DEFENSE THREAT REDUCTION AGENCY

BROAD AGENCY ANNOUNCEMENT

HDTRA1-17-S-0001

CHEMICAL / BIOLOGICAL TECHNOLOGIES

FY2017 Program Build

18 July 2016

TABLE OF CONTENTS

1.0 General Information

1.1 BAA Introduction

This publication constitutes a BAA as contemplated in Federal Acquisition Regulation (FAR) Part 35.016 and FAR 6.102(d)(2). Formal Request for Proposals (RFPs) regarding this announcement will not be issued.

1.2 BAA Open Period

This BAA will remain open from 18 July 2016 through 30 September 2016, 1400 Eastern Daylight Time (EDT). Phase I Proposals must be received by this time and date in order to be considered. Submission information is provided in Section 3.3 of this BAA.

1.3 Research Opportunity Description

The Defense Threat Reduction Agency (DTRA) Chemical and Biological Technologies (CBT) were established by the Department of Defense (DoD) to provide state-of-the-art defense capabilities to allow military forces of the United States to operate and to successfully complete their missions in chemical and biological warfare environments. The scope of mission efforts and the priorities assigned to specific projects are influenced by changes in military and civilian Chemical and Biological Defense (CBD) science and technology, advanced developments, operational requirements, military threat assessments, and national defense strategies. To keep pace with defense capability requirements, the CBD as part of its mission, routinely promulgates chemical and biological research. The comprehensive research program encompasses both intramural and extramural sources, and the role of each is vital to the fulfillment of the Program objectives.

DTRA is seeking optimum approaches to meet technology objectives within the areas listed below, with a goal to identify and select science and technology projects that can be transitioned to joint acquisition programs:

1. Detection – Chemical and Biological: The goal of the Detection area is to provide real-time capability to detect, identify, characterize, locate and warn against all known or validated CB warfare agents in addition to other chemical or biological threat materials (e.g., Toxic Industrial Chemicals).

2. Information Systems Capability Development: The goal of the Information Systems Capability Development area is to provide information technology superiority with respect to the Chemical, Biological, Radiological, and Nuclear (CBRN) environment.

3. Protection – Individual and Collective: The Protection Capability Area seeks to provide unencumbered full-dimensional protection to the war fighter for both personal protective gear (individual protection) and protection of large scale fixed or mobile environments (collective protection).

4. Hazard Mitigation: The goal of the Hazard Mitigation Capability Area is to develop

technologies that can rapidly restore pre-contamination capabilities with a minimum of logistical impact.

5. Threat Agent Science: The Threat Agent Science Capability Area seeks to maintain and develop scientific knowledge of current, non-traditional, and emerging threats in addition to studying areas such as low level toxicity, agent fate, and improved simulant materials.

6. Medical Pretreatments: The goal of the Pretreatments Capability Area is to conduct research in order to develop lead candidate vaccines and chemical pretreatments and protectants that can be administered before exposure to provide both specific and broad-spectrum protection against validated chemical or biological agents. Categories of threat agents addressed in this capability area include nerve agents, viruses, bacteria and toxins.

7. Medical Diagnostics: Medical diagnostics involves the diagnosis of infection by or exposure to bacterial, viral, or toxin agents (biological diagnostics) or of exposure to nerve, vesicant, respiratory and blood agents (chemical diagnostics) with the goal to rapidly identify the causative agent in a remote environment prior to onset of symptoms.

8. Medical Therapeutics: The goal of the Therapeutics Capability Area is to develop lead candidate medical treatments and pharmaceuticals that, when administered after exposure to a chemical or biological agent, mitigate or curtail the effects of that exposure and sustain forces operating in a CBW hazard area. Medical Therapeutics is segregated into biological countermeasures and chemical countermeasures.

9. Threat Surveillance - Chemical and Biological: The goal of the Threat Surveillance area is to deliver cutting edge Integrated Early Warning, Information Management and Applied Analytic capabilities to the warfighter; virtually connect them to these capabilities and other system users for rapid situational awareness, course of action (CoA) analysis and decision support.

1.4 BAA Process

This BAA will utilize a two-step process, consisting of the submission and evaluation of Phase I (White Paper Packages) and Phase II (Full) proposals. While all interested parties may submit Phase I proposals, submission of Phase II proposals will be by invitation only.

The evaluation status of Phase I and Phase II proposals will be provided at two points. An email will be sent to each Offeror after completion of White Paper package evaluations. The email will either inform the Offeror that their Phase I proposal is no longer under consideration, or it will provide instructions for the submission of a Phase II proposal. In a similar manner, Offerors that submit a Phase II proposal will receive an email informing them that their proposal is either no longer under consideration or has been selected for award pending successful price negotiations.

1.5 Award Vehicle

A full range of flexible acquisition related statutory authority arrangements available to DTRA are possible results from this announcement, including but not limited to, Contracts, Task Orders, and Other Transaction Agreements (OTA). **The Government does not intend to award grants or Cooperative agreements under this solicitation**. Each of these

procurement instruments offers different advantages, liabilities and responsibilities for Offerors and the Government. Except for OTAs, the Government actions under this BAA shall adhere to the requirements of the FAR and Defense Federal Acquisition Regulation Supplement (DFARS).

1.5.1 Contract Type

The Government intends to award Cost and Cost-Plus-Fixed-Fee (CPFF) contracts and, when in the Government's best interest, Fixed-Price contracts. Research and Development contracts are typically Cost-Reimbursement (Cost, CPFF) contracts. In accordance with FAR 16.301-3(a)(3), Cost-Reimbursement contracts require that the contractor's accounting system is adequate for determining costs applicable to the contract. **Determinations of accounting system inadequacy, or lack of evidence to support a determination of accounting system adequacy, will preclude the Offeror from receiving a contract.** The Government will typically rely on the findings of a DCAA accounting system audit in making a determination of accounting system adequacy.

1.5.2 Limitation on OTAs

Offerors are advised that an OTA may only be awarded if it meets one of the following criteria:

a. There is at least one nontraditional defense contractor participating to a significant extent in the prototype project, or
b. All significant participants in the transaction other than Federal Government are small business or non-traditional defense contractors, or
c. At least one third of the total cost of the prototype projects is to be paid out of funds provided by parties to the transaction other than the Federal Government.
d. The senior procurement executive for the agency determined in writing that exceptional circumstances justify the use of a transaction that provides for innovative business arrangements or structures that would not be feasible or appropriate under a contract, or would provide an opportunity to expand the defense supply base in a manner that would not be practical or feasible under a contract.

For purposes of determining whether or not a participant may be classified as a nontraditional defense contractor or small business and whether or not such participation is determined to be participating to a significant extent in the prototype project, the following definitions are applicable:

"Nontraditional defense contractor" means an entity that is not currently performing and has not performed, for at least the one-year period preceding the solicitation of sources by the Department of Defense for the procurement or transaction, any contract or subcontract for the Department of Defense that is subject to full coverage under the cost accounting standards prescribed pursuant to section 1502 of title 41 and the regulations implementing such section.

"Small Business" means a small business concern as defined under section 3 of the Small Business Act (15 U.S.C. 632).

"Participating to a significant extent in the prototype project" means that the nontraditional defense contractor or small business is supplying a new key technology or product, is accomplishing a significant amount of the effort wherein the role played is more than a nominal or token role in the research effort, or in some other way plays a significant part in causing a material reduction in the cost or schedule of the effort or an increase in performance of the prototype in question.

NOTE: Offerors are cautioned that if they propose the use of an OTA, the Government reserves the right to negotiate either a FAR based procurement contract, or OTA as it deems is warranted under the circumstances.

1.5.3 Contract Period of Performance Limitation

In accordance with FAR 17.204(e), contract periods of performance shall be limited to a maximum of five years, inclusive of all Options.

1.6 Points of Contact

E-mail address for all BAA correspondence and questions	Dtra.belvoir.J9.mbx.CB-BAA@mail.mil
BAA Announcements posted in Federal Business Opportunities, FedBizOpps	http://www.fbo.gov
DTRA Proposal Submission Website (requires registration prior to proposal submission)	http://www.dtrasubmission.net
DTRA Website	http://www.dtra.mil

1.7 Technical and Administrative Support by Non-Government Personnel

It is the intent of DTRA to use non-government personnel (e.g. contractor support personnel) in the review and administration of all submittals (Phase I and Phase II) for this BAA. Participation in the BAA requires the following DTRA Advisory and Assistance Services (A&AS) support contractor employees, contracted contract specialist support and proposal submission website support to have access to proposal information including information that may be considered proprietary: Engility Corporation; JAB Solutions, LLC; and SBG Technology Solutions, Inc. The contracts for provision of support personnel contain Organizational Conflict of Interest provisions and include contractual requirements for non-disclosure of proprietary contractor information. Additionally, Engility employees in their role as an A&AS support contractor to DTRA will provide technical input in an advisory role as subject matter experts (SMEs) to the Government reviewers in addition to providing administrative support in the management of the proposals and their technical review.

Phase II proposals, in some instances, may require other non-government personnel from Academia to serve as peer reviewers with access to proposal information including

information that may be considered proprietary. All individuals in these categories having access to any proprietary data shall execute nondisclosure agreements certifying that they will not disclose any information pertaining to this solicitation including any proposal submittals, the identity of any submitters, or any other information relative to the Offeror's proposal.

All Offerors to this BAA consent to the disclosure of their information to the aforementioned companies, their subcontractors, and Academia peer reviewers under these conditions.

1.8 Freedom of Information Act Disclosure

In the event that properly marked data contained in a Phase I or II proposal submitted in response to this BAA is requested pursuant to the Freedom of Information Act, 5 USC 552, the Offeror will be advised of such request and, prior to such release of information, will be requested to expeditiously submit to DTRA a detailed listing of all information in the white paper/proposal which the Offeror believes to be exempt from disclosure under the Act. Such action and cooperation on the part of the Offeror will ensure that any information released by DTRA pursuant to the Act is properly identified.

2.0 Eligibility

Except as specified below, this BAA is open to all responsible sources capable of responding to the Government's requirements. Intramural Offerors, as listed in paragraph 2.2, should respond to the JSTO-CBD FY17/21 Service Call if they wish to submit a proposal as a prime contractor.

2.1 Eligible Sources

Proposals submitted for this BAA will be considered from the following U.S. and Foreign Enterprises:

- Industrial/commercial concerns including small businesses.
- Accredited Degree granting colleges and universities.
- Not-for-profit organizations.
- Other Non-U.S. sources.
- DoD-sponsored Federally Funded Research and Development Centers (FFRDCs) specified in DFARS 235.017-1.
- University Affiliated Research Centers (UARCs), provided that it is permitted by the UARC's DoD sponsor.
- Department of Energy (DOE) sponsored FFRDCs and National Aeronautics and Space Administration (NASA) sponsored FFRDCs, provided that authorization is obtained from the DOE sponsor or NASA sponsor.

2.2 Non-Eligible Sources

The following entities may not participate as prime contractors nor furnish principal investigators in awards made under BAA but may act as subcontractors:

- Federal laboratories other than those DoD, DOE and NASA sponsored FFRDCs specified above.
- U.S. Government agencies and organizations.
- Academic institutions that are federal government organizations (e.g., Naval Postgraduate School).

3.0 Instructions to Offerors

To assure timely and equitable evaluation of proposals, Offerors must follow the instructions contained herein. Offerors are required to meet all solicitation requirements, including terms and conditions, representations and certifications, technical requirements, and proposal content and format requirements. Failure to meet a requirement may result in an offer being ineligible for award. Additionally, Offerors must clearly identify any exception to the solicitation terms and conditions and provide complete accompanying rationale. It is the Offeror's responsibility to ensure the completeness of the proposal. Evaluation of a proposal will be conducted only on the basis of the information contained within it and the Government will not assume that an Offeror possesses any capabilities not specified.

Proposals shall be clear, concise, and include sufficient detail for effective evaluation and for substantiating the validity of stated claims. The Offeror shall assume that the Government has no prior knowledge of the Offeror's capabilities.

3.1 Administrative Requirements

3.1.1 Registration to the DTRA Proposal Submission Website

All Offerors are required to register at the DTRA proposal submission website prior to submission of Phase I proposals. Detailed registration and submission instructions are available at the site.

The registration must be submitted by a central Business Point of Contact (BPOC) rather than individual Principal Investigator personnel. A BPOC is a person who is given the responsibility of coordinating all submissions from individual Principal Investigators at his or her work location and is the only individual who may access the DTRA proposal submission website. The intent is that all submissions from an organization be coordinated and submitted by a single, identified responsible party. Failure to register in accordance with instructions may render them ineligible for participation in this BAA.

Offerors must be aware that it is their responsibility to ensure that e-mail notifications reach the designated BPOC and that e-mail notifications are not blocked due to the use of 'spam blocker' software or other means that the recipient's Internet Service Provider may have implemented as a means to block the receipt of certain e-mail messages. Additionally, it is the responsibility of the BPOC to inform DTRA of any updates to e-mail addresses for both themselves as the registered BPOC and for the designated Principal Investigator.

IMPORTANT: Registration at the DTRA proposal submission website is NOT the same as registering at the System for Award Management or FedBizOpps websites. Failure to register at the DTRA proposal submission website will prevent an Offeror's submission of documents required and thus render the Offeror ineligible for participation in this BAA.

3.1.2 Registration to the System for Award Management (SAM) Website

DTRA requires that all Offerors be registered in the SAM database at the time of Phase I proposal submission. Contractors must keep their registration current for the life of the contract. Offerors may register with SAM online at http://www.sam.gov. Offerors will NOT be able to complete their SAM registration until SAM has confirmed the Offeror's Employer Identification Number (EIN) or Taxpayer Identification Number (TIN) with the Internal Revenue Service (IRS).

NOTE: It will take 24-48 hours for the IRS to validate the TIN. According to the IRS, if Offerors do not currently have an EIN and need to apply for one over the phone or Internet, they will be given a tentative EIN, but the EIN may not become active for up to two (2) weeks. Questions regarding an EIN may be directed at 1-800-829-4933.

3.2 Questions about this BAA

Questions regarding the technical and administrative content of this BAA must be sent to the following DTRA e-mail address: Dtra.belvoir.J9.mbx.CB-BAA@mail.mil. Questions and/or inquiries that are not submitted to the aforementioned e-mail address will be disregarded. All questions must include the BAA number in the subject line. DTRA will post answers to questions on the FedBizOpps website. It is the Offeror's responsibility to periodically check the FedBizOpps website to view postings of questions and answers, in addition to any applicable amendments to the BAA.

3.3 Proposal Submission Instructions

3.3.1 General Instructions

All proposals must be submitted electronically through the DTRA proposal submission website: http://www.dtrasubmission.net. Any proposal submitted by any means other than the DTRA proposal submission website **will not** be considered (e.g., hand-carried, postal service, commercial carrier, e-mail).

Offerors are responsible for ensuring submission of their Phase I proposals by the date and time specified in Section 1.2. **Time management is wholly the responsibility of the Offeror. If a timely submission is not fully uploaded prior to the cutoff date/time, the proposal will not be considered. No exceptions will be made.** The Offeror must verify the submission of their proposal package by printing the electronic receipt (time and date stamped) that appears on the final screen following compliant submission of a proposal to the DTRA proposal submission website.

Using the DTRA proposal submission website, all Offerors must prepare Proposal Cover Sheets for each Phase I and invited Phase II proposal submitted. All data point requirements must be completed in every cover sheet. Once the cover sheet is saved, the system will assign a unique proposal number for each Phase I submission and a different unique proposal number for each invited Phase II submission. Cover sheets may be edited as often as necessary until the submission period closes. All submissions must be dated and **unclassified**.

If multiple proposals are being submitted by the same Offeror in response to different Topic Areas, separate cover sheets must be generated for each proposal and the full proposal files must be uploaded with the associated cover sheet, since a unique document number will automatically be assigned to each submission by the electronic proposal tracking system. All documents submitted to the DTRA proposal submission website are considered works in progress and are not eligible for evaluation until the Offeror submits the final proposal package for consideration. Once all proposal files have been uploaded and the Offeror is ready to submit their application, select the green "Submit" button on the page. A confirmation message will appear on the page once the submission has gone through. Perform a virus check before uploading any proposal files. If a virus is detected, it may cause rejection of the file.

Offerors **must** submit proposals to the appropriate Topic. Failure to do so will render the proposal ineligible for evaluation and award.

3.3.2 Late Submissions and Withdrawal of Proposals

Offerors are responsible for access to the DTRA proposal submission website and for submitting electronic proposals so as to be received at the Government site indicated in this BAA no later than the closing date and time stated in Section 1.2, above. Untimely proposals will not be considered.

When sending electronic files, the Offeror will account for potential delays in file transfer from the originator's computer server to the Government website/computer server. Offerors are encouraged to submit their proposals early to avoid potential file transfer delays due to high demand or problems encountered in the course of the submission. Offerors should also print, and maintain for their records, the electronic date/time stamped receipt that appears on the final screen following submission of a proposal on the DTRA proposal submission website. All submissions shall be fully uploaded before the cut off time/date in order to be considered.

Proposals may be withdrawn by written notice received at any time before award. Withdrawals are effective upon receipt of notice via the e-mail address listed in Section 1.6.

3.4 Proposal Format Requirements

3.4.1 Submission File Format

Offerors shall submit each required proposal volume as a separate Portable Document File (PDF) compatible with Adobe Acrobat ® version 11.0.0 or earlier. Additionally, each Phase II proposal shall also contain a Statement of Work (SOW) provided in MS Word format and a Cost Spreadsheet provided in MS Excel format. Additional specific format requirements are provided below.

Movie and sound file attachments, or other additional files, will not be accepted. The proposal files must not be encrypted.

3.4.2 Phase I Proposal

Offerors must submit Phase I proposals in accordance with instructions provided in this section of the BAA; failure to do so may preclude consideration for Phase II proposal invite. Additionally, Offerors are required to complete a cover sheet using the DTRA proposal submission website. All Phase I proposals shall consist of a Quad Chart and White Paper conforming to the following format requirements:

3.4.2.1 Quad Chart

3.4.2.1.1 Format Requirements

- Paper size: 8.5 x 11 inches, Landscape orientation
- Font: Arial, 28 point bold for Header, 10 point for body
- Page Limit: No more than one (1) page. Pages in excess of the page limitation will not be read or evaluated.
- Format: MS PowerPoint
- Classification: Unclassified
- Restrictive Markings: The Quad Chart must not contain information deemed trade secret, confidential or proprietary by the Offeror.

3.4.2.2 White Paper

3.4.2.2.1 Format Requirements

- Paper size: 8.5 x 11 inches
- Spacing: Single-spaced
- Margins: One-inch
- Font: Times New Roman, not smaller than 12 point
- Page Limit: No more than six (6) pages. Pages in excess of the page limitation will not be read or evaluated.
- Classification: Unclassified
- Restrictive Markings: White papers containing proprietary information shall contain the restrictive markings reflected in Section 3.4.4.

3.4.3 Phase II Proposal

Offerors invited to submit a Phase II proposal must follow the instructions provided in

this section of the BAA; failure to do so may preclude consideration the proposal for award. All Phase II proposals shall consist of a Technical Volume, Cost Volume and Supplement Information Volume conforming to the following format requirements:

3.4.3.1 Technical Volume

The Technical Volume shall consist of the Offeror's Technical Proposal, Technical Approach and Basis of Estimate (BOE) and Statement of Work conforming to the following format requirements:

3.4.3.1.1 Technical Proposal

- Paper size: 8.5 x 11 inches
- Spacing: Single-spaced
- Margins: One-inch
- Font: Times New Roman, not smaller than 12 point
- Page Limit (Technical Approach): No more than fifteen (15) pages. Pages in excess of the page limitation will not be read or evaluated.
- Classification: Unclassified
- Restrictive Markings: Documents containing proprietary information shall contain the restrictive markings reflected in Section 3.4.4.

3.4.3.1.2 Technical Approach and BOE

- Paper size: 8.5 x 11 inches
- Spacing: Single-spaced
- Margins: One-inch
- Font: Times New Roman, not smaller than 12 point
- Page Limit: None
- Classification: Unclassified
- Restrictive Markings: Documents containing proprietary information shall contain the restrictive markings reflected in Section 3.4.4.

3.4.3.1.3 Statement of Work

- Paper size: 8.5 x 11 inches
- Spacing: Single-spaced
- Margins: One-inch
- Font: Times New Roman, not smaller than 12 point
- Page Limit: None
- Classification: Unclassified
- Restrictive Markings: The Statement of Work must not contain information deemed trade secret, confidential or proprietary by the Offeror or Contractor-specific references such as headers and footers with company name and/or logo. See Attachment 2 for more information.

3.4.3.2 Cost Volume

The Cost Volume shall consist of the Offeror's Cost Narrative / Supporting Documentation, Cost Spreadsheets, which shall conform to the following format requirements:

3.4.3.2.1 Cost Narrative / Supporting Documentation

- Paper size: 8.5 x 11 inches
- Spacing: Single-spaced
- Margins: One-inch
- Font: Times New Roman, not smaller than 12 point
- Page Limit: None
- Classification: Unclassified
- Restrictive Markings: Documents containing proprietary information shall contain the restrictive markings reflected in Section 3.4.4.

3.4.3.2.2 Cost Spreadsheets

- File Format: MS Excel 2010, or compatible format
- Format: In accordance with Attachment 4
- Formulas: All formulas shall be preserved.
- Page Limit: None
- Classification: Unclassified
- Restrictive Markings: Documents containing proprietary information shall contain the restrictive markings reflected in Section 3.4.4.

3.4.3.3 Supplemental Information Volume

The Supplemental Information Volume shall conform to the following format requirements:

- Paper size: 8.5 x 11 inches
- Spacing: Single-spaced
- Margins: One-inch
- Font: Times New Roman, not smaller than 12 point
- Page Limit: None
- Classification: Unclassified
- Restrictive Markings: Documents containing proprietary information shall contain the restrictive markings reflected in Section 3.4.4.

3.4.4 Restrictive Markings and Disclosure of Proprietary Information

The White Paper portion of the Phase I submission and all Phase II volumes submitted in response to this solicitation (with the exception of the SOW) may contain technical information and other data that the Offeror does not want disclosed to the public or used by the Government for any purpose other than proposal evaluation. Public release of

information in any submission will be subject to existing statutory and regulatory requirements. If proprietary information which constitutes a trade secret, proprietary commercial or financial information, confidential personal information, or data affecting national security is provided by an Offeror, it will be treated in confidence, to the extent permitted by law, provided that the following legend appears and is completed on the front of the submission:

> "For any purpose other than to evaluate the white paper/proposal, this data shall not be disclosed outside the Government and shall not be duplicated, used, or disclosed in whole or in part, provided that, if an award is made to the Offeror as a result of or in connection with the submission of this data, the Government shall have the right to duplicate, use, or disclose the data to the extent provided in the agreement. This restriction does not limit the right of the Government to use information contained in the data if it is obtained from another source without restriction. The data subject to this restriction is contained in page(s) __ of this white paper/proposal."

Any other legend may be unacceptable to the Government and may constitute grounds for removing the proposal from further consideration without assuming any liability for inadvertent disclosure. The Government will limit dissemination of properly marked information to official channels.

In addition, the pages indicated as restricted must be marked with the following legend: "Use or disclosure of the white paper/proposal data on lines identified by an asterisk (*) are subject to the restriction on the front page of this white paper/proposal." The Government assumes no liability for disclosure or use of unmarked data and may use or disclose such data for any purpose."

In the event that properly marked data contained in a white paper/proposal submitted in response to this BAA is requested pursuant to the Freedom of Information Act, 5 U.S.C. § 552, the Offeror will be advised of such request and, prior to such release of information, will be requested to expeditiously submit to DTRA a detailed listing of all information in the white paper/proposal which the Offeror believes to be exempt from disclosure under the Act. Such action and cooperation on the part of the Offeror will ensure that any information released by DTRA pursuant to the Act is properly identified.

By submission of a White Paper/proposal, the Offeror understands that proprietary information may be disclosed outside the Government for the sole purpose of technical evaluation. The Contracts Office will obtain a written agreement from the evaluator that proprietary information in the white paper/proposal will only be used for evaluation purposes and will not be further disclosed or utilized.

3.5 Proposal Content Requirements

3.5.1 Phase I Proposal

Offerors must submit Phase I proposals in accordance with instructions provided in this section of the BAA; failure to do so may preclude consideration for Phase II proposal

invite. All Phase I proposals shall consist of a Quad Chart and a White Paper conforming to the following requirements:

3.5.1.1 Quad Chart

The Quad Chart must be included in the Phase I proposal as well as in Volume III, Supplemental Information, of the Phase II proposal. Proposed Quad Charts must conform to the following template:

Heading:

- Title of Project
- Topic Number
- Principal Investigator
- Organization

Upper Left Quadrant:

- Objective – provide a clear and concise description of the goal of the effort.
- Description of Effort – provide a brief description of the technology proposed for investigation and the methodologies to be used during the course of investigation.

Lower Left Quadrant:

- Benefits of Proposed Technology – provide a brief description of the net advantages of the proposed technology over current practices and other competing technologies.
- Challenges: provide a bullet list of the technical or scientific challenges being addressed.
- Maturity – describe the maturity of proposed technology with respect to Technical Readiness Level (TRL) at project start and the anticipated TRL at project end. See Attachment 1 for TRL definitions.

Upper Right Quadrant:

- Picture or graphic illustrating proposed technology development

Lower Right Quadrant:

- Period of Performance – provide the project period of performance. If the project incorporates multiple periods of performance, separated by logical and meaningful milestones and go/no-go decision points, provide the duration of each period.
- Major goals/milestones and deliverables - provide a bullet list of the major project goals, milestones and deliverables. If utilizing multiple project periods of performance, provide the goals, milestones and deliverables for each period and for the overall project.

- Cost – provide a Rough Order of Magnitude (ROM) cost estimate. If utilizing multiple project periods of performance, provide the ROM estimates for each period and for the overall project.

3.5.1.2 White Paper

The white paper shall include the following sections in the order given below:

(1) Describe the following elements of the project technical approach.

- Project objectives and scope.
- Overview of tasks and methods planned to achieve each objective and the final deliverable and/or project end-state.
- Key personnel, including subcontractors and consultants. Offerors are cautioned to limit discussion to the minimum necessary to establish that the Offeror possesses sufficient technical expertise to successfully execute the technical approach.
- Facilities/Equipment necessary to carry out the proposed effort.

(2) Provide a project overview describing:

- How the technology addresses the topic requirement specified in Section 7 of this BAA.
- How and to what degree the scientific solution is relevant to DOD CBDP program goals.
- How the technology can be implemented or utilized by DoD end-users, and the impact of the technology on end-user mission capability.
- The current TRL of the technology and the anticipated TRL at the end of the proposed project.
- Any applicable technical and/or scientific challenges associated with the proposed project, and how the Offeror intends to address these challenges.

(3) Describe how the proposed project is achievable within the proposed schedule. Discuss potential risks and the actions that the Offeror will take to mitigate these risks and ensure that major milestones and objectives are successfully met within the proposed project schedule.

(4) Describe the estimated costs for the proposed technical approach. Explain how the cost estimate was derived. Provide a breakout of estimated costs by project milestone. If the proposed project includes multiple periods of performance, provide estimated costs by milestone for each project period.

3.5.2 Phase II Proposal

Offerors invited to submit a Phase II proposal must follow the instructions provided in this section of the BAA; failure to do so may preclude consideration the proposal for

award. All Phase II proposals shall consist of a Technical Volume, Cost Volume and Supplemental Information Volume conforming to the following requirements:

3.5.2.1 Technical Volume

The Technical Volume shall be comprised of a Technical Proposal, Technical Approach and BOE, and Statement of Work which conforms to the following requirements:

3.5.2.1.1 Technical Proposal

The Technical Proposal shall be submitted in accordance with the following:

3.5.2.1.1.1 Abstract

Offerors shall provide a brief abstract.

3.5.2.1.1.2 Scope

Offerors shall provide a detailed description of project scope, to include project objectives, background, programmatics and relevance.

A. Objective. Offerors shall state clearly and concisely the objective of the proposed project.
B. Background. Offerors shall provide the necessary technical and scientific background to support the scientific and/or technical merit of the proposed project.
C. Programmatic. Offerors shall describe their organization's program management plan for the proposed project. Offeror's shall list supporting and collaborating centers, and roles and responsibilities of each identified academic and/or industrial subcontractor supporting this project.
D. Relevance. Offerors shall describe the relevance of the proposed project in terms of DTRA mission, end-user needs and the state-of-the-art of the proposed technology.

3.5.2.1.1.3 Credentials

Offerors shall provide credentials and qualifications, limited to that which is directly relevant to the proposed work.

A. Summary of Organizational Credentials and Qualifications. Offerors shall describe their organizational qualifications and credentials to perform the proposed project.
B. Summary of Qualifications for PI and Key Personnel. Offerors shall list summary qualifications for the proposed Principal Investigator and other Key Personnel.

C. Summary of Facilities to Perform the Proposed Work. Offerors shall summarize the credentials of the primary performing center, and supporting academic and industrial subcontractors to perform the work. Offerors shall describe specific examples of similar work performed, and equipment and/or facilities available to perform the proposed work.

3.5.2.1.1.4 Performance Schedule and Expenditure Plan.

A. Gantt Chart.

Offerors shall provide a Gantt chart that lists each individual SoW task and provides the duration of performance for each.

B. Time-phased Expenditure Plan.

Offerors shall provide a time-phased expenditure plan, provided in chart format that provides estimated cost accrual by month, by project period. For example, if the proposed project includes three periods of performance, each lasting twelve months, the Offeror's chart will be broken out into three separate twelve-month periods.

3.5.2.1.1.5 References

Offerors shall list any relevant documents used to develop the technical approach.

3.5.2.1.2 Technical Approach and BOE

A. General. The Offeror shall address the following requirements:

1. Provide a detailed narrative summary of the proposed technical approach.
2. Provide project milestones and objectives. Explain why the proposed technical approach is valid and suitable to achieve SoW requirements and project milestones and objectives.

B. Risks. The Offeror shall address the following requirements:

1. Explain the risks associated with achieving proposed project goals, objectives and milestones (what will be done), and risks associated with the technical approach (how it will be done).
2. For all identified risks, Offerors shall indicate how they plan to manage these risks (e.g. avoidance, acceptance, mitigation, transfer) and provide a detailed narrative explaining the corresponding risk management actions that will be taken for each identified risk.

C. Approach and BOE. For **each proposed SoW task**, Offerors shall address the following:

1. Technical Approach: The proposed technical approach to execute the individual SoW task.

2. Milestones, Metrics, Objectives and Deliverables: The milestones, metrics, objectives and deliverables associated with the individual SoW task.

3. Basis of Estimate: The proposed resources to execute the technical approach, covering all cost elements in accordance with the below information and format requirements. No cost information shall be provided with the technical approach and BOE. Cost data is limited to the Cost Volume only. Address each of the following requirements.

a) Direct Labor

i. Direct Labor Breakout - provide a chart that lists each individual labor category assigned to this task and the number of hours allocated to each listed labor category.

ii. Direct Labor Justification – Offerors shall explain, in detail, how the estimate was developed (e.g. bottom-up analysis, analogy), the rationale supporting the chosen estimating technique, and why each proposed labor category, and the hours allocated to each labor category, is reasonable and necessary to execute the technical approach

b) Subcontracts

i. Subcontract Breakout - provide a chart that lists each individual subcontractor assigned to this task.

ii. Subcontractor Justification – Offerors shall explain, in detail, why each proposed subcontractor is appropriate and necessary to execute the technical approach.

c) Consultants

i. Consultant Breakout - provide a chart that lists each individual consultant assigned to this task and the number of hours allocated to each consultant.

ii. Consultant Justification – Offerors shall explain, in detail, why each proposed consultant, and associated level of effort/hours, is appropriate and necessary to execute the technical approach.

d) Materials/Supplies

i. Material/Supply Breakout - provide a chart that lists each individual material and supply item assigned to this task and the quantity for each.

ii. Material/Supply Justification – Offerors shall explain, in detail, how the estimate was developed (e.g. bottom-up analysis, analogy), the rationale supporting the chosen estimating technique, and why each proposed material and supply item is appropriate and necessary to execute the technical approach.

e) Equipment

i. Equipment Breakout - provide a chart that lists each individual equipment item assigned to this task and the quantity for each.

ii. Equipment Justification – Offerors shall explain, in detail, how the estimate was developed (e.g. bottom-up analysis, analogy), the rationale supporting the chosen estimating technique, and why each proposed equipment item is appropriate and necessary to execute the technical approach.

f) Travel

i. Travel Breakout - provide a chart that lists each individual travel event, and for each individual travel event, lists the following: a) reason for travel, b) destination, c) number of travelers, d) applicable labor categories, and e) duration of travel.

ii. Travel Justification – Offerors shall explain, in detail why each proposed travel event, and the proposed travelers (by labor category) are appropriate and necessary to execute the technical approach.

g) ODCs

i. ODC Breakout - provide a chart that lists each individual ODC item assigned to this task and the quantity for each.

ii. ODC Justification – Offerors shall explain, in detail, how the estimate was developed (e.g. bottom-up analysis, analogy), the

rationale supporting the chosen estimating technique, and why each proposed ODC item is appropriate and necessary to execute the technical approach.

The technical approach and BOE MUST clearly and accurately reflect the proposed SoW. Offerors must complete the above for each proposed project period of performance (e.g. Base Period, Option Period 1, etc.). Each proposed subcontractor must also provide a technical basis of estimate addressing each of the above requirements.

3.5.2.1.3 Statement of Work

The Statement of Work shall be submitted in accordance with the sample template provided in Attachment 2.

3.5.2.2 Cost Volume

All proposals are subject to the requirements of the Truth in Negotiations Act (TINA). A proposal tentatively selected for award exceeding the threshold listed in FAR 15.403-4(a)(1) will be required to submit a certificate of current cost and pricing data in the format described in FAR 15.406-2 upon conclusion of successful negotiations.

The responsibility for providing adequate supporting data and attachments lies solely with the Offeror. The cost proposal must include cost estimates sufficiently detailed for meaningful evaluation. Further, the Offeror must also bear the burden of proof in establishing reasonableness of proposed costs; therefore, it is in the Offeror's best interest to submit a fully supportable and well-prepared cost proposal. The basis and rationale for all proposed costs should be provided in the cost narrative so that Government personnel can place reliance on the information as current, complete, and accurate.

The Cost Volume shall contain the following content:

3.5.2.2.1 Cost Spreadsheet

The Offeror shall prepare the Cost Spreadsheet utilizing Attachment 4 – Cost Spreadsheet. The Cost Spreadsheet is in Microsoft Excel format. Offerors shall follow all instructions, including provided Notes, contained within the Cost Spreadsheet.

3.5.2.2.2 Cost Narrative/Supporting Documentation

All Offerors shall provide documentation, and analysis as required, to support the proposed costs contained within Attachment 4. Specific information requirements for this section are included in the Attachment 4 Notes.

3.5.2.3 Supplemental Information Volume

The Supplemental Information Volume shall be submitted in accordance with the content requirements provided in Section 8.1.

4.0 Evaluation Criteria

4.1 General Evaluation Information

Evaluation of proposals will be conducted based upon a technical subject matter expert review as described in FAR Subparts 6.102(d)(2) and 35.016. Each proposal will be evaluated based on the merit and relevance of the specific proposal as it relates to the DTRA program rather than against other proposals for research in the same topic area. All documents necessary for the review and evaluation of the Phase I and Phase II proposal submissions must be provided as described in Section 3 of this BAA.

4.2 Adjectival Ratings

With the exception of Phase II Factor 4 – Cost Realism, the Government will evaluate proposals using the adjectival ratings below. Phase II Factor 4 – Cost Realism will be assigned a rating of either Realistic or Not Realistic. Offerors are advised that a strength is an aspect of a proposal that has merit or exceeds specified performance or capability requirement in a way that will be advantageous to the Government during contract performance. A weakness means a flaw in the proposal that increases the risk of unsuccessful contract performance. A deficiency is a material failure of a proposal to meet a Government requirement or a combination of significant weaknesses in a proposal that increases the risk of unsuccessful contract performance to an unacceptable level.

Rating	Description
Outstanding (O)	The proposal is a technically exceptional submission pertinent to program goals and objectives. The proposal contains multiple strengths, exceptional features or innovations that should substantially benefit the program. The risk of unsuccessful performance is low.
Good (G)	The proposal is a technically thorough submission pertinent to program goals, and objectives. The proposal contains at least one strength which indicates the proposed approach will benefit the program. Weaknesses, if any, are more than offset by strengths. The risk of unsuccessful performance is low to moderate. The proposal may be recommended for acceptance but are at a lower priority than submissions rated 'Outstanding'.
Acceptable (A)	The proposal is a technically adequate submission pertinent to program goals, and objectives. Strengths and weaknesses are offsetting or will have little or no impact on contract performance. The risk of unsuccessful performance is no worse than moderate. The proposal may be recommended for acceptance but is at a lower priority than submissions rated either 'Outstanding' or 'Good'.

Marginal (M)	The proposal is a technically weak submission pertinent to program goals, and objectives. The proposal has one or more weaknesses which are not offset by strengths. The risk of unsuccessful performance is high. The proposal may be recommended for acceptance but is at a lower priority than submissions rated 'Outstanding', 'Good' or 'Acceptable'.
Unacceptable (U)	The proposal is not pertinent to program goals and objectives and contains one or more deficiencies. The proposal is unawardable.

4.3 Phase I Proposal

The evaluation of Phase I proposals will be based on the two factors listed below. Each factor will be assigned one of the following adjectival ratings: Outstanding (O), Good (G), Acceptable (A), Marginal (M) or Unacceptable (U). Any factor scored as "Unacceptable (U)" will render the offeror's proposal "Unawardable," and the proposal will not be considered further.

Phase I evaluation factors to be used to evaluate and select Quad Charts/White Papers are listed below in order of decreasing importance.

4.3.1 Factor 1 – Scientific and Technical Merit

The objective of this factor is to assess the extent to which the Offeror has an innovative, unique, high payoff, and comprehensive technical approach based on sound scientific principles. Offerors must demonstrate that their approach is innovative, unique, and responsive to the topic as presented in this solicitation; that the technical approach is sound; that they have an understanding of critical technical issues and risk and that they have a plan to reasonably mitigate those risks where possible. Significant improvements in chemical and biological technology capability above the 'state-of-the-art' are sought.

4.3.2 Factor 2 – Value to Mission Goals

The objective of this criterion is to assess the extent to which the Offeror's proposal provides a rapid path of application of the technology to the DoD. Offerors must demonstrate a clear knowledge of desired military capabilities and indicate the manner in which the technology will transition. Proposals must demonstrate how the proposed research supports the program goals and responds to the specific topic areas. Offerors must demonstrate that the new technology can be implemented or utilized by end-users as a means to improve their operational capabilities.

4.4 Phase II Proposal

The evaluation of Phase II proposals will be based on the four factors listed below. Factors 1 through 3 each will be assigned one of the following adjectival ratings: Outstanding (O), Good (G), Acceptable (A), Marginal (M) or Unacceptable (U). Factor 4 will be assigned a rating of Realistic or Not Realistic. Any factor scored as "Unacceptable (U)" or Not Realistic will render the offeror's proposal "Unawardable," and the proposal will not be considered further.

Phase II evaluation factors to be used to evaluate and select full proposals are listed below in

decreasing order of importance. Additionally, pursuant to FAR 35.016(e) fund availability shall be a consideration during evaluation.

4.4.1 Factor 1 – Scientific and Technical Merit

The objective of this factor is to assess the extent to which the Offeror has an innovative, unique, high payoff, and comprehensive technical approach based on sound scientific principles. Offerors must demonstrate that their approach is innovative, unique and responsive to the topic as presented in this solicitation; that the technical approach is sound; that they have an understanding of critical technical issues and risks and that they have a plan for mitigation of those risks. Significant improvements in chemical and biological technology capability above the 'state-of-the-art' are sought.

4.4.2 Factor 2 – Value to Mission Goals

The objective of this criterion is to assess the extent to which the Offeror has a credible and feasible scientific solution that best meets or exceeds the topic requirements and provides a rapid path of application of the technology to the Department of Defense. Offerors must demonstrate a clear knowledge of desired military capabilities and indicate the manner in which the technology will transition. Proposals must demonstrate how the proposed research supports the program goals and responds to the specific topic areas. Offerors must demonstrate that the new technology can be implemented or utilized by end-users as a means to improve their operational capabilities.

4.4.3 Factor 3 – Capability of the Personnel and Facilities to Perform the Proposed Effort

The objective of this factor is to assess the extent to which the Offeror's team has the requisite expertise, skills and resources necessary to perform the proposed program. This includes an assessment of the team's management construct, key personnel, facilities and past technical experience in conducting similar efforts of the proposed scope. Offerors must demonstrate that their team has the necessary background and experience to perform this project. Facilities should be detailed with discussion of any unique capabilities pertinent to the research. Subcontractors may include Government facilities or Agencies; however the unique expertise or specialized facilities provided through their inclusion must be clearly presented.

4.4.4 Factor 4 – Cost Realism

This objective of this factor is to establish that the proposed costs are reasonable and realistic for the technical approach offered and to assess the Offeror's practical understanding of the scope of the proposed effort. Proposals also will be evaluated for cost justification in relation to the scope of the proposed effort.

4.5 Basis for Selection Decision

Phase II proposal invitations will be extended to, and contract awards will be made to, the best proposals that are determined to be most beneficial to the Government with appropriate

consideration given to the evaluation factors, order of importance, and selection preferences. Other factors that may be considered include duplication with other research, program balance across research topics, and budget limitations. The Government may also evaluate the impact of any asserted data/software restrictions or patents during the selection and/or negotiation process, and may request additional information from the Offeror, as may be necessary, to evaluate the Offeror's assertions. Proposals may be selected for funding which are not rated as highly as others and which may be of higher risk and higher cost. Multiple awards are anticipated. The Government reserves the right to select for negotiation all, some, one, or none of the proposals received in response to this BAA.

4.6 Notification to Offerors

Selection and non-selection notifications will be sent via e-mail to Offerors - specifically, the registered business point of contact and the designated Principal Investigator as entered on the proposal cover page on the DTRA proposal submission website. The e-mail will be sent from the DTRA proposal submission website on or about the date specified in Section 6.0. Additionally, notification of apparent successful Offerors will be posted to http://www.fbo.gov on or about the date specified in Section 6.0.

4.7 Debriefing

The Government will provide written debriefings to Offerors if a request is submitted and received within three working days of Phase II proposal non-selection notifications.

Note: Debriefings will not be provided for Phase I proposal submissions.

4.8 Other Considerations

4.8.1 Negotiations

Phase II proposals selected for award will be subject to negotiations, which will include costs and price and may include technical scope. Additionally, the Government may elect to fund only part of a submitted proposal and may incrementally fund any or all awards under this BAA. The Procuring Contracting Officer (PCO) will have the ultimate authority and responsibility to make final scope determinations for selections of proposals that will not be totally funded to ensure the portion selected meets the solicited requirements and does not represent a substantial change to the original scope of work proposed.

During the course of negotiations, Offerors whose proposals are selected for potential award will be contacted to provide additional information required to facilitate the negotiation process and to allow for award. Offerors that are not responsive to Government requests for information in a timely manner, defined as meeting government deadlines established and communicated with the request, may be removed from award consideration. Offerors may also be removed from award consideration if the Offeror and the Government fail to negotiate mutually agreeable terms within a reasonable period of time.

4.8.2 Reserve List of Selected Proposals Subject to Availability of Funds

The Government reserves the right to create and maintain a reserve list of proposals for potential funding, in the event that sufficient funding becomes available. The reserve list will remain active and available for funding for up to 12-months after the date of selection. All awards are subject to the availability of funds.

4.8.3 Responsibility Determination

The PCO shall make a final determination on selectees' responsibility and responsiveness to BAA terms and conditions. Any of these determinations may render an impending proposal or selectee ineligible for contract award.

5.0 Contract Data Requirements Lists (CDRLs)

Resultant contracts will contain specific deliverable requirements contained within DD Form 1423 CDRLs. The CDRL lists those data deliverables that are required, under the terms of the contract, to be delivered to the Government in accordance with the information in the CDRL and the contract itself. The CDRL will identify the necessary information needed by the contractor to deliver acceptable data items to the Government. This includes a description of the data item, any acceptance criteria, the format of the deliverable, and any delivery information.

While Topic-specific deliverables will apply, all resultant contracts will contain the following general deliverable requirements:

Annual Project Spend Plan
Monthly Cost/Financial Status Report
Monthly Progress Report
Annual Report
Final Project Report
Meeting/Teleconference Minutes

Final CDRL requirements will be negotiated prior to contract award.

6.0 Estimated Milestones

MILESTONE SCHEDULE	DATE
BAA Posted to FBO	18 Jul 2016
Begin registration at the DTRA proposal submission website	18 Jul 2016
DTRA proposal submission website opens for receipt of Quad Chart/White Paper	18 Jul 2016
Deadline to submit questions	9 Sep 2016
Questions and Answers posted at FBO	23 Sep 2016
Phase I Proposal receipt deadline	30 Sep 2016
Phase II Proposals invited	17 Nov 2016
Phase II Proposal receipt deadline	23 Dec 2016

Announcement of Apparent Successful Phase II Offerors; non-selection notifications will follow within two weeks ("on or about" is used since this is an estimate)	20 Feb 2017
Estimated First Award Date ("on or about" is used since this is an estimate)	21 Jul 2017[1, 2]

Notes:
1: Actual award dates will vary based on complexity, statutory requirements, quality of proposal, pricing considerations, DCAA audits of proposed rates, type of instrument, number of awards, and other considerations. All dates are subject to change.
2: Awards will be made subject to the availability of funds.

7.0 Topic Requirements

Proposals will be accepted and considered that combine Basic Research with Applied Research, Applied Research, and/or Advanced Technology Development as specified in each topic. This BAA will not consider Advanced Component Development and Prototypes under Section 819 of Public Law 111-84. However, offerors may propose efforts necessary to evaluate integrated advanced development to expedite technology transition from the laboratory to operational use under a final option and limited to a period of one year while a new competitive effort can be awarded.

7.1 List of Topics

The DoD is interested in soliciting proposals in the following areas of Chemical and Biological Defense. The intent of these topics is to identify technologies that fill identified capability needs in the DoD Chemical and Biological Defense Program. The level of detail provided for each specific technology area and sub-area or order in which they appear is not intended to convey any information regarding relative priority.

This BAA is limited to projects that meet Technology Readiness Level (TRL) definitions in the TRL range 3-6. Upon completion of proposed development efforts, solutions should strive to meet a TRL in the range of 4-6. Proposals that address technologies at TRL 4 or greater should also be aware of the Manufacturing Readiness Level (MRL) considerations.

Topic: CBA-01
Challenging Agents by Novel Diagnostic Orthogonal (CANDO) Technology Program

Background: A myriad of bacterial and viral pathogens may manifest as severe acute systemic febrile illness with nonspecific symptoms. These pathogens are both extremely difficult to diagnose and self-limited in duration; lasting in the bloodstream for only a few days to weeks. Diagnosing these illnesses can be challenging and usually requires a high index of suspicion and clinical awareness. Several of the serious and potentially life threatening infections include brucellosis[1], epidemic typhus[2] and viral encephalitis[3]. In fact, limited data is available to support a diagnostic approach for viral encephalitis caused by Eastern, Western and Venezuelan equine encephalitis viruses. Many non-human primate (NHP) animal studies have shown that viremia is short-lived with variability in viral load. Previously developed real-time polymerase chain reaction (PCR) diagnostic assays

(amplification of pathogen target genes) for both brucellosis and epidemic typhus were terminated due to multi-center clinical trial performance below acceptance criteria.

Objective: This topic seeks proposals to deliver clinically relevant and diagnostically informative approaches for developing signatures and/or tests to identify and diagnosis severe acute systemic febrile illness caused by *Brucella spp*., *Rickettsia prowazekii*, Eastern equine encephalitis virus, Western equine encephalitis virus, and Venezuelan equine encephalitis virus. Enhancements over the current state of diagnostics for these pathogens are required. Analyte discovery efforts must be accompanied by studies to verify the diagnostic window and parameters of the analyte (i.e., appropriate body fluid/clinical sample matrix, time post-exposure, etc.) in relevant animal models. This topic will ultimately support the Joint Program Executive Office (JPEO) Joint Project Management Office for Medical Countermeasure Systems (MCS) Diagnostics program to develop diagnostic tests for acute brucellosis, epidemic typhus and arboviral encephalitis.

The goal is discovery and verification of diagnostic window and parameters of novel circulating analytes for diagnosis of acute brucellosis, epidemic typhus and arboviral encephalitis. Single or multiple approaches with accompanying diagnostic algorithm for each causative agent may be submitted; however, higher priority will be given to proposals that address more than one of the pathogens.

Science and Technology Needs: research should focus on answering the following knowledge gaps with the listed considerations.

- Analyte(s) Identification: define the appropriate analytes that can be targeted as an indication of the corresponding clinical disease. Analytes are preferably pathogen derived, highly specific to the causative agent, and detectable by nucleic acid amplification or affinity techniques. Host-based markers should be included only by exception due to validation challenges and an unclear pathway to regulatory clearance in the near- to mid-term (2-5 years).
    - Serological (antibody capture) methods must be developed and validated against well-characterized serum sample panels with relevant representation of pathogen species titers (sero-positivity and negativity), immunoglobulin class (IgM, IgG), titer, clinical, geographical metadata, etc.
    - DNA methods that target multiple or enhanced genetic element signatures, improved amplification and extraction efficiency though primer design and probe chemistry, extended and re-optimized cycling protocols, and/or ultrasensitive amplicon detection modality are examples of approaches that may address challenges.
    - Antigen capture immunoassays should focus on secreted, circulating and in vivo amplified bacterial pathogen antigen biomarkers.
    - Assay validation test plan must be presented for high TRL (≥5) proposed analyte tests.
- Clinical Matrix Identification: define the matrix or matrices where the analytes reproducibly accumulate to detectable levels during clinical disease. Non- (or minimally) invasive specimen matrices for measuring analytes are encouraged. Clinical matrices that are compatible with Army medical role 3 collection capabilities

would be the minimum standard for consideration (urine, whole blood, serum, sputum, nasopharyngeal swab).

- Diagnostic Window: define the time period when the analytes accumulate to detectable levels in the clinical matrix. Additional information that defines the expected analyte concentration in each matrix will inform the appropriate detection platform based on analytical capabilities (e.g. LFI, immunoassay instrument, etc.). The analytes would preferably be detectable within 7 days of symptom onset as this would align with a role 3 diagnostic as it relates to patient movement within the military medical roles of care.

Offerors are encouraged to develop R&D collaborations with other organizations in Government, academia, and the private sector to broaden and strengthen their knowledge, experience and capabilities. Additionally, offerors are encouraged to take advantage of specialized resources in the DoD and other Government agencies such as facilities/capabilities.

References:

1. Pappas G, et al. 2005. Brucellosis. *N Engl J Med*.
2. Bechah et al. 2008. Epidemic typhus. Lancet Infect Dis
3. Zacks. 2010. Encephalitic Alphaviruses. *Veterinary Microbiology*

Topic: CBA-02
Field Assays for Chemical Weapons Exposure

Background: Current methods for determination of human exposure to chemical warfare agents (CWAs) are limited, in that they rely upon visible signs and symptoms, inference from detection of the agent itself outside of the body, or lab-based mass spectrometric methods. The only current FDA-approved assay for determining chemical warfare agent exposure in the field is the Test-mate ChE Cholinesterase Test System [1] (a CLIA moderate complexity test based on the Ellman assay), which is approved for cholinesterase level measurement from fresh whole blood, derived from a 4-microliter finger stick and with a 4-min time to result. However, there are a variety of limitations of this assay. For example, the assay has a narrow operational temperature range, no data export capability, no controls, and a poor negative predictive value. Moreover, the assay's reliance upon a single exposure biomarker gives it an inability to distinguish between various possible CWAs which would call for variations in countermeasure responses.

Recent agent- and host-based signatures of exposure to nerve agents and other CWAs of current concern [2-6], together with the possibility of modifying assays under development for drugs of abuse [7] and adopting a multiplexed format with the potential ability to perform semi-continuous communication of assay results, offers the potential to address the inherent limitations of the Test-mate system. Coupling known biomarkers and recent assay developments will provide the warfighter with the ability to rapidly assess, in the field, whether exposure to a CWA has occurred and to achieve greater resolution as to the nature of the insulting agent and therefore the proper tactical and medical response, within specific military scenarios.

Objective: This topic seeks proposals that leverage known biomarkers of exposure to CWAs into assays for employment in any of the following contexts: (a) minimally invasive assays for high levels of exposure to long latency cholinesterase-inhibiting agents for which medical intervention could change the outcome; (b) low burden trigger to treat for presumptively exposed personnel without objective signs of exposure in high threat scenarios; or (c) high level exposures to long latency cholinesterase-inhibiting agents for which medical intervention could change the outcome. Assays should be applicable to multiple CWAs of current concern. The goal is to develop low-cost, FDA-cleared assays applicable to determining exposure to chemical warfare agents in a battlefield setting. This topic will ultimately support the JPEO MCS Diagnostics program to develop field diagnostic tests for chemical warfare agents.

Offerors shall address the following in their technical approach:

- A clear roadmap to FDA approval of a field assay for CWAs with 7 years, with clearly defined and measureable quantitative go/no-go decision points subject to validation by government-defined entities external to the performing team.
- Articulate consideration of how the assay would be applied within a field setting relevant to one or multiple of the contexts described above, including realistic limitations of such application(s).
- A robust plan for translation from appropriate in vitro and in vivo models to human relevance, as well as translation from any experiments which may initially employ chemical warfare agent simulants to those which employ the actual agents at appropriate facilities.
- A plan and appropriate partnerships to enable translation of successfully demonstrated assays to either current commercial platforms [8-10] or new platforms which will be commercialized.
  This topic is NOT seeking efforts which are focused purely on: new biomarker discovery, laboratory-based analysis or forensics methods, or computational modeling.

Offerors are encouraged to develop R&D collaborations with other organizations in Government, academia, and the private sector to broaden and strengthen their knowledge, experience and capabilities. Additionally, offerors are encouraged to take advantage of specialized resources in the DoD and other Government agencies such as facilities/capabilities.

References:

1. http://www.eqmresearch.com/
2. A. W. Tuin, *et al.* "Activity-Based Protein Profiling Reveals Broad Reactivity of the Nerve Agent Sarin," *Chem. Res. Toxicol. 22,* **2009**, 683-689.
3. D. Noort, *et al.* "Biomonitoring of Exposure to Chemical Warfare Agents," *Environmental Aspects of Converting CW Facilities to Peaceful Purpose.* NATO Science Series, *37,* **2002**, 21-29.

4. R. A. Evans *et al.* "Quantification of Sarin and Cyclosarin Metabolites Isopropyl Methylphosphonic Acid in Minipig Plasma Using Isotope-Dilution and Liquid Chromotography-Time-of-Flight Mass Spectrometry," *J. Anal. Toxicol. 32*, **2008**, 78-85.
5. http://www.ecbc.army.mil/about/posters/2015/B17.pdf
6. B. Li, *et al.* "Polyclonal Antibody to Soman-Tyrosine," *Chem. Res. Toxicol. 26*, **2013**, 584-592.
7. https://tools.thermofisher.com/content/sfs/manuals/10016007-DRI-Fentanyl-Assay-CJF-EN.pdf
8. https://www.luminexcorp.com/clinical/instruments/magpix/
9. http://www.philips.co.uk/healthcare/product/HCNOCTN496/minicare-i-20
10. https://www.abbottpointofcare.com/

Topic: CBA-03
Integrated Early Warning Ecosystem for Chemical and Biological Defense

Background: The Biosurveillance Ecosystem (BSVE) is a virtual, customizable, collaborative system that leverages existing commercial and government technologies. The BSVE is a cloud-based system that ingests a wide variety of data sources: open source data; social media, diagnostic data; and DoD, Interagency, national and international surveillance system data. Analytic applications "apps", developed and integrated by third parties, utilize the published BSVE Software Developer's Kit (SDK). These apps use data streams to provide alerts, near-real-time modeling, analyses, and visualize results. The BSVE supports the biosurveillance analysts' and decision-makers' needs by providing automated, intelligently suggested data, tools, and analyses. The BSVE also provides a user-friendly interface with modern collaboration and reporting features.

The BSVE architecture supports HTML5, Java, Python, R Shiny, PostgreSQL, MongoDB, and Hadoop.

Objective: This topic seeks proposals to broaden and enhance the current BSVE architecture and technologies to provide improved CBD situational awareness, a common analytical work bench for users, integration and fusion of a wide array of relevant data sources, and decision support tools for the tactical to strategic level command authorities. Focus areas of this topic include:

- Data & Integration:
  - Identifying optimal data sources and capture resolution (e.g., elements, frequency) to allow for efficient data transfer and actionable early warning
  - Acquiring data sources through the implementation of standards-based device-to-cloud connectivity for platforms to include open source information, medical diagnostic devices, wearable technology, environmental sensors, unmanned platforms and genomic sequences
  - Integrating real-time information from multiple end point sensors to a central data processing system capable of assessing alarm data and presenting validated, actionable alerts to the end user in a remote location
  - Processing real-time information through Natural Language Processing pipeline to enrich content (e.g., geospatial, demographic, key event details)

- System Enhancements:
  - Supporting future transition by validating across multiple scenarios with multiple users that information provided allows warfighters to take timely mitigating actions
  - Employing adaptable visualization functionality for standard and tactical displays (e.g., mobile devices and ocular displays)
  - Enabling collaborative, risk-based decision making
  - Maximizing flexibility of the central data processing software through working with collaborators to render it agnostic to source devices, with an aim to decrease integration costs and increase operational relevance
- System Integration and Security:
  - Decreasing risk of data intercept or manipulation through increasing the security of data communications
  - Application of a FEDRAMP certified approach with the intention of supporting Authority To Operate (ATO)
- Expertise:
  - Providing relevant subject matter expertise in areas such as: Epidemiology, Public Health, Geospatial Information Systems, Human Factors, Network Security, Enterprise Architecture, Computer Science, Agile Development, CBD Operational Warfighter Experience

Topic: CBA-04
Analytics and Data Sources to Support DoD Integrated Early Warning

Objective: Ensuring state of the art technologies are made rapidly accessible, this topic seeks proposals that develop analytic applications (apps) to acquire, synthesize and interrogate multiple sources of data (open source information, medical diagnostic devices, wearable technology, environmental sensors, unmanned platforms and genomic sequences) to provide high confidence in the prediction and early warning of chemical or biological events. Metrics shall be devised such that successful utilization of these analytic tools will result in a measureable impact on the event timeline or consequence. These technologies should be capable of residing in an existing DoD platform such as the current BSVE. Focus areas of this topic include:

- Development of analytic applications capable of fusing multiple, disparate data sources and providing an optimized anomaly detection alert based on unique mission objectives
- Quantification, in real-time, how the fusion of disparate data sources affects the alerting accuracy and timeline for a wide variety of CBD events
- Development of a robust Natural Language Processing capability to enrich CBD relevant content in real-time (e.g., geospatial, demographic, key event details) which may include machine learning approaches

Topic: CBA-05
Identification of Optimal Clinical Matrices for Etiologic Biothreat Agent Disease Diagnosis

Objective: This topic seeks to develop a comprehensive reference guide for detection of biothreat targets in body fluid matrices. Utilizing published literature as well as unpublished institutional studies, the reference guide will deliver a survey of clinically relevant and diagnostically informative studies in order to identify the optimal clinical matrices for biothreat targets. The data is to determine intended use statements of diagnostic devices, specifically at patient point of need (PON).

The survey must include identification of all relevant clinical matrices, identification of the optimal clinical matrix and the clinically relevant diagnostic window for pathogens (at a minimum: *Burkholderia pseudomallei/Burkholderia mallei, Bacillus* anthracis, *Yersinia pestis* and *Brucella spp.* The final deliverable will be a comprehensive report.

Offeror proposals shall address the following in their technical approach:

- Clinical Matrix Identification:
  - Study protocol/design: Specify type strain, animal model, route of exposure, exposure dose/$LD_{50,}$ collection time points, other relevant pathologic findings or human clinical sample collection metadata, etc.
  - Identification of optimal matrices for specific disease type (e.g. inhalational, cutaneous, etc.)
  - Specify presence of culturable agent and/or detectable surrogate analyte in clinical matrices that are compatible with PON collection capabilities (at a minimum: urine, blood, serum, sputum, nasopharyngeal swab):
    - Blood: whole blood (venipuncture vs capillary/fingerstick blood, plasma, serum). Identify anticoagulant used (if any).
    - Offerors are highly encouraged to include data on body fluid matrices where the pathogen/analytes reproducibly accumulate to detectable levels during clinical disease utilizing non-invasive or minimally- invasive sample collection: saliva, sweat, etc.
- Diagnostic Window: identify the time period when the analytes accumulate to detectable levels in each clinical matrix. Additional information that defines the expected analyte concentration in each matrix will inform the appropriate detection platform based on analytical capabilities. The analytes would preferably be detectable within 7 days of symptom onset as this would align with a diagnostic tests intended use as it relates to patient movement within military medical care.

Offerors are encouraged to develop collaborations with other organizations in Government, academia, and the private sector to broaden and strengthen their knowledge, experience and capabilities. No animal or human studies will be authorized for this program.

Topic: CBS-01
Development of New Platform Technology for Nerve Agent Prophylaxis

Background: The human body employs a wide variety of mechanisms in order to partially protect itself from the adverse effects of inhaled or absorbed toxicants. These interconnected mechanisms range, for example, from selective barriers such as the skin and various endothelial and epithelial partitions, to membrane efflux pumps, scavenging or catalyzing

proteins, radical scavengers, immune-mediated responses, and metabolic and excretion processes. However, since the body has only a limited capability to respond to extremely deadly toxicants such as chemical warfare agents (CWA), the Chemical and Biological Defense Program is pursuing the development of enhanced prophylaxis by modulation of one or more of these mechanisms in order to provide greater protection. In this vein, for example, it is known that natural variations among individuals and populations can lead to significant and measureable differences in the response to pharmaceuticals and toxicants of various classes. These variations can be due to genetic or environmental influences. In certain cases the specific phenotypic and genotypic loci contributing to such natural variation in the human host response to xenobiotics have been characterized. [1-6] As just one example, certain healthy human populations have a genetic variation, "Cynthiana variant," [7, 8] a condition of 2-3 fold increased levels of plasma butyrylcholinesterase, which leads to a lowered efficacy of certain drugs and toxicants that act at the nerve synapse.

Novel approaches to prophylaxis against CWA could be envisioned to focus on upregulating or otherwise modulating such natural resistance mechanisms to offer systemic protection to exposed individuals. When coupled with careful consideration of appropriate targeting modalities [9, 10] as well as drug delivery methods relevant to military operations in chemically contaminated environments, the potential exists for breakthrough approaches to new FDA-approved prophylactics to CWA. Appropriate exploitation of such relevant *in vivo* response pathways could address several of the limitations inherent in current work that relies upon exogenously-derived countermeasures, including problematic immunogenicity and bioavailability.

Objective: This topic seeks proposals to develop and advance physiological production and distribution of prophylactic medical countermeasures against chemical weapons of mass destruction. The aim of this topic is to ultimately provide the warfighter with increased protection, survival, reduced morbidity, and greater ability to operate in contaminated environments without complex pre-mission preparation. It is further envisioned that the developed prophylactic, whether based on modulation of endogenous protein expression or other innate protective responses, will ultimately be FDA approved. This topic is specifically focused on new platform approaches which have the potential for high impact on the military's ability to function in environments contaminated with nerve agents, via breakthroughs in relevant prophylactics.

- Innovative approaches are desired which induce or enhance the body's innate ability to respond to systemic exposure to nerve agents.
- Protective efficacy against 2-5 times the LD_{50} for an exposure modality relevant to military operations must be demonstrated. In addition, prophylaxis must be fully effective within three days of the initiation of the protective measure and must persist for at least ten days.
- Offerors shall demonstrate an understanding of how the prophylactic could be effectively administered in a military setting.
- Offerors shall outline a clearly defined regulatory pathway to FDA approval within 8 years, including clearly defined steps and measureable quantitative go/no-go decision

points subject to validation by government-defined entities external to the performing team.

- Offerors shall present a robust plan for translation from pharmacologically-relevant animal models to effects in humans, as well as translation from experiments which may initially employ nerve agent simulants to experiments which employ the actual agents at appropriate facilities.
- Offerors shall outline appropriate pharmacokinetic, pharmacodynamic, absorption-distribution-metabolism-excretion (ADME), toxicity and mechanism of action studies to support regulatory requirements.
- In addition, offerors shall describe relevant biomarkers associated with their approach and the status of required assays, in terms of whether they are validated, in development, or proposed.
- The maturity of supporting synthetic activities should also be described, together with an estimate of scale-up costs which may ultimately be required. Activities which will require subcontracts must be detailed together with contingency plans to mitigate risk.

Note that this topic is NOT seeking traditional drug discovery approaches which rely heavily upon computational methods, high throughput compound screening, or repackaging of approved countermeasure pharmaceuticals. The topic is also NOT seeking approaches already in discussion with the FDA in an Investigational New Drug (IND) context.

Funding Profile: Proposals are sought for projects with a funding level of $0.5-1.3M per year, with a one-year base period and up to four additional option years.

References:

1. M. Najarro, *et al.* "Identifying Loci Contributing to Natural Variation in Xenobiotic Resistance in Drosophila," *PLoS Genet. 11*, 2015, e1005663.
2. D. Epel, *et al.* "Efflux Transporters: Newly Appreciated Roles in Protection against Pollutants," *Environ. Sci. Technol. 42*, 2008, 3914-3920.
3. W. Osburn, *et al.* "Nrf2 signaling: An adaptive response pathway for protection against environmental toxic insults," Mutation Res./Rev. Mutation Res. 659, 2008, 31-39.
4. B. La Du, *et al.* "On the physiological role(s) of the paraoxonases," *Chemico-Biol. Interact. 119-120*, 1999, 379-388.
5. S. Georas, *et al.* "Environmental exposures and innate immunity in the lung," *J. Environ. Immunol. Toxicol. 2*, 2014, 1-3.
6. W. Jakoby, *et al.* "The Enzymes of Detoxication," *J. Biol. Chem. 265,* 1990, 20715-20718.
7. A. Yoshida, *et al.* "A Pseudocholinesterase Variant (E Cynthiana) Associated with Elevated Plasma Enzyme Activity," *Am. J. Hum. Genet. 21*, 1969, 486-498.
8. M. Naguib, *et al.* "Increased plasma cholinesterase activity and mivacurium resistance: report of a family," *Anesth. Analg. 89*, 1999, 1579-1582.
9. S. Kim, *et al.* "A tumor-targeting p53 nanodelivery system limits chemoresistance to temozolomide prolonging survival in a mouse model of glioblastoma multiforme," *Nanomed.: Nanotechnol., Biol., Med. 11*, 2015, 301–311.

10. E. Duysen, *et al.* "Adenovirus-mediated human paraoxonase1 gene transfer to provide protection against the toxicity of the organophosphorus pesticide toxicant diazoxon," *Gene Therapy 18*, 2011, 250-257.

Topic: CBS-02
Computational Rapid Identification & Scientific Threat AnaLysis (CRISTAL)

Background: Currently, there are many different software tools that have not been applied to the DoD's need to assess a compound's "potential to cause acute, debilitating toxicity." Some of these models might provide a valuable backbone for predicting physicochemical properties, environmental fate and acute toxicity. Many commercial models have been designed for pharmaceutical use in terms of structure-activity prediction, physiologically-based pharmacokinetics/pharmacodynamics, different products have been developed (government and commercial) to forecast physicochemical properties from molecular structure or to utilize fundamental experimental data to determine likely agent fate parameters. These models have all been developed for specific uses, but do not "talk" to each other to create a chemical characterization continuum.

Upon receipt of "Application of Modern Toxicology Approaches for Predicting Acute Toxicity for Chemical Defense,"(1) the Threat Agent Science (TAS) Program began an analysis of its current program to find where efficiencies could be gained, as well as where in silico approaches were already being employed. Through that analysis, many programs that look into physical, chemical and toxicological properties, as well as environmental agent fate, were identified as intrinsic components to the existing experimental program. These include:

- ACD Labs
- EPI Suite (EPA)
- GEO Pearl Pesticide fate model
- EFAST: Exposure and Fate Assessment Screening Tool (EPA)
- Simulations Plus ADMET Predictor
- Simulations Plus Gastroplus
- Simulations Plus MedChem Designer
- Simulations Plus MedChem Studio
- Other commercial and government modeling software tools that predict chemical or particle behavior or environmental and physiological response.

In addition to the programs listed above, "ChemDraw" is used by many chemists and toxicologists in initial design and analysis of chemicals, though many of the current computational tools will not import chemical structures from that software to use as a starting point. Ultimately, the capability should have multiple points for insertion and extraction of information. A "smart system" that is flexible enough to take in multiple streams of data in and extrapolate to useful endpoints.

In order to be successful, CRISTAL requires a combination of technical areas to ensure a comprehensive look at the problem which includes: physicochemical properties, chemical

disposition and metabolism, through acute toxicity predictions. A successful approach will require validation steps with available in vitro and in vivo data to support model reliability. The components of CRISTAL are not independent, or even linear, but parts of an integrated capability. The system needs to be able to coordinate between and around these disparate datastreams in a way that provides access to critical information that can inform decision makers and countermeasure developers in a timely fashion.

CRISTAL is divided into many parts:

1. Development of computational tools to predict physicochemical properties, acute systemic toxicity and/or environmental fate;
2. Development of medium- to high-throughput laboratory approaches to predict:
   a. laboratory animal and/or human *in vivo* acute toxicity of chemical threat agents and verify fidelity of computations and
   b. environmental agent fate in a variety of operationally relevant matrices (soils, grasses, asphalt, concrete, etc.) of chemical threat agents and verify fidelity of computations; and
3. Development of a tool to integrate currently used computational models and databases.

Part 1: Includes but is not limited to the development of computational tools to predict properties and fate for a broad range of chemicals. **(Proposals are not currently being solicited for Part 1 of CRISTAL.)**

A. Initial characterization of physicochemical properties along with *in-silico* approaches such as:
   a. Structure-activity relationship (SAR)
   b. Quantitative structure-property relationship (QSPR) (2)
   c. Quantitative structure-activity relationship (QSAR) (3)
   d. category and analogue approaches where prediction can extend to chemical families
B. Initial prediction of chemical disposition and metabolism

Objective: There is a need for development and integration of "non-testing approaches" that bring together multiple property evaluations and toxicity factors to enhance predictive characterization, environmental fate and toxicology for chemical threat agents. This area will seek to integrate disparate areas and fill identified gaps in computational and *in vitro, ex vivo,* non-mammalian, and non-vertebrate evaluation of potential threat agents and their activity on or in the human. This topic seeks proposals for Parts 2 and 3 of CRISTAL as reflected below.

Part 2: Development of medium- to high-throughput laboratory approaches to predict acute systemic toxicity and/or environmental agent fate. (Multiple proposals are being solicited in this area. Multiple awards are anticipated. Awards are expected range between $250,000.00 and $2,000,000.00)

A. Development of medium- to high-throughput laboratory approaches to predict acute systemic toxicity in laboratory animals and/or humans of chemical threat agents for operationally relevant routes of exposure (ocular, inhalation (nose-only and whole-body) and dermal) and verify fidelity of computations. Any effort proposed against this area MUST demonstrate the ability to place known organophosphate-, organphosphonate- and carbamate-pesticides, as well as G- and V-type chemical warfare agents in appropriate order of human systemic toxicity by one or more operationally relevant routes of exposure. Preference will be given to those approaches that can accomplish both "a" and "d" below.
    a. *In vitro, ex vivo,* non-mammalian, and/or non-vertebrate experimental approaches to increase throughput
    b. Absorption and deposition (noting differences between oral, dermal, inhalational routes of exposure)
    c. Metabolism
    d. *In vitro, ex vivo,* non-mammalian, and/or non-vertebrate experimental approaches to assess volatile chemicals
B. Development of medium- to high-throughput laboratory approaches to predict environmental agent fate in a variety of operationally relevant matrices (soils, grasses, asphalt, concrete, etc.) of chemical threat agents and verify fidelity of computations and provide information that is otherwise unavailable. The product would include properties and outputs suitable for operational modeling parameters (such as JEM, JWARN, HPAC).
    a. Physical Properties such as vapor pressure, viscosity, surface tension, density
    b. Partitioning between aqueous, organic and vapor phases, dissociation constants.
    c. Aqueous and thermal stability, sorption and interaction with operationally relevant matrices under operationally relevant conditions.

Part 3: Development of a tool to integrate existing computational tools and databases with flexibility to add components as identified or developed. (Multiple proposals are being solicited in this area. Multiple awards are anticipated. Awards are expected range between $250,000.00 and $1,200,000.00)

Tools and databases to be included in the initial integration include:

- ACD Labs
- EPI Suite (EPA)
- GEO Pearl Pesticide Fate Model
- EFAST: Exposure and Fate Assessment Screening Tool (EPA)
- Simulations Plus ADMET Predictor
- Simulations Plus Gastroplus
- Other commercial and government modeling software tools that predict chemical or particle behavior or environmental and physiological response.

In addition to the tool, it should be able to take output from "ChemDraw,"as well as the SMILES string, and be able to incorporate that into the above computational tools.

DTRA Threat Agent Science is seeking proposals for the areas specified above including: Development of medium- to high-throughput laboratory approaches for predicting acute systemic toxicity; Development of medium- to high-throughput laboratory approaches for predicting environmental fate; and/or Development of a tool to integrate the data from the laboratory methods and all of the multiple computation predictive tools that CRISTAL currently uses.

References:

1. National Academies of Sciences, Engineering, and Medicine. **Application of Modern Toxicology Approaches for Predicting Acute Toxicity for Chemical Defense**. Washington, DC: The National Academies Press, 2015. doi:10.17226/21775.
2. Katritzky, A. R., Lobanov, V. S., & Karelson, M. (1995). *QSPR: the correlation and quantitative prediction of chemical and physical properties from structure. Chem. Soc. Rev.*, *24*(4), 279-287.
3. Cherkasov, A., Muratov, E. N., Fourches, D., Varnek, A., Baskin, I. I., Cronin, M., ... & Consonni, V. (2014). *QSAR modeling: where have you been? Where are you going to?. Journal of medicinal chemistry*, 57(12), 4977-5010.
4. National Research Council. **Toxicity Testing in the 21st Century: A Vision and a Strategy**. Washington, DC: The National Academies Press, 2007. doi:10.17226/11970.

Topic: CBMV-01
Next-Generation Prophylaxis Platform Technologies

Background: There continues to be significant strides toward the development of rapid production platform prophylaxis technologies that launch prophylaxis medical countermeasures against emerging and unanticipated threat agents. A goal of platform prophylaxis technologies is to reduce risk and shorten the timeline of prophylaxis conception through clinical use. To achieve this goal, it is desirable to identify strategies that minimize the technological requirements for effective development of a desired prophylaxis. The platform prophylaxis technologies applicable to this topic are:

- Inactivated virus/bacterial vaccine production systems
- Bacterial polysaccharide production systems
- Monoclonal antibodies that prevent infectious diseases
- Aptamers
- Novel scavenger technologies
- Novel platform production technologies (excluding viral, bacterial and bacteriophage vectors, and nucleic acid vaccines).

Objective: This topic seeks proposals that will assess the feasibility of rapid production platforms for biological prophylaxis that ultimately could be used to protect the Warfighter from biological threat agents. This topic supports the Chemical and Biological Defense Program's modernization goals by developing next-generation platform technologies for rapid production of biological prophylaxis. The objectives of this topic are to:

- Support the development of platform prophylaxis technologies that fall into the following categories:
    - Inactivated virus/bacterial vaccine production systems

    - Bacterial polysaccharide production systems
    - Monoclonal antibodies that prevent infectious diseases
    - Aptamers
    - Novel scavenger technologies
    - Novel platform production technologies (excluding plants production, viral, bacterial and bacteriophage vectors, and nucleic acid vaccines).
- Exclude platform prophylaxis technologies containing components that invoke immunity which interferes with subsequent applications of the platform prophylaxis technology, such as targeting a second indication.
- Assess the utility of platform production technologies toward the development of a prophylaxis against one or more of the following:
    - Burkholderia mallei/pseudomallei
    - Francisella tularensis
    - Arenaviruses (E.g. Junin virus (JUNV), Lassa virus (LASV), or Machupo virus (MACV))
    - Biological toxins, with the priority being marine toxins.

The desired attributes of the platform prophylaxis production system are as follows:

- Offerors developing inactivated virus/bacterial vaccine production systems shall include plans to formulate the vaccine with an adjuvant that will minimize the primary series dose amount and number requirement.
- Offerors developing bacterial polysaccharide production systems shall use systems amenable to Food and Drug Administration Good Manufacturing Practice guidelines. If using a host bacterial strain for polysaccharide production, Offerors shall aim to develop single-step allelic exchange processes for the production strain development.
- Offerors developing aptamer ideally will consider D- and L-isomer nucleic acid and amino acid components, with high-throughput microarray screening strategies.
- Offerors developing novel scavenging technologies will focus on broad-spectrum neutralization.
- Offerors shall include plans to develop high-affinity antibodies to optimize protection.
- Offerors shall include preliminary data demonstrating the utility of the platform system for production of a prophylaxis against an infectious disease or biological toxin.
- Offerors shall define how the platform prophylaxis technology reduces risk, offers manufacturing efficiencies and reduces the timeline to produce material acceptable for clinical use.
- Offerors shall include a plan to evaluate the prophylaxis candidate(s) in a small-animal model.
- Offerors should aim to induce a rapid onset of immunity, ideally measurable protective responses by 28 and no later than 90 days. Ideally, platform prophylaxis technologies shall induce durable immunity that persists greater than 1 year after the primary series, although thermally stable, single-dose formulations that afford a shorter duration of protection would be acceptable. It is envisioned that protection will be achieved with a single dose (preferred). The primary series shall not be more than 3 doses.

- It is recommended that Offerors include plans for interaction with the Food and Drug Administration to seek review of the proposed plans and to receive any additional guidance for model development selection and characterization.

Deliverables will include:

- A technical data package describing the methods, study results, compositions, formulations and other requirements that are specific for the proposed platform technology.
- A straw-man proposal as to how the platform will be utilized, including logistics, producibility and regulatory metrics, by the DoD to provide a means for rapid, flexible and agile manufacturing of medical countermeasures (MCM) to meet emergency and urgent Warfighter needs.

Advanced Development and Manufacturing (ADM) Utilization: The DoD has awarded a contract (W911QY-13-C-0010) to establish an ADM capability. In addition to providing a BSL-3 capable, multiproduct manufacturing facility for biologic products, the ADM and a consortium of teaming partners can support development of medical countermeasures from discovery through FDA approval. This includes the facilities, equipment and expertise necessary to perform nonclinical, clinical, process development, and regulatory activities. Please contact the BAA to obtain POC information for the program office managing the ADM contract. Nota bene: The decision to, or NOT to, use the ADM is totally independent of, NOT a criterion for, and will have NO bearing on the decision to select a proposal for funding.

Topic: CBMV-02
Development of a *Coxiella burnetii* Reactogenicity Model

Background: *Coxiella burnetii*, an obligate intracellular bacterium, is the etiologic agent of Q fever, an acute febrile disease that can progress to become a serious chronic illness that results in inflammation of the liver, lung, heart and brain. *C. burnetii* is readily transmitted between hosts and environmental reservoirs, with human infection primarily occurring via the inhalation of infectious aerosols. Currently, a formalin-inactivated vaccine (Q-VAX) is licensed in Australia; however, safety and utilization constraints render it unsuitable for US Warfighters. This vaccine provides near-complete protection in humans, however serious side effects have been observed in individuals either previously exposed to the pathogen or previously vaccinated. Common side effects include tenderness, erythema and oedema at the injection site, and transient headaches.
Uncommon reactions can include immune abscesses at the injection site, subcutaneous lumps that have the potential to disperse without intervention, hyperhidrosis, lymphadenopathy, granuloma, myalgia and athralgia[1, 2]. To decrease the incidence of adverse reactions, individuals must undergo a pre-vaccination screening consisting of two assays, a skin and serological test, which measure different arms of the immune system and past medical history.

While pre-vaccination screenings have significantly lowered the incidence of vaccine-related hypersensitivity, skin and blood tests are time consuming, costly, and may be incorrectly

applied or misinterpreted. Most importantly, patient populations with previous exposure to Coxiella are unable to be vaccinated. Therefore, efforts are underway to develop safer Q fever vaccines that will eliminate the requirement for pre-vaccination screening, yet retain vaccine efficacy and safety.

Development and licensure of a Q fever vaccine will proceed under the United States Food and Drug Administration (FDA) Animal Rule. When human clinical trials are not feasible or ethical, the Animal Rule enables licensure of candidate vaccines and therapeutics to proceed when efficacy is demonstrated in well-characterized animal models that reflect human disease. Therefore, suitable models with pre-exposure to *C. burnetii* which mimic reactogenicity will be required for the development and licensure of candidate vaccines. While the Hartley guinea pig model, which displays common adverse reactions such as the formation of sterile abscesses and granulomas at the inoculation site[3], is reliable, it does not recapitulate the uncommon pathologies associated with vaccination of humans who are already sensitized to Q fever antigens and who may therefore experience serious hypersensitivity reactions if vaccinated. This reactogenicity model will enable identification, development and subsequent licensure of Q fever vaccines that do not cause adverse reactions in humans.

Objective: This topic seeks proposals focused on development and standardization of a reactogenicity model for assessing vaccine-related adverse reactions that are similar to those observed in humans. Models should display hypersensitivity to a reference material (e.g. Q-Vax or inactivated *C. burnetii*) following pre-exposure to *C. burnetii.* Potential models may incorporate:

- A tiered evaluation by which a primary model is utilized as an antigen/candidate screen (e.g., delayed type hypersensitivity (DTH) skin test) followed by a secondary model to evaluate specific adverse reactions (e.g., pathology model).
- An *ex vivo* human mimetic system to evaluate the human immune response (e.g. vaccinated vs un-vaccinated or naïve vs infected donor response).

Consideration will be given to proposals that include the following:

- Models should be directly applicable to the discovery, evaluation and development of vaccines against Q fever as a result of aerosol exposure to *C. burnetii*.
- Characterization of the immune response and pathology (if animal model is developed) following pre-exposure to *C. burnetii* should be performed.
- Models should address the adverse reactions shown below:
  - Common Adverse Reactions: fever, joint swelling, injection site inflammation, induration, and oedema;
  - Uncommon Adverse Reactions: endocarditis, systemic manifestations such as lymphadenopathy, hyperhidrosis, abscess formation, and granuloma.
- Models should be planned to have sufficient statistical power to make down-selection decisions on vaccine candidates at a reasonable cost.
- Models that are less burdensome on the time of investigators and facilities will be preferred over those more burdensome

This topic supports Chemical and Biological Defense Program goals by providing a suitable model for safety testing of Q fever vaccine candidates and subsequent licensure under the FDA Animal Rule.

Regulatory Compliance: It is anticipated that a new Q Fever vaccine will need to be approved by the US Food and Drug Administration (FDA) under the Animal Rule. The Animal Rule provides a pathway for FDA approval of a new vaccine (21 CFR 19 601.90) in the event that human clinical trials are not feasible or ethical. The Animal Rule enables efficacy to be demonstrated in well-characterized animal models that reflect human disease. **Therefore, the model development to be funded under this Topic must be designed from the start for eventual compliance with the Animal Rule.** It is recommended that Offerors include plans for interaction with the Food and Drug Administration to seek review of the proposed plans and to receive any additional guidance for model development selection and characterization. FDA recently updated their relevant Draft Guidance, Product Development Under the Animal Rule (see references).

FDA-regulated studies subject to the Animal Rule submitted for approval of a specific therapeutic or vaccine must be conducted in accordance with preexisting requirements under the Good Laboratory Practices (GLP) regulations (21 CFR part 58). This GLP requirement does not apply to the research done to develop an animal model to comply with the Animal Rule, but in developing such models the steps necessary for GLP compliance must be anticipated and executed. In particular, the model will require validation. These requirements are discussed in the applicable FDA guidances. Additional information on FDA guidances is available on FDA's Web site. In addition, FDA guidances related to medical countermeasures for chemical, biological, radiological, and nuclear (CBRN) agents can be accessed through FDA's Medical Countermeasures initiative (MCMi) Web site.

ADM Utilization: The DoD has awarded a contract (W911QY-13-C-0010) to establish an ADM capability. In addition to providing a BSL-3 capable, multiproduct manufacturing facility for biologic products, the ADM and a consortium of teaming partners can support development of medical countermeasures from discovery through FDA approval. This includes the facilities, equipment and expertise necessary to perform nonclinical, clinical, process development, and regulatory activities. Please contact the BAA to obtain POC information for the program office managing the ADM contract. Nota bene: The decision to, or NOT to, use the ADM is totally independent of, NOT a criterion for, and will have NO bearing on the decision to select a proposal for funding.

References:

1. Marmion BP, Ormsbee RA, Kyrkou M, Worswick DA, Izzo AA, Esterman A, Feery B, Shapiro RA. Vaccine prophylaxis of abattoir-associated Q fever: eight years' experience in Australian abattoirs. Epidemiol Infect. 1990 Apr; 104(2):275-87.
2. http://www.csl.com.au/docs/742/54/Q-VAX_CMI_clean-final-28-january-2014.pdf#search=q-vax
3. Wilhelmesen, CL and Waag, DM. Guinea Pig Abscess/Hypersensitivity Model for Study of Adverse Vaccination Reactions Induced by Use of Q Fever Vaccines. Comparative Medicine. Vol 50, No 4: 374-378. Aug 2000.

Topic: CBMV-03
Development of a Pan-Arenavirus Vaccine that can Elicit Broad Sterilizing Immunity in the Respiratory Mucosa

Background: An ideal vaccine for the Department of Defense is one that is safe and can effectively provide sterilizing, cross-reactive immunity against aerosolized biological weapons, particularly in the respiratory mucosa. It's well known that mucosal surfaces represent the most important portal of entry for pathogens, as the respiratory tract, in particular, is continuously exposed to environmental antigens and airborne microbes, and thus employs a complex network of mechanisms that enable specific and non-specific responses to prevent infection. However, development of vaccines that can induce effective mucosal protection has been hampered by knowledge gaps in the basic immunological mechanisms responsible for the induction of broad, sterilizing mucosal immunity. Arenaviruses, which cause hemorrhagic fever in humans, have potential use as aerosolized bioweapons. Various vaccine platforms have been investigated in animal models, including a ML29 reassortant vaccine against Lassa virus that provided sterilizing immunity to subcutaneous challenge in Guinea pigs1. Additionally, significant progress in delineating the mechanisms of pathogenesis of arenaviruses revealed a critical role for cell-mediated immunity in cross-reactive protection in mucosal infection models of Lassa virus and lymphocytic choriomeningitis virus (LCMV)2,3. Despite this progress, a vaccine that can induce an effective immune response to provide sterile protection across various strains and sub-strains of arenaviruses is lacking. Therefore, this topic seeks proposals that aim to develop a pan-arenavirus vaccine that can induce sterile immunity in the respiratory mucosa. Of critical interest are proposals that aim to characterize immune mechanisms, mediators, cells or pathways that provide an understanding of broad, sterilizing immunity in the lung and nasal tract.

Objective: The topic seeks proposals that will develop a pan-arenavirus [i.e. Junin virus (JUNV), Lassa virus (LASV), and/or Machupto virus (MACV)] vaccine that can induce sterile, cross-strain immunity in the respiratory tract. Additionally, proposals which seek to understand the immunological mechanisms in the respiratory mucosa that are responsible for sterile protection are being solicited. Proposals should also include plans for interaction with the Food and Drug Administration to seek review of the proposed plans and to receive any further guidance for vaccine design and characterization. Proposals that address the following will be given consideration:

- Vaccine candidate(s) formulated for at least one dose administered mucosally.
- Demonstration of immunogenicity and efficacy.
- Characterization of the immune response after vaccination and challenge. Analyses may include, but are not limited to, innate, humoral and cell-mediated immune responses such as quantitative and functional analyses of IgA and IgG, lung resident memory T cells, innate lymphoid cells, and respiratory epithelial cells.
- The proposal should include a plan to determine a correlate or surrogate of mucosal protection.

- The project should evaluate vaccine candidate(s) in animal models challenged via aerosol.
- Proposals should aim for focused immunodominance, rapid onset of immunity, reduced dose requirements, and immunological memory for durability.
- Applicants should describe how their vaccine candidates would be manufactured and provide at least proof-of-concept data to demonstrate manufacturability and the feasibility for scale up.

Candidates that demonstrate low logistical burden to improve compatibility with military operations (CONOPS) will be given priority. Factors will include ease of administration without specialized medical devices, minimal or no cold-chain requirement, storage stability, minimal number of administrations to generate protective immunity and early onset of protection ($\leq$ 30 days preferred, < 90 days maximum).

This topic supports the Chemical and Biological Defense Program's goals by providing a pan-arenavirus vaccine and key information regarding the immunological mechanisms required to induce broadly sterilizing mucosal immunity, which will be of great value to current and future vaccine development programs.

ADM Utilization: The DoD has awarded a contract (W911QY-13-C-0010) to establish an ADM capability. In addition to providing a BSL-3 capable, multiproduct manufacturing facility for biologic products, the ADM and a consortium of teaming partners can support development of medical countermeasures from discovery through FDA approval. This includes the facilities, equipment and expertise necessary to perform nonclinical, clinical, process development, and regulatory activities. Please contact the BAA to obtain POC information for the program office managing the ADM contract. Nota bene: The decision to, or NOT to, use the ADM is totally independent of, NOT a criterion for, and will have NO bearing on the decision to select a proposal for funding.

Topic: CBMB-01
Advanced Bacterial Antimicrobials and Anti-infectives with Novel Mechanisms of Action

Objective: This topic seeks milestone-driven proposals focused on the development of antimicrobial therapies that have the potential to potently and specifically treat multiple drug resistant bacterial infections, including those caused by priority DoD bacterial threat agents (*B. pseudomallei, F. tularensis, B. anthracis, Y. pestis,* and/or *C. burnetii*). Proposals shall include drug candidates with supporting data for a unique, novel mechanism of action that does not overlap with marketed antibacterials for which drug resistant strains have been identified. Broad spectrum activity is desirable but not absolutely essential to this solicitation. Strategies to reverse antibiotic resistance in the disease state and those directed towards host targets have the potential to be effective against one or more diseases are favored. As such, proposals for non-traditional therapeutics are encouraged provided they have demonstrated therapeutic activity when used alone or in combination with existing licensed products. Novel monotherapies targeting topoisomerases/gyrases will not be considered.

For the purposes of this topic, a lead candidate will have demonstrated feasibility of manufacturing, *in vitro* and *in vivo* evidence of efficacy against biothreat bacterial agents, and sufficient characterization to allow the development of a draft Target Product Profile (TPP). Priority will be given to proposals that fulfill more advanced stages of development either previously, through work conducted in this proposal, or through conjunction of other complementary work outside this proposal. Candidates that have initiated Phase I clinical studies for safety, tolerability and PK for clinical indications are of particular interest. Responsive proposals will include preliminary data for candidate products toward a defined Target Product Profile and a regulatory plan (both required in a phase II proposal, if invited).

Respondents to this topic must have documented expertise in drug discovery and development, including demonstrated knowledge of regulatory guidelines and submission procedures for candidate products directed against biological threats. The offeror is expected to comply with Animal Rule Guidance for development of MCMs against biowarfare threats.

The following are not of interest and considered outside of the scope of the topic:

- Basic research, discovery of new targets or candidates, or refinement of lead series to identify a candidate.
- Efforts focused on therapeutics for non-BWA strains solely or non-resistant strains of *F. tularensis, B. anthracis*, *Y. pestis*, and/or *C. burnetii* without a concurrent approach against MDR surrogates.

Offerors are encouraged to develop R&D collaborations with other organizations in government, academia, and the private sector to broaden and strengthen their capabilities. Where possible, Offerors are encouraged to take advantage of specialized resources in DoD and other Government agencies such as facilities/capabilities for biocontainment, collections of biothreat pathogens, Core testing, or advanced manufacturing.

Because collections of AMR and MDR BSL-3 biodefense pathogens are not currently available to the broad community, predicted efficacy for AMR and/or MDR biodefense pathogens may be demonstrated using clinical isolates of other pathogens with variable or high-level characterized resistance to specific antibiotics (i.e. Methicillin Resistant *Staphylococcus aureus* (MRSA), *Klebsiella pneumonia, Pseudomonas aeruginosa, Acinetobacter baumannii, Escherichia coli,* etc.). However, these non-biothreat BSL-2 strains should only be used to assess the ability of a therapeutic, or combination of therapeutics, to overcome resistance mechanisms and effectively inhibit microbial growth, etc. Therefore, efforts should not focus on the development of antibiotics that are specific to these surrogate pathogens or their mechanisms of pathogenicity. Additionally, the government currently offers a Core testing capability to perform *in vitro* and/or *in vivo* screening of compounds (lead, advanced, or licensed) alone or in combination against an extensive panel of biodefense pathogens, as well as a panel of MDR ESKAPE pathogens, to generate MIC90 and/or murine survival data at no cost and with no intellectual property implications to the providing party. Respondents interested in acquiring additional information may inquire through the BAA. It should be noted that during the course of performance of proposals selected for funding, *in vitro* performance of promising candidates

or combinations of candidates will be validated, at the cost of the government, by this Core testing capability per government use rights.

ADM Utilization: The DoD has awarded a contract (W911QY-13-C-0010) to establish an Advanced Development and Manufacturing capability (ADM). In addition to providing a BSL-3 capable, multiproduct manufacturing facility for biologic products, the ADM and a consortium of teaming partners can support development of medical countermeasures from discovery through FDA approval. This includes the facilities, equipment and expertise necessary to perform nonclinical, clinical, process development, scale-up, purification, and regulatory submission activities. Respondents interested in discussing potential collaborations with the ADM may inquire through the BAA.

Topic: CBMB-02
Innovative Technological Approach to Treat Active Filovirus Infections

Background: Ebola and Marburg hemorrhagic fevers (EHF and MHF) are caused by the Filoviridae family of viruses, Ebolavirus and Marburgvirus, respectively. These severe diseases have high mortality rates, approaching nearly 90% in humans. EHF and MHF are classified as select agents; World Health Organization Risk Group 4 Pathogens (requiring Biosafety Level 4-equivalent containment), National Institutes of Health/National Institute of Allergy and Infectious Diseases Category A Priority Pathogens, and Centers for Disease Control and Prevention Category A Bioterrorism Agents. Therefore, post-exposure measures against these pathogens and their sequelae; viral hemorrhagic fevers are a high priority.

Objective: This topic seeks proposals for the development of a broad novel and innovative technological approaches to treat (post-exposure therapeutic) pan-filovirus infections (Marburg, Sudan and Ebola). This topic supports Chemical and Biological Defense Program goals by developing therapeutic medical countermeasures against members of the Filoviridae family of viruses. Outcomes from these studies are intended to provide options for Emergency Use Authorization (EUA) candidates for regulatory review and potential for interim fielding for limited, defined populations in the event of a declared emergency. This MCM will be used to treat the Warfighter following a biowarfare assault, unintentional or natural exposures to these viruses.

Guidance for Offeror Proposals:

Broad-spectrum pan-filovirus or pan-ebolavirus therapeutic candidates are highly desirable. Medical devices to reduce viral load including hemofiltration and viral ligand binding devices will be considered.

Novel or repurposed compounds targeted at reducing mortality and/or morbidity may include viral replication inhibitors, blockers of viral uptake, translocation, modulators of the host response, enhancement of viral degradation and clearance interruption of cell pathways resulting in viral infection will be considered. Additionally, other medical countermeasures which increase efficiency and benefit of palliative medicine such as those aimed at preventing or treating systemic inflammatory response syndrome (SIRS) of infected subjects,

disseminated coagulopathy, and other compounds that mitigate organ failure/damage during an active infection will be considered.

Efforts will be prioritized according to preliminary data in order of decreasing priority:

- Preliminary Data:
    - Proposals with an extensive body of preliminary data demonstrating correlates of efficacy *in vitro* and *in vivo* with optimized assays and conditions in place to develop and characterized pharmacodynamic (PD) and pharmacokinetic (PK), cytotoxicity, ADME. These will include evidence of viral inhibition and clearance, or demonstrated reduction of mortality and/or morbidity for any combination of pathogens.
    - Proposals with limited preliminary data demonstrating limited correlative efficacy *in vitro* and *in vivo* with incompletely characterized and validated assays and conditions in place to develop and characterize PD and PK, cytotoxicity, ADME and viral inhibition and clearance for any combination of pathogens.
    - Proposals with only *in vitro* data demonstrating potential therapeutic efficacy. Proposals without *in vitro* preliminary data, but with similar data and/or validated approaches in other models or systems.

Priority will be given to submissions which provide Proof of Concept (POC) and Proof of Principle (POP) data from validated small and large animal models of filovirus induced disease. Submissions should include scope of work, development paths and regulatory strategy and may encompass both research and development domains of research. Translational science indicating the safety and potential for disease-modifying effects of potential candidates should outline the basis for the submission. Aerosol viral challenge studies are highly desirable.

Offerors are encouraged to develop R&D collaborations with other organizations in Government, academia, and the private sector to broaden and strengthen their capabilities. Where possible, Offerors are encouraged to take advantage of specialized resources in DoD and other Government agencies such as facilities/capabilities for biocontainment, collections of biothreat pathogens, Core testing, or advanced manufacturing.

Topic: CBMB-03
Antibody-based Therapeutic and/or Prophylactic Protection against Viral Pathogens

Background: The changing landscape of biological threats necessitates approaches to provide rapid, prophylactic protection and therapeutic support against pathogens of interest. Advances in antibody engineering and rapid and versatile platform technologies render monoclonal antibodies a potential suitable countermeasure to address this issue, especially given their inherent specificity and long half-lives in the circulation.

Objective: This topic is seeking proposals to exploit platform technologies to generate candidate monoclonal antibodies that when administered prophylactically or therapeutically are effective against aerosolized alphaviral induced disease and proceed to develop lead

candidates for preclinical and clinical testing. This topic will support CBD Program goals by generating monoclonal antibody-based candidates for prophylactic or therapeutic administration that provides protection or therapy against infections by alphaviruses (Venezuelan, Eastern, and/or Western Equine Encephalitis). Proposals can involve approaches that include single monoclonal antibodies or cocktails. Proposals are sought that will minimize logistical considerations pertaining to the Concept of Operations (i.e. minimizing the number of doses, investigation of low- or non-invasive routes of administration, maximizing bioavailability, etc.). Moreover, proposals are encouraged to consider the cost of goods of the final product by taking advantage of economical means of production where feasible. Utilization of novel antibody-based platforms such as single domain antibodies or bispecific antibodies is encouraged. Research in this area may include any or all of the following:

1. Discovery of efficacious monoclonal antibodies
    - In silico approaches to determine likely protective epitopes
    - In vitro and in vivo evaluation of neutralization efficacy to down-select to candidates for further testing

2. *In vivo* testing of candidate monoclonal antibodies for prophylaxis or therapeutic in relevant animal model(s)
    - Determination of effective dose
    - Determination of the time to onset of protection (or therapeutic window if there is also potential for post-exposure therapeutic use)
    - Determination of the duration of protection post-administration to include biodistribution and bioavailability studies
    - Determination of optimal routes of administration and dosing

3. The following are example metrics to which the proposed work could strive
    - Demonstration of greater than 90% protection in the animal model against aerosol exposure
    - Therapeutic efficacy >1 hour post exposure
    - Achievement of protection with one, intramuscular dose
    - Achievement of protection within <48 hours
    - Achievement of protection >3 months post-administration
    - Proposals that exploit flexible, single-use bio-manufacturing technologies are desired

Topic: CBMB-04
Drug Discovery and Development of Therapeutics for Encephalitic Alphavirus Infections

Background: Select alphaviruses can cause severe disease in humans and represent a significant threat to public health. Venezuelan (VEEV), eastern (EEEV), and western equine encephalitis (WEEV) viruses, are causative agents of debilitative, acute, and sometimes fatal encephalitis in North, Central, and South America. These alphaviruses are naturally maintained in a zoonotic cycle between nonhuman vertebrate hosts and mosquito vectors. Natural human cases are rare and occur through the bite of an infected mosquito. VEEV,

EEEV, and WEEV are of interest to the biodefense community, based on historical weaponization programs, ease of genetic manipulation and high-titer production, stability, and ability to infect by aerosol route. Given this threat, there is a critical need for anti-alphavirus therapeutic(s) effective against VEEV, EEEV, WEEV, or all three. Currently, there are no licensed drugs available for the treatment of VEEV, EEEV, and WEEV infections. This represents a significant capability gap in the DoD Joint Chemical and Biological Defense Program's research program.

Objective: This topic seeks milestone-driven proposals focused primarily on the discovery or repurposing of novel small molecule therapies or adjuvant therapies for the alphaviruses of greatest concern to the DoD Joint Chemical and Biological Defense Program (i.e. VEEV, EEEV, and WEEV). Proposals focused on other approaches will also be considered, but should focus on development of more mature candidates with compelling data provided demonstrated efficacy against VEEV, EEEV, and/or WEEV.

The ultimate goal of the program is to deliver at least one lead and one backup chemical series effective against alphaviruses as identified through in vitro and challenge in pre-clinical animal models. Compounds active in vitro will progress through a methodical medicinal chemistry campaign to establish the pharmacophore and to build SAR on appropriate targets, in vitro ADME, and safety properties to, in turn, enable the selection of compounds for evaluation of pharmacokinetics, tolerability, and biomarker-driven in vivo efficacy and safety studies. In the most advantageous scenario, the project would identify a superior compound or series with clear intellectual property that could be later optimized for advanced pre-clinical testing. Each proposal may target a known viral target and must utilize an experimental SAR-driven medicinal chemistry effort to identify and optimize chemical series. Responsive proposals will focus on, and will include preliminary data and down-selection criteria for ease of drug manufacture, and establishing proof-of-concept for candidate products towards a defined Target Product Profile (that will be submitted at the Phase II stage). Phase I Clinical Trials are supported under this topic.

Characteristics of successful proposals for this topic may include the following:

- Milestone driven drug development plan with clear and quantitative go/no go decision points through Phase I Clinical Trials.
- A clearly outlined starting point for chemical matter that utilizes an experiment-driven, chemistry approach with a solid screening methodology for VEEV, EEEV, or WEEV.
- For library screening and in silico structure-guided drug design, priority is given to performers with established expertise in this area. Utilization of industry partners, research organizations, or dedicated academic high-throughput screening centers is encouraged.
- Outlining a logical screening funnel with an overview of how experiments and metrics will be used to translate in vitro findings to in vivo effects.
- Ability to provide treatment in the CNS and/or olfactory nerve.

The following are considered outside the scope of the topic:

- Identification of host proteins that play a critical role in the virus lifecycle (host target ID); and,
- Efforts relying too heavily on SINV and SFV as model systems.

Topic: CBMB-05
Pharmacological and Biologic Intervention to reduce inflammation and seizures caused by viral encephalitis.

Background: Alphaviruses can cause severe disease in humans and represent a significant threat to public health. VEEV, EEEV, and WEEV viruses, are causative agents of debilitative, acute, and sometimes fatal encephalitis in North, Central, and South America. These alphaviruses are naturally maintained in a zoonotic cycle between nonhuman vertebrate hosts and mosquito vectors. Natural human cases are rare and occur through the bite of an infected mosquito. However, VEEV, EEEV, and WEEV are of interest to the biodefense community due to possible aerosol delivery of this family of viruses as warfare agents. Brain inflammatory diseases such viral encephalitis and bacterial meningitis are the subject of extensive translational research to develop therapies addressing the underlying inflammation and seizures.

Objective: This topic seeks proposals for the development of a novel and innovative technology to treat post-exposure alphavirus infection. It is aimed at mitigating the deleterious effects of an active alphaviral infection, namely reducing or eliminating encephalitis, seizures and/or other validated clinical markers of morbidity. This topic supports Chemical and Biological Defense Program goals by developing therapeutic medical countermeasures against members of the Genus Alphavirus from the Togaviridae Family. This MCM will be used to treat the Warfighter following a biowarfare assault, unintentional or natural exposures to these viruses.

Characteristics of successful proposals for this topic may include the following:
Pan-alphavirus candidates are highly desirable. Novel or repurposed compounds targeted at reducing viral encephalitis, seizures or demonstrated beneficial effects on mortality and/or other clinical markers of morbidity.

Efforts will be prioritized according to preliminary data in order of decreasing priority:
- Proposals with an extensive body of preliminary data demonstrating correlates of efficacy in vitro and in vivo with optimized assays and conditions in place to develop and characterized PD and PK, cytotoxicity, ADME.
- Demonstrated reduction of mortality and/or morbidity for any combination of pathogens, with normalization of neuronal electric activity with or without reduction in number and intensity of seizures as well as reduction or elimination of encephalitis after viral challenge. Viral inhibition and clearance is desirable but not required.
- Proposals with limited preliminary data demonstrating limited correlative efficacy *in vitro* and *in vivo* with incompletely characterized and validated assays and conditions in place to develop and characterize PD and PK, cytotoxicity, ADME, and neuronal activity for any combination of pathogens.

- Proposals with only in vitro data demonstrating potential therapeutic efficacy. Proposals without *in vitro* preliminary data, but with similar data and/or validated approaches in other models or systems.

Topic: CBMB-06
Development and Integration of Novel MCM Delivery and Bioagent-MCM Co-Localization Platforms

Background: Traditional approaches in biodefense MCM programs face significant and sometimes greater obstacles on the path to success than non-defense driven pharmaceutical industry due to the fact that biowarfare agents (BWAs) including bacteria, viruses and biotoxins are difficult to eradicate and BWA-caused infections/intoxications are harder to cure and often quickly lethal. In addition to the constrained resources dedicated to biodefense MCMs, limited market share and low commercial interest impede the development of MCMs against BWAs. Development/employment of revolutionary technologies, such as an integrated BWA-collection-and-MCM-delivery platform to track, collect, and eradicate BWAs, is needed to help biodefense programs bridge the 'valley of death' and overcome these challenges.

Objective: This topic seeks proposals to capture, integrate and/or develop emerging technologies that can provide novel approaches to physically and pharmacologically mitigate infection/intoxication of threat agents. If successful, the technologies should sequester threat agents at their sites of entry or during their initial circulation so that further dissemination to replication or infection site(s) can be avoided in addition to carrying the MCM payload to wherever and whenever the BWAs are present including infection sites for BWA eradication. A desirable improvement of such technologies will be to carry MCMs with triggerable, on-demand drug release to kill the pathogens while they are entrapped or sequestered. Together, successful technologies are expected to provide novel capacities in combating BWAs.

Proposals should address material needs and methods for recognizing and collecting agents, co-localizing agents with MCMs, and utilizing agent-specific and/or the body's response to infection as targeting guide and drug release trigger. Precisely directed or triggered MCM release within the MCM-BWA complex or within infected cells will be ideal although MCM release in target tissue(s) is also acceptable. Since this is a platform instead of a drug development program, the use of a marker (or prototype) antibiotic, antiviral and/or antitoxin of small molecules or monoclonal antibodies (mAbs) for POC purpose of a technology is acceptable.

The following desired components, alone or in combination, should be addressed for one class of BWAs as the program threshold. Yet, a technology should be able to demonstrate acquired ability or rationalized potential to take on multiple BWAs (broad spectrum platform) as the program goal.

- Technologies to recognize and collect BWAs by specific ligand binding polymers, receptor and antibody approaches, or other bioengineering/nanotechnology means to

allow early stage *in vivo* collection and an eventual eradication of pathogens are encouraged.

- Integration of pathogen sequestration into MCM delivery systems which seek to provide restriction of pathogen replication and dissemination, co-localization of pathogen with drug, within-trap triggered release and kill, and tissue-specific targeting of MCMs are desired. Examples may include the pulmonary, lymph nodes/spleen, and central nervous system (CNS) sites of infection or intoxication.
- Methods that encompass site-specific cellular receptor-ligand interactions are sought. The delivery of molecules (e.g., small molecules, antisense, and/or mAbs) to specific pathogens or inside host cells and subcellular compartments is desirable.
- Methods of sustained and biologically responsive delivery of potential therapeutics/marker MCMs to sites of emerging pathology. On-demand delivery and release kinetics of therapeutic candidates is desired. Preferential or localized delivery with controlled release of MCM payloads is sought to minimize drug (dose) related toxicities and enhance/enable efficacy.
- Novel delivery systems such as engineered viral particles including bacteriophages, red blood cell ghosts, engineered cells, and various nano-particles (polymeric, protocells, liposomes, multi-lamellar constructs, etc.) which can release their diversified payloads in response to pathogen specificity or disease biomarkers including host cytokine/immune responses are sought.
- Other novel technologies that can satisfy the objectives of this topic will also be considered.

The use of engineered cells, mammalian cell-nanoparticle complexes, artificial membrane constructs, engineered bacteriophages, viral like particles (VLPs) BWA-trapping systems and any other biocompatible nano-carriers are those among the many technologies that will be considered. Those technologies that trap, restrict or confine BWAs, restrict their movement at sites of entry or during initial general circulation, and thus block dissemination/replication/infection as well as infection site eradication of threat agents are sought. The ability to target infected cells or subcellular compartments at sites of infection is strongly encouraged. The ultimate goal is to co-localize the pathogenic agent and MCMs, and to initiate biologically responsive release of the therapeutic payloads during various stages from BWA exposure, infection to disease progression. It is expected that the offerors will consider technologies to entrap pathogens and to cause local release of MCMs to kill them wherever and whenever the pathogens go. Technologies that explore responsive delivery of MCMs, therapeutics, host immune modulators are of interest.

The deployment of site-directed targeted delivery of MCMs to either pathogen, cells of interest, effector cells or tissues/organs are of great interest. As pathologies of the CNS are of concern, methods are of interest to overcome or transiently modify blood brain barrier (BBB) function to enable effective CNS MCM delivery. These may include the ability to use chaperone delivery systems that allow access to the CNS.

Technologies that demonstrate site localization and pathology- or biomarker-dependent release of payloads are highly encouraged. Technologies with supporting preliminary data will receive a higher priority. To demonstrate the platform and enabling nature of such

technologies, offerors must consider one (initially) or more (eventually) classes of BWAs of interest to DTRA, including Alphavirus (VEEV, EEEV, WEEV) and Filovirus (Ebola and Marburg), *Burkholderia* spp and *Francisella tularensis*, and Botulinum Neurotoxin (BoNT).

Acceptable maturity of technology can range from early *in vitro* POC to late preclinical/clinical application demonstration in other medical fields but has to rationalize the possibility and relevance in biodefense application. Collaboration among technology developers and MCM developers are encouraged during proposal phase or after funding award to advance suitable technologies and MCMs rapidly toward military applications in Biodefense.

Offerors are encouraged to take advantage of specialized resources in DoD and other Government agencies such as facilities/capabilities for biocontainment, collections of biothreat pathogens, Core testing, or advanced manufacturing. Respondents interested in discussing potential collaborations may inquire through the BAA/Call.

8.0 Other Information

8.1 Supplemental Information Volume Content Requirements

This volume contains supplemental data. Additional details about each specific item are located in the sections referenced below. This Volume must address all of the items listed below. If any particular item is not relevant to the proposed effort, include a reference to the requested information and state that the particular information is not applicable in order to confirm a negative response.

8.1.1 Authorized Negotiators

Offerors must include the name, title, mailing address, telephone number, fax number, and e-mail address of the company, BPOC and any personnel authorized to negotiate with the Government and who is authorized to obligate the Offeror contractually.

8.1.2 Confirmed Proposal Expiration Date

Offerors shall provide written confirmation that cost proposals will remain valid for a period of one year after the Phase II submission closing date. Offerors may be asked to revalidate their proposal expiration date.

8.1.3 Collaboration with Government Laboratories and Federally Funded Research and Development Centers (FFRDC)

Proposed collaboration with a DoD laboratory should be clearly identified in the proposal, and must be supported with a letter of intent from that laboratory's Commander.

Offerors choosing to use the services of Government Laboratories in the performance of work proposed may be required to enter into a Cooperative Research and Development Agreement (CRADA) with the Laboratory. A CRADA is not a FAR-based agreement; it is authorized by 15 U.S. Code Section 3710(a). A CRADA will be separate from the DTRA procurement instrument, with its own unique terms, in particular related to Intellectual Property. It would be prudent for the Offeror to discuss those unique terms with the Laboratory prior to submitting a proposal under this BAA. DTRA will not facilitate, nor be involved in, the negotiation of the agreements with Government Laboratories.

8.1.4 Additional FFRDC Requirements

DoD-sponsored FFRDCs should review DFARS 235.017 to ensure compliance with the requirement for an Organizational Conflict of Interest (OCI) Risk Mitigation Plan, which should accompany the Phase II proposal submission.

In accordance with FAR 17.503(e), DoE Order 481.1C and DoE Acquisition Regulation DEARS 970.1707-3, DoE FFRDC participants must provide a copy of the written certification from the DoE sponsor authorizing its performance of the proposed effort. The DoE sponsor must provide written certification that the proposed work –

(1) is consistent with or complimentary to missions of DoE and the facility to which the work is to be assigned,
(2) will not adversely impact programs assigned to the facility, and
(3) will not create a detrimental future burden on DoE resources.

In accordance with FAR 17.503(e), 35.017(a)(2) and 35.017-3, FFRDC participants (other than DoE FFRDCs) must provide documentation from the FFRDC sponsor authorizing its performance of the proposed effort.

8.1.5 Representations and Certifications

Representations and Certifications must be completed at the time of Phase II submission. The Offeror must complete the annual representations and certifications electronically via the SAM website at http://www.sam.gov. After reviewing the SAM information, the Offeror verifies by submission of the offer that the representations and certifications currently posted electronically have been entered or updated within the last 12 months, inclusive of the following:

- FAR 52.209-7 Information Regarding Responsibility Matters;
- FAR 52.209-11, Representation by Corporations Regarding Delinquent Tax Liability or a Felony Conviction under any Federal Law;
- FAR 52.204-20, Predecessor of Offeror;
- DFARS 252.203-7005 Representation Relating to Compensation of Former DoD Officials;
- DFARS 252.204-7008 Compliance with Safeguarding Covered Defense Information Controls;

- DFARS 252.203-7996, Prohibition on Contracting with Entities that Require Certain Internal Confidentiality Agreements-Representation (DoD Deviation O0003, Oct 2015); and
- DFARS 252.247-7022 Representation of Extent of Transportation by Sea

NOTE: If any of the above mentioned provisions are not contained in the SAM database, the Offeror is required to complete and submit Attachment 5 – Representations & Certifications.

Additionally, the Offeror is required to verify that the electronic representations and certifications are current, accurate, complete, and applicable to this BAA, including the business size standard applicable to the NAICS code referenced (541711) for this BAA, as of the date of this offer and are incorporated in this offer by reference (see FAR 4.1201).

8.1.6 Protection of Human Subjects

If the proposed work involves human subjects or materials, Offerors are required to outline the human use, to include the source of the human subjects or materials involved in the work. Further information may be required if the proposal is successful.

All work under any award made under this BAA involving human subjects must be conducted in accordance with 32 CFR 219, 10 U.S.C. § 980, and DoD Instruction 3216.02, and, as applicable, 21 CFR parts 11, 50, 56, GCP, the ICH as well as other applicable federal and state regulations. Contractors must be cognizant of and abide by the additional restrictions and limitations imposed on the DoD regarding research involving human subjects, specifically as regards to vulnerable populations (32 CFR 219 modifications to subparts B-D of 45 CFR 46), recruitment of military research subjects (32 CFR 219), and surrogate consent (10 U.S.C. § 980).

DTRA Directive 3216.01 establishes the DTRA Human Subjects Protection Program, sets forth the policies, defines the applicable terms, and delineates the procedures necessary to ensure DTRA compliance with federal and DoD regulations and legislation governing human subject research. The regulations mandate that all DoD activities, components, and agencies protect the rights and welfare of human subjects of study in DoD supported research, development, test and evaluation, and related activities hereafter referred to as "research." The requirement to comply with the regulations applies to new starts and to continuing research.

The DTRA Directive requires that research using human subjects may not begin or continue until the DTRA Research Oversight Board (ROB) has reviewed and approved the proposed protocol. Contractors and subcontractors are required to submit a valid federal assurance for their organization (institution, laboratory, facility) that has been issued by either DoD or the Department of Health and Human Services, and documentation of review of proposed protocols by the local Institutional Review Board (IRB) to include consent forms for any planned research using human subjects to the ROB for its review through the contracting officer's representative (if assigned) or the

contracting officer. The ROB review is separate from, and in addition to, local IRB review.

A study is considered to involve human research subjects if: 1) there is interaction with the subject (even simply talking to the subject qualifies; no needles are required); and 2) if the study involves collection and/or analysis of personal/private information about an individual, or if material used in the study contains links to such information.

Written approval to begin research or to subcontract for the use of human subjects under the proposed protocol will be provided in writing from the DTRA ROB, through the contracting officer. Both the contractor and the Government must maintain a copy of this approval. Any proposed modifications or amendments to the approved protocol or consent forms must be submitted to the local IRB and the DTRA ROB for review and approval. Examples of modifications/amendments to the protocol include but are not limited to:

- a change of the Principal Investigator;
- changes in duration or intensity of exposure to some stimulus or agent;
- changes in the information requested of volunteers, or changes to the use of specimens or data collected; or
- changes in perceived or measured risks or benefits to volunteers that require changes to the study.

Research pursuant to such modifications or amendments must not be initiated without IRB and ROB approval except when necessary to eliminate apparent and immediate hazards to the subject(s).

Research projects lasting more than one year require IRB review at least annually, or more frequently as required by the responsible IRB. ROB review and approval is required annually. The contractor or subcontractor must provide documentation of continued IRB review of protocols for ROB review and approval. Research must not continue without renewed ROB approval unless necessary to eliminate apparent and immediate hazards to the subject(s).

Clauses regarding human subjects research will be included in all contracts involving human subjects research. Non-compliance with any provision of this clause may result in withholding of payments under the contract pursuant to the terms and conditions. The Government shall not be responsible for any costs incurred for research involving human subjects prior to protocol approval by the ROB.

8.1.7 Animal Use

If the proposed research involves the use of live nonhuman vertebrate animals, Offerors are required to describe the proposed animal use and type of animals being used. The Animal Care and Use Review Office (ACURO), a component of the USAMRMC Office of Research Protections (ORP), must review and approve all animal use prior to the start

of working with animals. Therefore, the contractor will be required to complete and submit the animal use appendix titled "Research Involving Animals", after award of contract, which can be found on the ACURO website: (https://mrmc-www.army.mil/index.cfm?pageid=Research_Protections.acuro). Allow two to four months for regulatory review and approval processes for animal studies. Offerors are to build the review time into their project schedules.

DoD Directive 3216.01, dated September 13, 2010, provides policy and requirements for the use of animals in DoD-funded research. The DoD definition of animal is any live nonhuman vertebrate. All proposals that involve the use of animals must be in compliance with DoD Directive 3216.01 and AR 40-33. For animals, the provisions include rules regarding animal acquisition, transport, care, handling, and use in: (i) 9 CFR parts 1-4, Department of Agriculture rules that implement the Laboratory Animal Welfare Action of 1966 (U.S.C. 2131-2156); and (ii) the "Guide for the Care and Use of Laboratory Animals," National Institutes of Health Publication No. 86-23.

8.1.8 Biological Defense Research Program (BDRP) Requirements: Biosecurity and Select Agent Use; Chemical Agent Use

Proposals must specify what Select Agent work will be conducted at the Offeror's facility and what Select Agent work will be performed in other facilities. Proposals also must provide the source of the Select Agents, any appropriate registration information for the facilities, and specify the Laboratory Biosafety Level. All Select Agent work is subject to verification of information and certifications.

For those contractors conducting research with Bio-safety Levels 3 and 4 material, a Facility Safety Plan must be prepared and made available during the project award phase in accordance with 32 Code of Federal Regulations (CFR) 626.18. DTRA requires that research using Select Agents not begin or continue until DTRA has reviewed and approved the proposed agent use.

Proposals that will employ the use of chemical agents, either neat agent or dilute agent, the Offeror must provide approved Facility Standard Operating Procedures that conform to Federal, State, and local regulations and address the storage, use and disposition of these chemical materials.

8.1.9 Organizational Conflict of Interest

Certain post-employment restrictions on former federal officers and employees may exist, including special Government employees (including but not limited to Section 207 of Title 18, United States Code, the Procurement Integrity Act, 41 U.S.C. 423, and FAR 3.104). If a prospective Offeror believes that a conflict of interest exists that relates to the above restrictions, the situation should be raised to the DTRA Contracting Officer before time and effort are expended in preparing a proposal. Send notification of potential conflict of interest via an e-mail message to the e-mailbox listed in the BAA.

All Offerors and proposed subcontractors also must affirmatively disclose whether or not

they are providing scientific, engineering and technical assistance (SETA), A&AS or similar support, through an active contract or subcontract, to any DTRA technical office(s), the Joint Program Executive Office for Chemical and Biological Defense (JPEO), Assistant to the Secretary of Defense for Nuclear, Chemical, and Biological Defense Programs (ATSD-NCB), or the Office of the Special Assistant for Chemical and Biological Defense and Chemical Demilitarization Programs (OSA (CBD&CDP)). All disclosures must state which office(s) the Offeror supports, and identify the prime contract number. Disclosures must be furnished at the time of proposal submission. All facts relevant to the existence or potential existence of organizational conflicts of interest (FAR 9.5) must be disclosed, including facts not specifically described above. The disclosure must include a description of the action the Offeror has taken or proposes to take to avoid, neutralize, or mitigate such conflict.

8.1.10 Export Control Notification

Offerors are responsible for ensuring compliance with all export control laws and regulations that may be applicable to the export of and foreign access to their proposed technologies. Offerors may consult with the Department of State with any questions regarding the International Traffic in Arms Regulation (ITAR) (22CFR Parts 120 – 130) and/or the Department of Commerce regarding the Export Administration Regulations (EAR) (15 CFR Parts 730-774). The Department of State publishes guidance on the ITAR at http://www.pmddtc.state.gov. Department of Commerce guidance on the EAR is located at http://www.bis.doc.gov.

8.1.11 Intellectual Property

8.1.11.1 Patents

Offerors must list any known patents, patent applications, or inventions which the Offeror may be required to license in order to perform the work described in the Offeror's proposal, or which the Government may be required to license to make or use the deliverables of the contract should the Offeror's proposal be selected for award. For any patent or patent application listed above, the Offeror must provide the patent number or patent application publication number, a summary of the patent or invention title, and indicate whether the Offeror is the patent or invention owner. If a patent or invention is in-licensed by the Offeror, identify the licensor.

If any listed patent, patent application or invention is owned or licensed by the Offeror, the Offeror must provide a statement, in writing, if it either owns or possesses the appropriate licensing rights to patent, patent application or invention to perform the work described in the proposal and/or to grant the Government a license to make or use the deliverables for this program. If any listed patent, patent application or invention is not owned or licensed by the Offeror, then the Offeror must explain how it will obtain a license, how the Government may obtain a license and/or whether the Offeror plans to obtain these rights on behalf of the Government.

Be advised that no patent, patent application or invention disclosure will be accepted if identified in the Data Rights Assertion list described in subsection 8.1.11.2 below. Existing inventions, patents and patent applications should be discussed in the above list. Government rights in any technology that might be invented or reduced to practice under the contract are addressed in the patent rights clause to be included in the contract.

8.1.11.2 Data Rights

Offers submitted in response to this BAA shall identify, to the extent known at the time an offer is submitted to the Government, the technical data or computer software that the Offeror, its subcontractors or suppliers, or potential subcontractors or suppliers, assert should be furnished to the Government with restrictions on use, release, or disclosure, in accordance with DFARS 252.227-7017, Identification and Assertion of Use, Release or Disclosure Restrictions, and DFARS 252.227-7028, Technical Data or Computer Software Previously Delivered to the Government. The Offeror's assertions, including the assertions of its subcontractors or suppliers or potential subcontractors or suppliers, shall be submitted as an attachment to its offer in the following format, dated and signed by an official authorized to contractually obligate the Offeror. If the Offeror will deliver all technical data and computer software to the Government without restrictions, enter "NONE" in this table under the heading "Technical Data or Computer Software to be Furnished with Restrictions."

Identification and Assertion of Restrictions on the Government's Use, Release, or Disclosure of Technical Data or Computer Software.

The Offeror asserts for itself, or the persons identified below, that the Government's rights to use, release, or disclose the following technical data or computer software should be restricted:

Technical Data or Computer Software to be Furnished With Restrictions*	Basis for Assertion**	Asserted Rights Category***	Name of Person Asserting Restrictions****
(LIST)*****	(LIST)	(LIST)	(LIST)

*For technical data (other than computer software documentation) pertaining to items, components, or processes developed at private expense, identify both the deliverable technical data and each such item, component, or process. For computer software or computer software documentation identify the software or documentation.

**Generally, development at private expense, either exclusively or partially, is the only basis for asserting restrictions. For technical data, other than computer software documentation, development refers to development of the item, component, or process to which the data pertain. The Government's rights in computer software documentation generally may not be restricted. For computer software, development refers to the software. Indicate whether development was accomplished exclusively or partially at private expense. If development was not accomplished at private expense, or for computer software documentation, enter the specific basis for asserting restrictions.

***Enter asserted rights category (e.g., government purpose license rights from a prior contract, rights in SBIR data generated under another contract, limited, restricted, or government purpose rights under this or a prior contract, or specially negotiated licenses).

****Corporation, individual, or other person, as appropriate.

*****Enter "none" when all data or software will be submitted without restrictions.

Date _____

Printed Name and Title _____

_____

Signature _____

Offerors responding to this BAA requesting an OTA shall specifically identify any asserted restrictions on the Government's use of intellectual property contemplated under those award instruments. For this purpose, Offerors must propose specific Intellectual Property terms and conditions and a data deliverable list. Offerors are encouraged to model their data rights assertions list to the template provided in DFARS 252.227-7017.

8.1.12 Subcontracting Plan

Any Offeror, other than small businesses, submitting a proposal for an award with a value more than the amount listed in FAR 19.702(a)(1) and that has subcontracting possibilities, must submit a subcontracting plan in accordance with FAR 19.7. Pursuant to Section 8(d) of the Small Business Act (15 U.S.C. § 637(d)), it is the policy of the

Government to enable small business and small disadvantaged business concerns to be considered fairly as subcontractors to contractors performing work or rendering services as prime contractors or subcontractors under Government contracts, and to assure that prime contractors and subcontractors carry out this policy.

A subcontracting plan identifies the Offeror's approach to awarding subcontracts to small business, small disadvantaged business, women-owned small business, service-disabled veteran owned small business, and Historically Underutilized Business Zone (HUB Zone) small business concerns, on this effort. A DCMA approved master plan may be submitted in lieu of an individual contract plan. The narrative in the subcontract plan must address each element listed in FAR 19.704(a)(1)-(11). The emphasis of the plan must be to maximize small business participation to the maximum extent practicable. The current DoD subcontracting goals are as follows:

Percentage of subcontracted dollars	
Small Business	34.5%
HUB Zone Small Business	3%
Small Disadvantaged Business	5%
Women-Owned Small Business Concerns	5%
Service-Disabled Veteran Owned Small Business	3%

Note: Provide rationale if the Small Disadvantaged Business goal cannot be achieved per DFARS 219.705-4(d), or if subcontracting possibilities do not exist (reference FAR 19.705-2(c)).

8.1.13 Identification of Team Members

Offerors shall include a list of team members (e.g. subcontractors/consultants) that are being proposed. Offerors shall also include the estimated percentage of the effort to be performed by the Offeror and percentage of work to be performed by proposed team members.

8.1.14 Statement of Current and Pending Support

Offerors must include a statement of current and pending support of all related work that is currently receiving or may potentially receive financial support. This information must be included for each investigator listed in the proposal.

8.1.15 Modified Pre-award Checklist – SF 1408

Any offeror awarded a cost type contract must be in compliance with FAR 16.301-3 "Limitations" restrictions. Specifically, the Offeror's accounting system must be adequate for determining costs applicable to the contract; and will be subject to DCAA audit and surveillance during performance to provide reasonable assurance that efficient methods and effective cost controls are being used. Any Offeror that has not been subject to a DCAA pre or post-award accounting system audit is required to submit a Modified Preaward Checklist (SF 1408), which will expedite the pre-award survey of the accounting system by DCAA. Refer to www.dcaa.mil for further assistance preparing an

adequate cost proposal. Offeror's that have been subject to an DCAA accounting system audit shall provide the resultant audit report in lieu of the SF1408.

8.1.16 Forward Pricing Rate Agreement/Provisional Billing Rates

Offerors shall include a copy of any current Forward Pricing Rate Agreements or Provisional Billing Rate Agreements with Government agencies, such as Defense Contract Management Agency (DCMA), the Office of Naval Research (ONR) or the Department of Health and Human Services (DHHS). If no agreement has been made with a Government representative, Offerors shall provide all rates, factors, and bases by year utilized in the development of the proposal and the basis of those rates and factors.

9.0 List of Attachments

ATTACHMENT 1: Technology Readiness Level Definitions

ATTACHMENT 2: Statement of Work Template

ATTACHMENT 3: Standard Form 1408

ATTACHMENT 4: Cost Spreadsheet

ATTACHMENT 5: Representations & Certifications Worksheet