliance with the associated FFRDC sponsor agreement and terms and conditions.

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

If reply is "No", please explain:

14. Does your proposal include a response regarding Organizational Conflicts of Interest?

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

If reply is "No", please explain:

15. Does your proposal include a completed Data Rights Assertions table/certification?

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

If reply is "No", please explain: