Office of Biomedical Advanced Research and Development Authority (BARDA) Broad Agency Announcement (BAA)

BAA-18-100-SOL-00003

Office of Acquisitions Management, Contracts, and Grants (AMCG)

200 C Street SW

Washington, DC 20201

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INTRODUCTION

This Broad Agency Announcement (BAA), which sets forth research and development (R&D) areas of interest (AOI) for the Office of Biomedical Advanced Research and Development Authority (BARDA), is issued under paragraph 6.102(d)(2)(i) of the Federal Acquisition Regulation (FAR). Proposals selected for award are considered to be the result of full and open competition and in full compliance with 41 U.S.C. § 3301. A formal Request for Proposal will not be issued. Paper copies of this announcement will not be issued. The U.S. Government (Government) reserves the right to select for award and fund all, some, or none of the proposals in response to this announcement. All proposals will be treated as sensitive competitive information and the contents only disclosed for the purpose of evaluation.

Offerors that are not responsive to the 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.

The Government reserves the right to award the instrument best suited to the nature of the research proposed and may award any appropriate contract type under the FAR.

OVERVIEW INFORMATION

Agency Name:

U.S. Department of Health and Human Services (HHS), Office of the Secretary, Office of the Assistant Secretary for Preparedness and Response (ASPR), Office of Biomedical Advanced Research and Development Authority (BARDA), 200 C Street SW, Washington, DC, 20201

Issuing Office:

Department of Health and Human Services (HHS), Office of the Secretary (OS), Office of the Assistant Secretary for Preparedness and Response (ASPR), Office of Acquisitions Management, Contracts, and Grants (AMCG), 200 C Street SW, Washington, DC, 20201

Development Opportunity Title:

Office of Biomedical Advanced Research and Development Authority (BARDA) Broad Agency Announcement (BAA)

Announcement Type and Date:

Broad Agency Announcement, November 6, 2017 as: BAA-18-100-SOL-00003

This Broad Agency Announcement combines versions of three related Broad Agency Announcements (BARDA CBRN BAA, BARDA Influenza BAA, and BARDA SST BAA), which have been re-issued annually.

This BAA is available on the following websites:

- Federal Business Opportunities - FBO.gov[1]
- MedicalCountermeasures.gov[2]
- Public Health Emergency - PHE.gov[3]
- Grants.gov[4]

Amendments to this BAA will be posted to the websites listed above when they occur. Interested parties are encouraged to check these websites periodically for updates and amendments.

Eligible Offerors:

This BAA is open to ALL responsible sources. Offerors may include single entities or teams from private sector organizations, Government laboratories, and academic institutions.

To be eligible for award, a prospective recipient must meet certain minimum standards pertaining to financial resources, ability to comply with the performance schedule, prior record of performance, integrity, organization, experience, operational controls, technical controls, technical skills, facilities, and equipment.

Federally Funded Research and Development Centers (FFRDCs) and Government entities (Government/National laboratories, military educational institutions, etc.) are subject to applicable direct competition limitations and cannot propose to this BAA in any capacity unless they address the following conditions. FFRDCs must clearly demonstrate that the proposed work is not otherwise available from the private sector AND must provide a letter on letterhead from their sponsoring organization citing the specific authority establishing their eligibility to propose to government solicitations and compete with industry, and compliance with the associated FFRDC sponsor agreement and terms and conditions. This information is required for FFRDCs proposing to be primes or subcontractors. Government entities must clearly demonstrate that the work is not otherwise available from the private sector and provide written documentation citing the specific statutory authority (as well as, where relevant, contractual authority) establishing their ability to propose to government solicitations. Specific supporting regulatory guidance, together with evidence of agency approval will be required to establish eligibility. BARDA will consider eligibility submissions on a case-by-case basis; however, the burden to prove eligibility for all team members rests solely with the Proposer.

Historically Black Colleges and Universities (HBCU), Minority Institutions (MI), Small Business concerns, Small Disadvantaged Business concerns, Women-Owned Small Business concerns, Veteran-Owned Small Business concerns, Service-Disabled Veteran-Owned Small Business concerns, and HUB Zone Small Business concerns are

[1] https://www.fbo.gov/
[2] https://www.medicalcountermeasures.gov/
[3] http://www.phe.gov/
[4] http://www.grants.gov/

encouraged to submit proposals and to join other entities as team members in submitting proposals.

In accordance with federal statutes, regulations, and U.S. Department of Health and Human Services (HHS) policies, no person on grounds of race, color, age, sex, national origin, or disability shall be excluded from participation in, be denied the benefits of, or be subjected to discrimination under any program or activity receiving financial assistance from the HHS.

Research and Development Opportunity Description:

The Office of Acquisitions Management, Contracts, and Grants (AMCG) on behalf of the Office of Biomedical Advanced Research and Development Authority (BARDA) solicits proposals for the advanced research and development of medical countermeasures (MCM) for chemical, biological, radiological and nuclear (CBRN) agents, pandemic influenza, and emerging infectious diseases that threaten the U.S. civilian population. BARDA anticipates that R&D activities awarded under this BAA will serve to advance candidate medical countermeasures towards licensure or approval by the U.S. Food and Drug Administration (FDA). This BAA will also serve to advance the knowledge and scientific understanding of candidates' platform technologies, modeling and forecasting, and visual analytics.

The purpose of this BAA is to solicit proposals that focus on research and development in the following solicited AOI as listed here and further described in Part I of this announcement. The BAA does not support the acquisition of products or the construction of facilities.

Research and Development Areas of Interest:

Development and technical objectives are described in Part II. Efforts proposed by Offerors may cover all aspects of MCM Advanced Research and Development, including Non-Clinical Research and Development, Process Development, Platform Development, Formulation, Manufacturing, and Clinical Evaluation.

Technological Maturity:

Offerors must identify in their Quad Chart and White Paper the current Technology Readiness Level (TRL) of their product, and the TRL identified should meet or exceed the requirements of the given Development Area of Interest. Each White Paper should also contain sufficient supporting information and data to justify the TRL rating. Criteria for determining the appropriate TRL for a product can be found in Attachment 1. Note that all activities within a TRL (or sublevel) must be completed to have achieved that TRL status. One TRL criteria document is provided for use with diagnostics and medical devices (Attachment 1A) and one TRL criteria document is provided for use with therapeutics and vaccines (Attachment 1B). TRL requirements for enabling technologies or products that are not directly applicable to the TRL criteria will be considered on a case-by-case basis.

Number of Awards:

Multiple awards of various values are anticipated and are dependent upon the program priorities, proposals' scientific/technical merits, how well the proposals fit BARDA's areas of interest, and available funds. Anticipated funding for the program is subject to congressional appropriations. The program funding is subject to change due to government discretion and funding availability.

Type of Award:

A contract award under this BAA may utilize Cost-Reimbursement, including Cost (C), Cost-Sharing (CS), Cost-Plus-Incentive-Fee (CPIF), and Cost-Plus-Fixed-Fee (CPFF) Contracts, and Firm-Fixed-Price (FFP) Contracts.

Offerors submitting Full Proposals should submit cost-sharing contract (or cost contract) proposals. When cost sharing is proposed, the amount of cost participation should depend on the extent to which the R&D effort or results are likely to enhance the Offeror's expertise, capability, or competitive position.

If an Offeror does not believe that a Cost-Sharing contract (see FAR 16.303) (or Cost contract [see FAR 16.302]) is appropriate, then the Offeror should provide the reason in writing under "B. Basic Cost/Price Information" of the Cost Proposal (Part VI, Stage 2, Volume II – Cost Proposal Attachments). The reason should include an explanation (i) as to why there is no probability that the Offeror would receive any present or future benefits from an award, (ii) of the R&D expected to be of only minor value to the Offeror, or (iii) of a statute that precludes the use of cost sharing.

If the Government contemplates the award of a cost-reimbursement type contract, the Offeror must demonstrate prior to award that its accounting system is adequate for administering a cost-reimbursement contract. Offerors should propose the type of arrangement they believe best satisfies the requirement.

The Government may also elect to make awards in the form of grants and cooperative agreements, and Other Transactions (OT) agreements, as authorized for BARDA under the Pandemic and All Hazards Preparedness Reauthorization Act (2013).

The costs of preparing responses to this BAA are not considered an allowable direct charge on any resultant award.

Application Process:

Stage 1: Prepare a cover sheet, Quad Chart, and White Paper in accordance with the preparation guidance. Offerors must submit their Quad Chart and White Paper in accordance with the instructions provided in Part V. The Quad Chart and White Paper should describe the effort in sufficient detail to allow evaluation of the concept's technical merit and its potential contribution to the BARDA mission. BARDA will evaluate White Papers based on the criteria provided in Part VII.

Offerors whose Quad Chart and White Paper receive a favorable evaluation will be invited via e-mail to submit a Full Proposal. Offerors whose Quad Chart and White Paper did not receive a favorable evaluation will be notified via e-mail, and will be provided with information on technical issues and concerns that BARDA has regarding the proposed product. This written feedback is the only response that will be provided to unsuccessful Stage 1 Offerors.

Stage 2: Offerors must submit their Full Proposals in accordance with the instructions provided in Part VI. Full Proposals will be evaluated against criteria as described in Part VII. Proposals that do not conform to the requirements outlined in the BAA or to the instructions provided in the invitation letter will not be considered for further action.

Submission Deadlines and Government Response Time:

Table 1: Submission Deadlines and Government Response Time

Proposal Stage	Deadline for Submission*	Government Response
Stage 1: Quad Chart and White Paper	A Quad Chart and White Paper may be submitted on any day during the open period of the BAA. Submission deadlines are as follows: January 31, 2018 April 30, 2018 July 31, 2018 October 31, 2018 January 31, 2019 April 30, 2019 July 31, 2019 October 31, 2019 The final White Paper submission deadline is October 31, 2019.	A receipt confirmation will be sent within 1 week. A decision will be made within 90 calendar days of the submission deadline.
Stage 2: Full Proposal	As specified in the Invitation Letter. A Full Proposal may be submitted on any day during the open period of the BAA. Full Proposal submission deadline is October 31, 2019.	A receipt confirmation will be sent within 1 week. A decision will be made within 90 calendar days of receipt of Full Proposal.

*Submissions must be submitted no later than 4:30 PM Eastern Standard Time for each due date.

Contact and Submission Information:

All inquiries and submissions regarding this BAA must be sent to:

BARDA-BAA@hhs.gov.

Technical questions only should be directed to the Technical Point of Contacts (POC) listed under each area of interest. The Technical POCs are located in "Part I: Research and Development Areas of Interest."

Limitation on Communication After Submission:

Be advised that after a White Paper (or Full Proposal) has been submitted, all communications related to that submission must be through the Contracting Office at BARDA-BAA@hhs.gov. Communications following the Government response to a White Paper or Full Proposal submission must be through the Contracting Officer identified in the response letter.

When submitting a Full Proposal following receipt of White Paper Response Letter from the Contracting Officer, submit the Full Proposal to BARDA-BAA@hhs.gov, carbon copy (cc) the Contracting Officer, and reference the Response Letter in the first paragraph of the email.

Do not cc or blind carbon copy (bcc) the technical POCs or any other individuals within Program during submission of a Full Proposal. Similarly, do not cc or bcc the technical POCs or any other individuals within Program when sending inquires to BARDA-BAA@hhs.gov or directly to the Contracting Officer.

Preliminary Inquiries:

The Government realizes that the preparation of a development proposal often represents a substantial investment of time and effort by the Offeror. In an attempt to minimize this burden, BARDA encourages organizations and individuals interested in submitting proposals to make preliminary inquiries as to the general need for the type of R&D effort contemplated before expending extensive effort in preparing a detailed proposal or submitting proprietary information.

TechWatch Program:

Offerors are encouraged to participate in the TechWatch program prior to any White Paper or Full Proposal submissions. Participation in the TechWatch program affords Offerors an opportunity to present their capabilities to BARDA scientific subject matter experts and program managers, as well as Office of Acquisitions Management, Contracts, and Grants (AMCG) acquisition professionals. These personnel can evaluate products/technologies, suggest techniques and strategies for meeting technical and regulatory challenges, provide insight on how a product or technology may address BARDA's objectives, and provide general information about BARDA's mission and programs. To request a TechWatch meeting and for more information about the TechWatch program, Offerors should visit the TechWatch website[5]. Entities with a White

[5] https://www.medicalcountermeasures.gov/barda/advancing-innovation/techwatch.aspx

Paper or proposal currently under review under any ASPR solicitation are not eligible to schedule a TechWatch meeting related to that submission.

Special Instructions:

Special instructions will be advertised via the BAA as they become apparent. These additional instructions would be tailored to specific AOI and may have unique submission due dates. The information requested in these instructions should be used along with Part VI of the BAA to format and prepare the Technical (Volume I) and Cost (Volume II) Proposals. Offerors shall follow the instructions in Part VI of the BAA, and include the information requested therein.

Proposal Handling and Submission Information:

Treatment of Submission Documents: All proposals are treated as Offeror's proprietary information prior to award and the contents are disclosed only for the purpose of evaluation. The Offeror must indicate any limitation to be placed on disclosure of information contained in the proposal in accordance with the instructions as set forth in FAR 52.215- 1(e) "Restrictions on disclosure and use of data."

Classified Submissions: Classified proposals will not be accepted. All submissions must be Unclassified.

Use of Color Proposals: All proposals received shall be stored as electronic images. Electronic color images require a significantly larger amount of storage space than black-and- white images. As a result, Offerors' use of color in proposals should be minimal and used only when necessary for details. Do not use color unless necessary.

Post-Employment Conflict of Interest: There are certain post-employment restrictions on former federal officers and employees, including special government employees (Section 207 of Title 18, U.S.C.). If a prospective Offeror believes a conflict of interest may exist, the situation should be emailed to the appropriate Contracting Officer, prior to expending time and effort in preparing a proposal. The appropriate HHS personnel will discuss any conflict of interest with prospective Offeror.

Unsuccessful Proposal Disposition: Proposals will not be returned. The original of each proposal received will be retained by ASPR pursuant to FAR 4.805 and all other non-required copies destroyed.

Government Notice for Handling and Submitting Proposals: Refer to Attachment 6 for inclusion requirement of the Government notice.

BACKGROUND

This Broad Agency Announcement (BAA) sets forth advanced development areas of interest for the Office of Biomedical Advanced Research and Development Authority (BARDA), a component of the Office of the Assistant Secretary for Preparedness and Response (ASPR) within the Office of the Secretary (OS) of the U.S. Department of Health and Human Services (HHS). This BAA is issued under paragraph 6.102(d)(2) of the Federal Acquisition Regulation (FAR), and proposals selected for award are considered to be the result of full and open competition and in full compliance with The Competition in Contracting Act of 1984, 41 U.S.C. 253.

BARDA is the lead federal agency for supporting advanced development of MCM to protect the United States against public health emergency threats, including CBRN agents, emerging infectious diseases, and pandemic influenza. The Pandemic and All Hazard Preparedness Reauthorization Act authorizes BARDA to promote (i) innovations in technologies that may assist MCM advanced research and development, (ii) research and development of tools, devices, and technologies, and (iii) research to promote strategic initiatives, such as rapid diagnostics, broad spectrum antimicrobials, and vaccine manufacturing technologies. The continuing threat of terrorism, pandemic influenza, and emerging diseases underscores the compelling need to develop new and improved MCM for protecting all segments of the civilian population. BARDA is soliciting proposals for the advanced research and development of MCM for CBRN agents; the ever-present and ever-evolving threat of novel influenza; and the re-emergence and emergence of infectious diseases that threaten the U.S. civilian population. This BAA will support the development of candidate products and diagnostic tools to meet the challenging requirements of CBRN MCM (e.g. post- exposure efficacy, extended shelf life, storage, distribution, and dispensing).

The priorities of the BARDA Influenza and Emerging Infectious Diseases Division are closely aligned with the *Public Health Emergency Medical Countermeasures Enterprise Review*[6] (August 2010), the President's Council of Advisors on Science and Technology's Report to the President on Reengineering the Influenza Vaccine Production Enterprise to Meet the Challenges of Pandemic Influenza[7] (August 2010), the *BARDA Strategic Plan 2011-2016*[8] (October 2011), and HHS Pandemic Influenza Plan[9] (June 2017).

Vaccines, therapeutics, diagnostics, ventilators, and respiratory protective devices are essential for protecting all segments of the civilian population from pandemic influenza and other emerging infectious diseases. This BAA will support advanced development activities of medical countermeasures for influenza and other emerging respiratory viruses to be specified by BARDA. BARDA priorities for influenza vaccines are focused on those vaccines that induce long-lasting and broad (heterotypic and/or heterosubtypic) immunity in all populations compared to currently licensed influenza vaccines. In addition, BARDA will prioritize support for vaccines that induce broad immunity so as to prime the population against newly emerging influenza viruses or other respiratory viruses of pandemic potential. BARDA is also prioritizing broadly reactive

[6] https://www.medicalcountermeasures.gov/media/1138/mcmreviewfinalcover-508.pdf
[7] http://www.whitehouse.gov/sites/default/files/microsites/ostp/PCAST-Influenza-Vaccinology-Report.pdf
[8] https://www.medicalcountermeasures.gov/media/745/bardastrategicplan9-28--508.pdf
[9] https://www.cdc.gov/flu/pandemic-resources/pdf/pan-flu-report-2017v2.pdf

immunotherapeutics, such as monoclonal antibodies, that will be effective in treating severely ill, hospitalized patients of all ages who are infected with influenza or other emerging infectious diseases. Such therapeutics will demonstrate effectiveness when given later than 48 hours after onset of symptoms. Additional focus will be placed on MCM and devices suitable for use in at-risk populations such as children, pregnant women, the elderly, and persons with compromised immune systems. BARDA will endeavor to prioritize projects that provide benefits to all populations, while also allowing for focused development projects or studies for at-risk populations where necessary.

BARDA's CBRN priorities are aligned with the preparedness mission of the HHS Public Health Emergency Medical Countermeasures Enterprise (PHEMCE), as articulated in the 2016 PHEMCE Strategy and Implementation Plan[10]. Specifically, HHS has generally adopted a strategy of developing and acquiring MCM for post-event response to CBRN threats. Preventive measures are appropriate only for threats of such potential catastrophic consequence that a pre-event strategy will be examined in order to reduce vulnerability and mitigate post-event consequences. Currently, no pre-event MCM strategies are deemed necessary and feasible at this time for the U.S. civilian population. Therapeutics and diagnostics or the use of post-event prophylaxis will be the preferred strategy for all other threats. Priority will be placed on MCM that focus on post-event prophylaxis or post-exposure treatment. Some CBRN programs are reaching maturity and their intended goal, and receive less emphasis in this process. More emphasis will be placed upon product candidates that have multi-purpose indications (i.e., CBRN usage and commercial indication for public health needs). Additional focus will be placed on supporting the development of medical countermeasures suitable for use in special populations such as children, pregnant women, the elderly, and persons with compromised immune systems, prioritizing and supporting projects that provide benefits to all populations where possible and exploring focused development projects or studies where necessary. To that end, BARDA supports the advanced research and development, and acquisition of MCM such as vaccines, therapeutics, and diagnostics.

BARDA addresses the many challenges to the development of MCM that mitigate the effects of CBRN, pandemic influenza, and emerging infectious disease threats by leveraging commercial technologies, innovative methodologies, and resources used by academia and the private sector. BARDA invests where it has identified gaps or opportunities in technical capabilities that improve the execution of its mission, and is currently focusing on several enabling technologies: standardized technologies (platforms) for rapid MCM development; predictive modeling and novel quantitative analysis capabilities; and visual analytics tools. The refinement of existing platform technologies and the development of innovative new platform technologies for rapid response vaccine, therapeutic, and diagnostic development is an essential part of a paradigm shift in product development from a "one-off" to a "plug-and-play" approach, that can expedite the technical and regulatory path from threat identification to safe, effective human use. Predictive modeling and quantitative analysis plays a key role in determining how large a pandemic or CBRN incident may be and informing development and manufacturing of critical MCM to address the crisis. Visual analytics capabilities, applications, and tools allow visual access to increasingly larger and more complex data sets in an easily understandable format to support the breadth of BARDA's MCM product development.

[10] https://www.medicalcountermeasures.gov/media/36937/2016_phemce_sip.pdf

Awards resulting from this BAA may also benefit from multiple core services that BARDA already provides and will provide in the future. These core services include an animal study network, flexible manufacturing facilities, and technical expertise in development, manufacturing, regulatory affairs, quality systems, and clinical studies.

For additional requirements information, visit:

- The Pandemic and All Hazard Preparedness Act[11] Pub. L. No. 109-417, 42 U.S.C. § 241 et seq. (PAHPA) and

- The Pandemic and All Hazard Preparedness Reauthorization Act Pub. L. No. 113-5[12], (PAHPRA).

Learn more about legal authorities, policies, and committees[13] and strategies and reports[14] for pandemic influenza, Chemical, Biological, Radiological, and Nuclear Medical Countermeasures.

[11] http://www.gpo.gov/fdsys/pkg/PLAW-109publ417/pdf/PLAW-109publ417.pdf
[12] http://www.gpo.gov/fdsys/pkg/PLAW-113publ5/pdf/PLAW-113publ5.pdf
[13] http://www.phe.gov/preparedness/legal/Pages/default.aspx
[14] https://www.medicalcountermeasures.gov/federal-initiatives/strategies-and-reports.aspx

Part I: Research and Development Areas of Interest

This section presents an overview of the research and development projects that BARDA seeks to support through this BAA.

Offerors contemplating submitting Quad Charts and White Papers are strongly encouraged to contact BARDA technical POC for the respective area of interest. Be advised that after a White Paper (or Full Proposal) has been submitted, all communications related to that submission must be through the ASPR's Office of Acquisitions Management, Contracts, and Grants (AMCG).

Area of Interest #1: CBRN Vaccines

1.1. Anthrax and Smallpox. Submissions for anthrax and smallpox vaccines will not be considered during the open period of this BAA, unless specifically announced through special instructions.

1.2 Sudan ebolavirus and Marburg virus. BARDA is interested in advanced development projects for monovalent vaccines against Sudan ebolavirus and Marburg virus. The proposed vaccine candidate must have demonstrated protection from lethal challenge in non-human primate studies. Preference will be given to candidate products with one or more of the following:

- Phase 1 clinical data
- active Investigational New Drug (IND) with the FDA
- safety toxicity data
- preliminary formulation
- stability indicating assay
- demonstrated small scale manufacturing process

The objective of this program is to advance projects through the end of Phase 2 clinical development. Multivalent candidates will be considered only upon completion of phase 2 clinical study with clear guidance from FDA on regulatory pathway.

1.3 Expansion of availability of licensed anthrax and smallpox vaccines to at risk populations: BARDA is interested in programs to expand availability of licensed anthrax and smallpox vaccines for at risk populations, e.g. pediatric populations. Interested parties should refer to the Presidential Commission for the Study of Bioethical Issues report "Safeguarding Children: Pediatric Medical Countermeasures"[15]

Technical Point of Contact: Dr. Eric Espeland; Eric.Espeland@hhs.gov

Contracting Point of Contact: Jonathan Gonzalez; Jonathan.Gonzalez@hhs.gov

[15] https://www.medicalcountermeasures.gov/BARDA/Documents/PCSBI_Pediatric-MCM508.pdf

Area of Interest #2: Antitoxins and Therapeutic Proteins

2.1 Development of peptide or small molecule antitoxins, and other novel compounds, with innovative formulations offering enhanced long-term stability. The candidate must be at TRL-6 (active IND and human safety data).

2.2 Development of antibody treatments and other therapeutic agents for viral hemorrhagic fevers viruses. Programs must be at TRL-5 with a lead candidate identified.

2.3 Development of antibody treatments and other therapeutic agents against smallpox. Programs must have evidence for antiviral activity against orthopoxviruses. Programs at higher TRLs will be given priority.

Technical Point of Contact: Dr. Chia-Wei Tsai; Chia-Wei.Tsai@hhs.gov

Contracting Point of Contact: Erin Greninger; Erin.Greninger@hhs.gov

Area of Interest #3: Antibacterials

In accordance with the Pandemic and All-Hazards Preparedness Act (PAHPA) of 2006 and reauthorized in 2013 (PAHPRA), BARDA has the responsibility to ensure that the United States has a sufficient supply of vaccines and drugs to respond to public health emergencies caused by pandemic influenza, emerging infectious diseases, and chemical, biological, and radiological and nuclear threats. BARDA recognizes the dual utility of antimicrobials for the treatment and prevention of diseases caused by bacterial and viral threat agents and clinically relevant drug resistant pathogens. To achieve its' national security mission, BARDA seeks to establish public-private partnerships with industry to accelerate the advanced research, clinical development, and regulatory approval of new antibacterial products for the treatment or prevention of infections. Of particular interest to the Government are proposals, which aim to:

3.1 Develop and test antibacterial products that are in development for post-exposure prophylaxis (PEP) and treatment efficacy against one or more of the following biodefense threat agents: *Bacillus anthracis*, *Yersinia pestis*, *Francisella tularensis*, *Burkholderia mallei*, and *Burkholderia pseudomallei*. Minimum inhibitory concentration (MIC) data for multiple strains of one or more of these biothreat agents is required; data from non-clinical studies evaluating the antibacterial candidate against any of these biothreat agents in relevant animal models of infection will strengthen a proposal.

3.2 Develop new small molecule drugs that treat or prevent resistant bacterial infections either alone or in combination with other therapeutics;

3.3 Develop non-traditional antibacterial therapeutics that treat or prevent resistant infections. Examples include, but are not limited to antibody-based approaches, host-directed therapies including immune modulators, antimicrobial peptides, bacteriophage, microbiome approaches, and inhibitors of quorum sensing or expression of bacterial virulence factors.

Products should also possess activity against one or more of the pathogens categorized by the CDC as an "Urgent" or "Serious" public health threat in the September 2013 CDC

Report titled “Antibiotic Resistance Threats in the United States, 2013”. Competitiveness will be enhanced if the proposed candidate possesses activity against Gram negative pathogens.

Under this area of interest, most aspects of drug development are considered permissible including clinical studies, nonclinical studies, safety, toxicology, pharmacokinetics/pharmacodynamics (PK/PD), and microbiological studies, manufacturing, analytical assay development and validation, regulatory submission preparation, and the development and use of diagnostics to enhance clinical trial enrollment.

Qualities that strengthen the competitiveness of a proposal include:

- Candidates demonstrating substantial improvements over existing antimicrobial products are of greatest interest including novel first in class compounds with unprecedented mechanisms of action. If a candidate belongs to an existing class (same/similar chemistry and pathogen target) of antimicrobial products, there must be significant advantages such as overcoming existing resistance mechanisms and/or greatly improved therapeutic properties.

- Greater technological advancement of the candidate: Successive progression through TRLs and corresponding completion of commercial drug development activities will increase the attractiveness of proposals. Data from IND enabling toxicology studies is a requirement improved upon by having filed an IND, and further made attractive with progression into and completion of Phase 1, 2, and 3 clinical studies.

- Regulatory feasibility: Evidence of supportive regulatory correspondences from the FDA concerning the development plan of the candidate will strengthen a proposal submission.

- Special populations: Antimicrobials that offer therapeutic benefit to special populations, particularly pediatric subjects, are an important and underserved area. Proposals that have specific plans and proposed activities to advance a product for approved use in special populations will be viewed more favorably.

- Cost sharing: Proposals that demonstrate a commitment of resources from the Offeror in the form of sharing the cost of the proposed development plan are most advantageous.

Learn more about Antibacterials[16].

Technical Point of Contact: Dr. Christopher Houchens; Christopher.Houchens@hhs.gov

Contracting Point of Contact: Erin Greninger; Erin.Greninger@hhs.gov

Area of Interest #4: Radiological/Nuclear Threat Medical Countermeasures

Injuries resulting from accidental or intentional radiation exposures (from radiological dispersal devices (RDD) or nuclear detonations) are likely to be complex and could

[16] https://www.medicalcountermeasures.gov/barda/cbrn/broad-spectrum-antimicrobials.aspx

include combined injuries from radiation exposure concomitant with mechanical trauma or thermal burns. Radiation causes severe systemic injury at the cellular level including DNA damage and reactive oxygen species production that result in additional cellular physiological etiologies, including cellular apoptosis, loss of progenitor cells, endothelial cell damage, altered metabolism, and induction of inflammatory responses. These systemic injuries lead to the development of infection/sepsis and the clinical manifestations of vascular injury, coagulopathies, ischemia, and resultant multi organ failure.

This area of interest is focused on development of medical countermeasures (MCMs) to treat radiation injury. Programs proposing work in this area of interest should be at a TRL for the radiation, or related, indication of TRL 5 (i.e., completed all activities described for TRL 5); Submissions not meeting the TRL 5 maturity requirement will not be reviewed. Additionally, Offerors should have held a pre-IND meeting with FDA to discuss licensure as an MCM prior to the submission of a White Paper to the BARDA BAA, and should be prepared to provide the minutes from the meeting, if requested. Development programs should plan to address the needs of at-risk populations.

There are several considerations when proposing a product development program for BARDA Area of Interest 4 – Radiological/Nuclear Threat Medical Countermeasures:

Radiological and Nuclear Strategic Considerations

a) Concept of Operations (CONOPs) for Radiological and Nuclear Incidents

An emergency response to a radiological/nuclear event will likely follow two general phases of treatment: field care and definitive care. The field care treatment phase is generally defined as the first 72 hours of the emergency response, during which time resources and trained personnel are expected to be exceedingly scarce, thus delaying and limiting access to treatment. The definitive care treatment phase extends beyond the initial 72 hours of the emergency response and includes the full range of medical care necessary to manage a patient's condition, with treatment administered at medical centers and hospitals operating at surge capacity. BARDA priorities include the repurposing of already approved therapies for a new Acute Radiation Syndrome (ARS) indication or advanced development of new therapies. Desirable MCM characteristics to improve flexibility and usability in a mass casualty incident include ease of storage (e.g. storage at room temperature), favorable deployment and route of administration, and efficacy when administered a minimum of 24 hours or later after a radiation exposure. Efficacy should be based on improved survival outcome or mitigation of clinical endpoints of radiation injury. Priorities for the definitive care treatment phase could also include blood products, cellular therapies and products that enhance the engraftment and/or activity of these therapies.

b) Repurposing Commercially Available Products

BARDA may support evaluation of FDA approved drugs with existing commercial markets for repurposing to expand current indications. For proposed novel products, Offerors should identify a relevant commercial indication and propose activities that offer leveraging opportunities for both the MCM and commercial indication. A clear business strategy should be included in the plan.

c) Addressing Multiple Relevant Indications or Multiple Threat Areas

BARDA prioritizes MCMs that have the potential to treat multiple relevant indications or multiple threat areas (e.g., radiation injury combined with mechanical trauma; radiation and chemical injury).

Radiological and Nuclear Programmatic Priorities

4.1 Advanced Development of MCMs to treat radiation injury due to acute exposure to ionizing radiation. BARDA could support:

a) Evaluation of licensed products for repurposing. Products should have a label indication that could reasonably be expanded to include use in a mass casualty event to treat radiation injury due to acute exposure to ionizing radiation. The proposed development plan could include activities for additional commercially relevant indications.

b) Novel therapeutics to address thrombocytopenia due to acute exposure to ionizing radiation.

c) Novel therapeutics to address systemic injury responses due to acute exposure to ionizing radiation (mechanical trauma can be included as a second indication). Priority target pathways include coagulopathy, fibrinolysis, vascular injury and sepsis.

Note that the development of field use anti-neutropenics (second generation anti-neutropenics) will not be supported under this funding opportunity.

4.2 Blood Products: Advanced development of next generation blood products that will enhance our ability to respond to mass casualty events and meet blood product treatment gaps. Proposed intended use can be radiation injury, mechanical trauma or both (see considerations above). Potential areas of blood product development include but are not limited to:

a) Development of cell products derived from stem-cells and their progenitors to produce safe and non-alloimmunizing human red blood cell, platelet, or white blood cell products for use in transfusing humans;

b) Technologies for reliably producing hematopoietic stem cells and their progenitors, including optimization of directed differentiation and engraftment of functional and safe hematopoietic cells

c) Technologies to improve cell processing, optimization of ex vivo expansion, scale up, production, and Good Manufacturing Practice (GMP) manufacturing of human-derived or stem-cell derived blood products.

4.3 Decorporation Agents: Development of decorporation agents, which are either passive (limited generally to the blood pool) or active chelators (preferred; seeks intracellular or distributed depots). BARDA will continue to fund projects to support advanced research and development of Prussian blue formulations appropriate for children under the age of two years.

BARDA encourages innovation. For Area of Interest 4: Radiological/Nuclear, innovations could range from pre-clinical through licensure development plans or strategies. For

example, product development plans might include a systems biology approach, blood pharming strategies, or novel regulatory strategies, such as the development of species specific products for approval under the animal rule.

Learn more about Radiological and Nuclear Medical Countermeasures[17].

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Area of Interest #5: Chemical Threat Medical Countermeasures

Area of Interest #5 includes medical countermeasures (MCMs) that treat the acute health effects of chemical threats, are easy to administer in a mass-casualty situation, and are rapidly effective as post-exposure therapies. The MCMs should be safe and effective for the entire population, including infants, children, adolescents, elderly, pregnant women and immunocompromised individuals. The technical readiness level (TRL) for candidates should be at TRL 4 (i.e. completed all activities described for TRL 4) or higher; in vivo activity and potential for efficacy consistent with the product's intended use as an MCM against a threat agent (i.e. dose, schedule, duration, and route of administration) must be demonstrated. Offerors should have held a pre-IND meeting with the FDA for licensure as an MCM prior to the submission of a White Paper to the BARDA BAA. Strong preference will be given to drug candidates that are already approved or are in clinical development for a conventional indication similar to that arising from exposure to a chemical agent. Specific AOI within Chemical Threat Medical Countermeasures include:

5.1 Pulmonary Agents: Development of MCMs to prevent and treat lung damage (including pulmonary edema and fibrosis) resulting from exposure to agents such as chlorine and phosgene.

5.2 Vesicants: Development of MCMs that limit harmful aspects of exposure to vesicating agents such as sulfur mustard and Lewisite. Needs include MCMs designed to treat lung, skin, and ocular as well as systemic effects.

5.3 Blood/Metabolic Agents: Development of MCMs to treat acute poisoning from agents such as cyanides. Antidotes should be easily administered by first responders in personal protective equipment. Preference is given to those cyanide antidotes that are also effective against smoke inhalation-related exposure.

5.4 Nerve Agents and Organophosphorus (OP) Pesticides: Development of MCMs to treat seizures that are refractory to treatment with benzodiazepines. These drugs, in most cases, will be used after benzodiazepine therapy has failed.

5.5. Novel MCM Delivery Mechanisms: Development of improved methods of administration for new and existing MCMs. The candidates should be amenable to use by emergency medical personnel or first responders dealing with large numbers of exposed individuals in mass casualty situations.

Learn more about Chemical Medical Countermeasures.

[17] https://www.medicalcountermeasures.gov/barda/cbrn/radiological-and-nuclear-countermeasures.aspx

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Area of Interest #6: Burn Medical Countermeasures

BARDA has a responsibility to treat burn injuries and associated complications effectively in the civilian population resulting from natural calamities as well as various threats such as detonation of a nuclear device. Timely treatment, delivery of burn care and management of injuries is dependent on infrastructure and is labor intensive. Treatment is also influenced by various factors like burn size area and depth, as well as other comorbidities and confounding factors. In a mass casualty, limited available capacity, throughput, and ability to provide effective temporizing treatment to the large number of patients is expected to create bottlenecks in the ability to provide quality treatment and care for victims.

In collaborative efforts to address these complications, BARDA has worked with the burn care community to identify key procedures and technologies that may address these bottlenecks and can improve delivery of care in an event resulting in high numbers of burn victims. The paradigm in delivery of care requires consideration of treatment window, urgency, and resources at the location. Termed 'field care' and 'definitive care,' they are further described below.

Field Care is generally defined as the first 72 hours of the emergency response, where the primary goal is to provide initial and temporary stabilization and life-saving interventions. Treatment will likely be administered at or near the incident site or at peripheral assembly sites for triage and evacuation to other medical facilities for further definitive care. Resources and trained personnel are expected to be exceedingly scarce. MCMs should be compatible with the published RTR medical response system (*Prehosp Disaster Med*. 2009 May-Jun; 24(3):167-78). Emphasis is placed on the MCMs having attributes such as: ease of administration, high therapeutic index, robust stability, and ease of storage and deployment.

Definitive Care is the treatment phase that extends beyond the initial 72 hours of the emergency response when it is expected that the patient have been transferred to a medical facility. The primary goal is to manage a patient's condition fully. This includes access at that facility or others for a range of therapeutic and curative (or palliative) interventions, and the expertise and coordination that can occur for the initial acute phase as well as convalescent, restorative, rehabilitative, and preventive medical care. Treatment will primarily be administered at medical centers and hospitals, which may be operating at surge capacity. The challenges of providing definitive burn care are heightened in a mass casualty event creating a resource and infrastructure constrained environment.

Guidelines for Advanced Development of MCMs: BARDA is interested in the development of advanced therapeutic modalities for delivery of care for burn injuries in a mass casualty. It is imperative that products for consideration must address two goals: (1) clearly specify the target(s) for treatment within the burn care continuum and the value proposition from the potential to address critical bottlenecks in delivery of care in a mass casualty; and (2) clearly specify the value proposition of the products to integrate into and advance the care paradigm in the current standard of care to achieve market

sustainability, such as compatibility to other indications in wound care. Under this BAA, MCMs which have efficacy as treatments or have the ability to manage morbidity of burn injuries when administered during definitive care and reduce the overall cost of care are of particular interest compared to products for use in field care. Also, products currently marketed for other commercial indications, but which are found to be or are justifiable to be effective in improving the current standard of burn care, are of significant interest.

In meeting the above goals, the proposed MCMs could have one or more attributes making them especially amenable for use in a mass casualty. Such attributes include reducing resource needs (surgical needs, time and facilities), contributing to autograft sparing, enabling faster triage and assisting decision-making or the ability to temporize and stabilize patients to postpone or manage resources for advanced procedures. Proposed MCMs must clearly show a "clinically meaningful benefit to the patient," as defined by FDA, to support their indication. To that end, it is recommended to use FDA guidance on endpoints for treatment (e.g., full closure endpoints) and demonstrate via reasonable methods that they have been reached or surpassed within relevant models and studies. It is expected that Offerors have had input from the FDA prior to submission of a White Paper or proposal for consideration. BARDA may request documentation to support evidence of FDA input, such as a copy of the resulting meeting minutes.

The Technology Readiness Level (TRL) for technologies or treatments meeting the above goals should be at TRL 5 or higher (i.e.: completed all activities described for TRL 5; as described in Attachment 1). Specifically, Offerors should have held a pre-IND, pre-IDE, or pre-submission meeting with FDA to discuss licensure/clearance/approval as a MCM prior to the submission of a White Paper to the BARDA BAA.

Innovative MCMs: BARDA is also open to considering proposals for novel innovative technologies at a relatively lower TRL. Innovative technologies and potential MCMs that can be justified to provide a generational leap compared to the current standard of care in effectiveness, cost (both of the product and/or the overall patient treatment), and ease of use within a mass casualty setting are of particular interest. To be considered an innovative technology, submissions need to share some data for the value proposition and a sound rationale to justify its ability to transform or revolutionize burn care. Offerors must also have a defined regulatory path towards approval, a minimum of preclinical toxicity data, where appropriate, and proof-of concept efficacy data using a relevant *in-vivo* model system shown to appropriately mimic the human response.

Market Sustainability: Given the limited commercial burn market, all submissions must have a market sustainability plan. Such plans may include but are not limited to other clinical indications in conventional care while addressing one or more treatment goals, especially in definitive care for thermal burns as listed below (under Thermal Burn Product Areas of Specific Interest). Additionally, any submission must provide a defined capability to be transitioned into the burn care treatment community without the need for extensive retraining or interruption of the current continuum within the standard of care.

Thermal Burn Product Areas of Specific Interest:

- **6.1 Products to prevent or control burn wound conversion:** For a product to be considered, Offerors must demonstrate preliminary efficacy data to modulate wound healing. Proposed products must therefore contribute towards autograft sparing when applied to deep partial thickness burns and savings in

resources. Appropriate value propositions should be provided such as rationale for ease in administration and/or use in large TBSA burns in a mass casualty within a short timeframe. Products, which are non-autologous and used off-the-shelf for any patient would be of significant interest.

- **6.2 Smart imaging systems:** For a product to be considered, Offerors must demonstrate preliminary effectiveness to improve the performance in one or both of these actions compared to the current standards. Common desirable attributes include but are not limited to being non-invasive, mobile/portable, compliant with data security, and having user-friendly interfaces.

    - Identification of burn depth and/or assessment of a burn wound's healing potential without further intervention such as grafting. Desired attributes may include improvements for faster, comprehensive, and more accurate non-invasive, wound depth identification, real-time feedback and a model for decision support in signal triage.

    - Ability to multiplex or be multifunctional, i.e., one system that could have different modules and more than one function. For example, detect burn depth and have ability to detect traumatic injury complication associated with mass casualties, such as high impact injuries leading to quicker diagnosis of internal bleeding and the damage caused by trauma to the abdomen such as liver or spleen lacerations or perforation of other organs. Additional range of products includes but not limited to those products that could screen for and detect potential injuries to internal organs (such as by using ultrasounds to detect pooled blood, measure brain pressure to predict death risk).

- **6.3 Products promoting wound closure:** For a product to be considered, Offerors must demonstrate preliminary data and rationale to function as an adjunct to accelerate wound closure of deep partial thickness and full thickness thermal burn wounds. Preliminary data demonstrating the ability to accelerate time to full wound closure as defined by FDA guidance (FDA, Guidance for Industry: Chronic Cutaneous Ulcer and Burn Wounds- Developing Products for Treatment 2006) would be valuable. Desired attributes include MCMs which could be manufactured to be ready to use off-the-shelf without the need for additional procedures (e.g., allogenic products) and which have market sustainability as discussed above.

- **6.4 Products for temporizing burn injuries:** For a product to be considered, Offerors must share preliminary data and rationale on its ability to temporize full thickness burn wounds and therefore delay the need for autografting for an extended period beyond current standard of care. Desired attributes include safe temporization for more than 30 days without removal or re-application, storage at room temperature for extended periods of time and ability to use off-the-shelf.

- **6.5 Countermeasures for Cutaneous Radiation Injuries (CRI):** For a product to be considered, Offerors must share preliminary data in established models and/or human clinical conditions such as those caused by radiation oncology procedures, e.g., Radiation Dermatitis (RD). Acceptable data could

include but are not limited to: prompt and evidence-based wound management regimens that may lead to the reduction in patient's morbidity, the prevention of wound progression, and the acceleration of the CRI injury. The Offeror must also provide clear definition of their intended clinical window of opportunity within which to effectively use the product post-injury. Products should be able to treat CRI Grades I, II, and III.

- **6.6 Products for treatment of inhalation injuries:** For a product to be considered, Offerors must demonstrate preliminary efficacy data and the rationale for the mode of action to cause a reduction of morbidity and mortality due to complications resulting from inhalation injury. Products may include imaging devices, devices and methodologies for precision ventilation and inhalation management that may contain drugs and biologics which meet the goals for reducing morbidity and mortality associated with inhalation injuries.

Learn more about Thermal Burn Medical Countermeasures.

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Area of Interest #7: Diagnostics

The clinical diagnostics area of interest #7 consists of: Innovations (7.1), biothreats (7.2), antibiotic resistance (7.3), radiation exposure/biodosimetry (7.4), chemical threat exposure (7.5), influenza (7.6) and emerging diseases (7.7) and novel platform development (7.8).

Definitions for the purpose of this AOI:

- A "diagnostic" is defined as including an assay and, if required, an instrument, that together are FDA cleared or approved. Assays that use diagnostic instruments that have routine applications in clinical laboratories and/or point of care settings are preferred. New diagnostic platforms may be proposed (7.8) if they will have broad applications (e.g., CBRN, pandemic influenza, antibiotic resistance, emerging disease threats and common infectious diseases or routine healthcare analytes) and provide significant improvement in diagnostic capability (e.g., ease of use, time to result, higher sensitivity).

- Point of care (POC) is defined as a test that can be used in near patient, non-laboratory settings such as emergency departments, doctor's offices, clinics, pharmacies, and field triage centers. It should be easy to use, portable, and preferably CLIA-waivable, and provide results in less than 30 minutes.

- Molecular assays are defined as nucleic acid amplification tests (NAAT).

Technical Readiness Level:

- Offerors should propose development projects that have reached a TRL equal to or greater than that specified in each sub-section below. A product can be described as achieving a TRL only if all relevant activities identified in that TRL have been completed. For a detailed list of TRL definitions for diagnostics

development see Attachment 1A of this BAA. Development programs at lower maturity levels should consider funding opportunities offered by The National Institute of Allergy and Infectious Diseases (NIAID) or other Federal agencies that fund earlier stage R&D projects.

- Where TRL 4 or higher is expected, Offerors must have finalized the selection of targets and provide adequate feasibility data for both the proposed assay(s) and the platform demonstrating that clinically relevant sensitivity of the diagnostic target (e.g., nucleic acid, antigen, protein, toxin, antibody) is achievable in relevant clinical matrices. Assays with strong supportive feasibility data supporting the claimed use case will receive higher consideration. Platform performance data may include testing with surrogate agents, (e.g. B. cereus, or relevant common disease analytes). BARDA is not interested in White Papers or proposals that fail to include convincing feasibility data.

Animal samples, if required for proposed studies, will be provided as Government Furnished Material (GFM).

Design, manufacture, labeling, and packaging of test components must be compliant with current Good Manufacturing Practice (cGMP) as set forth in the Quality System Regulation, 21 Code of Federal Regulations (CFR) Part 820, and qualified for use in CLIA-regulated settings.

7.1 Diagnostic Innovations

This section encourages innovative technologies that will provide capabilities for novel diagnostics with improved performance, as well as for their expedited development, manufacturing, and use for existing and emerging threats. Projects may be at an earlier stage of development (TRL 3).

7.1.1 Development and evaluation of innovative sample collection devices that enable at least one of the following improvements:

- direct testing without separate sample preparation
- improved target collection, concentration and or/recovery resulting in improved sensitivity
- target stabilization for transfer to a laboratory setting or downstream testing
- enable reliable and consistent self-collection, or collection by non-expert personnel.

Sample collection devices should generate specimens that can be tested using novel and existing platforms and be applicable to BARDA priority threats. TRL 3 or greater.

7.1.2 Identify and validate host biomarkers of early infection that would be applicable to biothreats and influenza and may also have utility for emerging diseases. Characterization studies should demonstrate that markers are reliably detectable in earliest stages of disease/infection to be useful for both rule-in and rule-out indications and/or indicate disease severity or potential clinical outcome. Examples of host biomarkers include but are not limited to host proteins, antigens, and genetic markers

and physiologic indicators. Priority will be given to solutions that have the greatest diagnostic potential to inform patient management decisions, and have the potential to be transferred to platforms accessible for near patient testing. TRL 3 or greater.

7.1.3 Identify and validate pathogen markers of early infection that would be applicable to biothreats or influenza. Characterization studies should demonstrate that markers are reliably detectable in earliest stages of disease/infection to be useful for both rule-in and rule-out indications and/or indicate disease severity or potential clinical outcome. Examples of pathogen markers include but are not limited to nucleic acids, proteins, antigens, and toxins. Priority will be given to solutions that will have the greatest diagnostic potential to inform patient management decisions, and have the potential to be transferred to platforms accessible for near patient testing. TRL 3 or greater.

7.1.4 Development of external (wearable) biometric sensors or monitors that can reliably detect clinically relevant biomarkers that are detectable in early stages of disease/infection. Markers must be applicable to CBRN and/or influenza and should be applicable to other common infectious diseases. Sensors/monitors must include capability to provide information electronically to users and health care providers. TRL 3 or greater.

7.1.5 Development of novel device technology that helps move diagnostics closer to POC and home use. The technology should significantly reduce size, weight, cost, time to result, complexity of use, maintenance, waste and/or power consumption of diagnostic platforms/instruments and/or cartridges. TRL 3 or greater. Key AOI includes:

- fluidic management
- detection methodology
- sample processing capabilities
- ease of use
- manufacturability
- longer shelf life

7.1.6 Development of improved assay chemistry that will provide:

- shorter testing times
- improved analytical sensitivity and specificity
- higher throughput
- reduced reagent use
- reduced device complexity, size, or cost

Proposed enhancements should not increase the cost per test. TRL 3 or greater.

7.2 Biothreat Agent Diagnostics

Biothreat Agents of Interest include (listed alphabetically): *Bacillus anthracis* (anthrax), *Botulinum toxin* (botulism), *Burkholderia mallei* (glanders) and *Burkholderia pseudomallei* (melioidosis), ebolaviruses and Marburg virus, *Francisella tularensis* (tularemia), *Rickettsia prowazekii* (typhus), *Yersinia pestis* (plague) and smallpox (orthopox genus virus assays acceptable).

7.2.1 Advanced development, clinical evaluation, and FDA clearance/approval of rapid, accurate POC diagnostic systems for *Bacillus anthracis* infection (anthrax). Assays designed to quantitatively detect lethal factor protein and at least one other toxin marker (lethal toxin protein, edema factor protein, or protective antigen protein) will be considered. Assays must detect targets at clinically relevant concentrations present during the early stages of disease. These systems designed for ease-of-use by non-expert personnel (i.e., CLIA waived/waivable). If an instrument is used, it should be small, lightweight, portable, and have at least one FDA-cleared assay for common infectious diseases or other routine healthcare analytes. TRL 4 or greater.

7.2.2 Advanced development, clinical evaluation, and FDA clearance/approval of rapid, accurate POC diagnostic systems for *Burkholderia pseudomallei* infection (meliodosis). Assays must detect targets at clinically relevant concentrations present during the early stages of disease. These systems designed for ease-of-use by non-expert personnel (i.e., CLIA waived/waivable). If an instrument is used, it should be small, lightweight, portable, and have at least one FDA-cleared assay for common infectious diseases or other routine healthcare analytes. TRL 4 or greater.

7.2.3 Advanced development, clinical evaluation, and FDA clearance/approval of rapid, accurate POC diagnostic systems for biothreats defined above. Assays must detect targets at clinically relevant concentrations present during the early stages of disease. If needed, studies to characterize the relationship of markers to the diagnostic window of opportunity and their clinical utility in patient specimens, including determination of the most appropriate sample type and matrix should be included in the proposal (see Innovations sub-section 7.1.2). TRL 4 or greater.

7.2.4 Advanced development, clinical evaluation, and FDA clearance of automated, high-throughput diagnostic assays for determining infection due to the biothreats defined above.

- Single threat and multiplex biothreat assays will be considered. TRL 4 or greater.
- It is preferred that high throughput assays are developed and optimized for use with existing diagnostic instrument platforms that have a large number of US clinical laboratory placements, and that are FDA-cleared for other “routine health-care” applications.
- Assays must detect targets at clinically relevant concentrations present during the early stages of disease. If needed, studies to characterize the relationship of markers to the diagnostic window of opportunity and their clinical utility in patient specimens, including determination of the most appropriate sample type and matrix should be included in the proposal (see Innovations sub-section 16.1.2).

7.3 Antibiotic Resistance Diagnostics for priority bacterial pathogens

BARDA is providing support to advance innovative rapid and improved diagnostics to

detect drug resistant urgent and serious priority public health pathogens* and to characterize their resistance profiles, both for biological threats and routine healthcare conditions.

*Refer to the CDC report "Antibiotic Resistance Threats in the United States,"

7.3.1 Advanced development, clinical evaluation, and FDA clearance/approval of direct specimen diagnostic tests to guide targeted therapeutic decisions for priority bacterial pathogens by identifying the pathogen(s) and their resistance or susceptibility to relevant antibiotics without additional sample preparation. The assay must be highly sensitive and specific, and useful for multiple specimen types (e.g., sterile and mixed flora sites). Pathogen identification should be available in less than 30 minutes. TRL 4 or greater.

7.3.2 Advanced development, clinical evaluation and FDA clearance/approval of CLIA waivable, rapid platforms and assays for use in POC settings that will be useful to reliably distinguish between Viral and Bacterial infections in order to inform appropriate use of antibacterials and antivirals. The assay must be highly sensitive and specific, and useful for multiple infection types (e.g., respiratory, bloodstream). Results should be available in less than 30 minutes. TRL 4 or greater.

7.3.3 Advanced development, clinical evaluation and FDA clearance/approval of multiplex molecular assays for use in moderate complexity and high complexity laboratory settings that identify priority bacterial pathogens and genetic determinants of antibiotic resistance in a single direct specimen analysis. The assays must be highly sensitive and specific, and useful for multiple specimen types (e.g., sterile and mixed flora sites). TRL 4 or greater.

7.3.4 Advanced development and clinical evaluation of POC tests to enable antibiotic clinical trials, i.e., rapidly rule in/rule out pathogen of interest, and assess resistance profile from clinical specimens. Tests should be designed for use in POC settings. Although these tests may not require FDA clearance/approval, development pathway should ensure usability for all intended applications. TRL 4 or greater.

7.3.5 Advanced development, clinical evaluation, and FDA clearance/approval of clinically applicable specimen-to-result sequencing solutions with user-friendly simplified workflow and bioinformatics tools appropriate for use in a clinical diagnostics laboratory to identify pathogens with known and novel resistance determinants directly from a broad range of clinical specimen types. TRL 4 or greater.

7.3.6 Advanced development, clinical evaluation, and FDA clearance/approval of novel phenotypic susceptibility platforms and assays for use in moderate and high complexity laboratory settings that will shorten the time required to reliably and accurately identify resistance or susceptibility to relevant antibiotics. All results should be available in less than 8 hours. TRL 4 or greater.

7.4 Radiation exposure (Biodosimetry) Diagnostics

7.4.1 Development of a dosimetry self-assessment tool in order to determine if an individual (adults and children) has absorbed ionizing radiation at a dose equal to or greater than 2 Gy. Devices that leverage items routinely carried upon a person will receive higher consideration. TRL 4 or greater.

7.4.2 Advanced development, clinical evaluation, and FDA clearance/approval of accurate, low cost radiation biodosimetry tests that will significantly improve clinical response capability for a radiation incident. Submissions must be TRL-4 or greater and include NHP or human data demonstrating that the assay can discriminate absorbed dose.

- High-throughput laboratory assays that have an accuracy (estimating the actual dose absorbed) of at least 90% with an error of plus or minus 0.5 Gy over 1 to 14 days post-exposure", can be run on commercially available laboratory instruments, and have a turnaround time under 4 hours are required.

- For point of care, tests that require minimal resources and can be used in triage/field setting to determine absorbed dose >= 2 Gy threshold with high specificity and a turnaround time under 15 minutes are required.

7.5 Chemical Threat Diagnostics

Submissions for Chemical Agent Diagnostics will not be considered during the open period of this BAA, unless specifically announced through amendments or special instructions.

7.6 Influenza Diagnostics

Influenza assays must provide results that prompt early consideration for antiviral drug use, and at a minimum, differentiate Influenza A and B. Development should include evaluation of reactivity to emerging novel, avian and swine influenza viruses.

7.6.1 Advanced development, clinical evaluation and FDA clearance/approval of home-use tests that detect influenza, and at a minimum, differentiate Influenza A and B viruses. Diagnostics should demonstrate performance at least equivalent to existing FDA cleared diagnostics, and should include an integrated patient management solution incorporating:

- use case, acceptance by clinicians and patients,

- electronic information transfer to heath care provider for rapid treatment/patient management decisions.

TRL 4 or greater.

7.6.2 Advanced development, clinical evaluation and FDA clearance/approval of CLIA waivable, low cost influenza diagnostic tests suitable for use in POC settings and

- differentiate Influenza A and B viruses, and seasonal influenza A viruses from non-seasonal influenza viruses,

- demonstrate clinical sensitivity and specificity that is an improvement over existing assays,

- have electronic transmission capability.

If an instrument is used, it should be small, lightweight, portable, and have at least one

FDA-cleared assay for other common infection disease or routine health-care analyte, TRL 4 or greater.

7.6.3 Advanced development, clinical evaluation, and FDA clearance/approval of methods to enable more rapid identification of novel influenza viruses, human-animal reassortant influenza viruses, or emerging respiratory viruses with the goal to identify and diagnose both seasonal and novel influenza infections. Methods such as targeted or whole genome nucleotide sequencing that can be readily used in clinical laboratory settings may be proposed. TRL 4 or greater.

7.7 Emerging Diseases Diagnostics

Submissions for Emerging Disease Diagnostics will not be considered during the open period of this BAA, unless specifically announced through amendments or special instructions.

7.8 Hardware/Software platform development or improvement

In general, assays that can be performed using diagnostic platforms that are/will be readily available for routine applications in clinical laboratories and/or point of care settings are preferred. New diagnostic platforms may be proposed if they can be used for CBRN, pandemic influenza and/or emerging disease threats and provide significant innovation and improvement in diagnostic capability (e.g., ease of use, time to result, higher sensitivity, simplified sequencing). These devices must be developed using assays for BARDA priority biothreats, antibiotic resistant priority bacterial pathogens, pandemic influenza or biodosimetry and also have uses for common infectious diseases or routine healthcare analytes.

7.8.1 Advanced development, clinical evaluation, and FDA clearance of novel, improved *in vitro* diagnostic (IVD) devices that provide rapid, accurate results and can be used in POC settings. Proposal for new platform must also describe development of at least one assay relevant to BARDA priorities (biothreats, pandemic influenza, antibiotic resistance for priority bacterial pathogens, biodosimetry). Proposed technology must demonstrate significant improvements over exiting technology, meet TRL 4 or greater, and offer these essential elements:

a. Small footprint, easily portable

b. Lightweight – less than 5 lbs. preferred

c. Rapid results - sample to answer in under 30 minutes (15 minutes preferred)

d. Broad assay menu with highly accurate assays

e. Able to process multiple specimen types (e.g., blood, nasal swabs)

f. Battery operation option

g. Supports electronic data transmission

h. Able to operate in non-temperature/humidity controlled environments.

i. Low cost

7.8.2 Advanced development of simplified next generation sequencing platforms and analysis tools, making them more suitable for use in CLIA regulated laboratories. TRL 4 or greater.

Learn more about Biothreat Diagnostics and Biodosimetry[18].

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Area of Interest #8: Influenza and Emerging Infectious Diseases (IEID) Vaccines

Offerors for Area of Interest #8 should propose activities for products that can currently be described as having a maturity level equal to or greater than Technology Readiness Level (TRL) 6 (e.g. as evidenced by release of a finalized report for a Phase 1 clinical study for the same indication as proposed activities), unless otherwise specified. A product can be described as achieving a TRL if it has completed all activities identified in that TRL. The Technology Readiness Level ranking criteria can be found in Attachment 1B of this BAA.

Under this Area of Interest, BARDA is seeking technologies that will improve preparedness against influenza and emerging infectious diseases with pandemic potential. Successful Offerors will provide evidence that the proposed vaccine product represents a transformative improvement in key vaccine attributes as compared to currently licensed products.

8.1 Advanced development of more effective vaccines. Candidates, which have achieved TRL 6 or greater, and that will improve preparedness against influenza and emerging infectious diseases with pandemic potential are desired. Specifically for influenza, support for advanced development of new influenza vaccine candidates with the potential to stimulate broader (across influenza subtypes and/or within influenza subtypes), durable and more effective immunity than currently licensed products. The Offeror should provide data or a plan for validation of vaccine potency and release assays that are specific for the new influenza vaccine candidate. The Offeror should provide a regulatory strategy for FDA approval of the vaccine candidate and data demonstrating transformative improvements in immunogenicity/efficacy as compared to existing FDA licensed vaccines. Proposed clinical activities (Phase 1b/Phase 2 studies) should support development toward FDA licensure and evaluate key vaccine attributes, such as dose schedule, mechanism of action, time to onset of protection, broader cross-protection across influenza A virus subtypes, induction of priming immunity against viruses of pandemic potential, efficacy in multiple age groups, and multiyear duration of protection. Efforts might include development, qualification and validation of correlates of protection assays used to evaluate the immune response to the new influenza vaccine candidate. BARDA may request responses to this BAA for vaccine against specific emerging pathogens of pandemic potential. BARDA will prioritize vaccine candidates against specified emerging infectious diseases that have reached the TRL6 level, however, earlier stage candidates may be considered.

[18] https://www.medicalcountermeasures.gov/barda/cbrn/diagnostics-and-biodosimetry.aspx

8.2 Innovative vaccine production enhancements. Support for improvements in vaccine production and platform technologies that accelerate the availability of vaccines against viruses with pandemic potential.

Enhancements include but are not restricted to:

1. Virus:
    a. development or implementation of new technology platforms that promote high-yield or improved cross-reactivity
    b. methods and technologies that will allow the assessment of improved vaccine performance
2. Manufacturing:
    a. up-stream and downstream methods to improve production yields
3. Assay:
    a. methods to decrease the time required to produce essential potency reagents for vaccine release testing
    b. development or implementation of new potency determination methods that relieve virus strain-specific standard reagent dependencies.

Development programs at a maturity level less than TRL 6 should consider funding opportunities offered by The National Institute of Allergy and Infectious Diseases (NIAID) or other Federal agencies that fund earlier stage R&D projects.

Learn more about NIH/NIAID's Resources for Influenza Researchers[19] and NIAID's Microbiology and Infectious Diseases Resources[20].

Technical inquiries about funding through NIAID programs can be directed to:

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Area of Interest #9: Influenza and Emerging Infectious Diseases (IEID) Therapeutics

Offerors for Area of Interest #9 should propose activities for products having a maturity level equal to or greater than Technology Readiness Level (TRL) 6 (as evidenced by release of a final report for a Phase 1 clinical study and a US IND), unless otherwise indicated. A product can be described as achieving a TRL if it has completed all activities identified in that TRL. The Technology Readiness Level ranking criteria can be found in Attachment 1B of this BAA.

[19] https://www.niaid.nih.gov/research/influenza-resources
[20] https://www.niaid.nih.gov/research/microbiology-and-infectious-diseases-resources

BARDA seeks to develop novel therapeutics for the treatment of influenza A and B infections, as well as for the treatment of disease caused by emerging infectious diseases of pandemic potential to be determined by BARDA.

9.1 Influenza Therapeutics

For new influenza therapeutics, BARDA prefers a novel mechanism of action and demonstrated advantages when compared to FDA approved therapeutics for influenza. The proposed therapeutic should preclude the rapid emergence of drug resistance and have proven broad influenza strain neutralization activity (minimum for influenza A: H1N1, H3N2, H5N1, and H7N9). Data demonstrating H7N9 neutralization is required. Combination therapeutics that include novel investigational compounds and licensed therapeutics would also be applicable. Please address the Combination Rule if a combination therapy is proposed. Demonstrating efficacy of the proposed drug at least 72 hours after symptom onset appropriate viral challenge animal models is required. Therapeutics with antiviral activity at later time points will be viewed more favorably. The strongest proposals will have data demonstrating activity against strains from both influenza A and B viruses.

Because there are no treatments approved for severely ill, hospitalized influenza patients, the strongest proposals will include a clinical development plan that addresses treatment of this population. Therapeutics that offer benefit to special populations, such as pediatrics and the elderly will be viewed more favorably. Therapeutics must have an active Investigational New Drug application filed with the FDA and have demonstrated safety in a Phase 1 study as evidenced by a final clinical study report.

9.2 Emerging Infectious Disease Therapeutics. BARDA may request responses to this BAA for therapeutics against specific emerging pathogens of pandemic potential. BARDA will prioritize candidates against specified emerging infectious diseases that have reached the TRL6 level, however, earlier stage candidates may be considered.

9.3 Immunomodulators. Immunomodulators that improve the clinical response to and/or resolution of symptoms associated with influenza or emerging infectious diseases will be considered. Product candidates must demonstrate efficacy as measured by a significant reduction in morbidity, mortality, viral titers, or a significant change in immunological markers (for example) in relevant influenza or emerging infectious disease animal models. Proposed candidates must have an active Investigational New Drug application filed with the FDA and have demonstrated safety in a Phase 1 study as evidenced by a final clinical study report.

9.4 Innovative approaches to improve clinical trial execution for hospitalized influenza patients. BARDA seeks to drive innovation in the hospitalized clinical trial space by promoting activities that improve the efficient enrollment of these trials. These activities fall in the following areas:

a. **Real-time influenza surveillance reporting**. BARDA seeks novel solutions that result in accurate, real-time influenza surveillance data down to the zip code level. The strongest proposal will provide a solution that reports de-identified data daily during the northern hemisphere influenza season and should cover the continental US. The reported data should distinguish outpatient data versus hospitalized data. This data may also be used to develop models for influenza forecasting (See Area of Interest #13)

b. Data sets that measure the number of hospitalized influenza patients per hospital in a defined geographic area. BARDA seeks de-identified hospitalized data sets that report the number of patients hospitalized with influenza in a given geographic area. The strongest proposals will provide data down to the zip code level, will cover the continental US, and will provide data for at least the last 5 northern hemisphere influenza seasons.

c. Use electronic health record data to improve future enrollment by identifying the optimal target population characteristics and comparing alternative endpoints.

1. Offerors will use de-identified electronic health records to identify the inclusion/exclusion criteria resulting in a more optimal target population for the evaluation of new investigational therapeutics in hospitalized influenza clinical trials.

2. Offerors will use existing de-identified hospital data sets or electronic health record data to compare alternative endpoints in response to early vs. late treatment of oseltamivir. The strongest proposals will provide a head to head comparison of the vital sign endpoint to a multi-category ordinal scale in early vs late treatment with oseltamivir.

d. Integration of wearable or in-home diagnostics with telemedicine platforms to support early administration of antiviral drugs under appropriate healthcare systems.

Note: Development programs at a maturity level less than TRL6 should consider funding opportunities offered by The National Institute of Allergy and Infectious Diseases (NIAID) or other Federal agencies that fund earlier stage R&D projects.

Learn more about NIH/NIAID's Resources for Influenza Researchers[21] and NIAID's Microbiology and Infectious Diseases Resources[22].

Technical inquiries about funding through NIAID programs can be directed to:

DMIDResources@niaid.nih.gov

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Area of Interest #10: Respiratory Protective Devices

Technical Readiness Level:

Offerors should propose development projects that have reached a TRL equal to or greater than that specified in each sub-section below. A product can be described as achieving a TRL only if all relevant activities identified in that TRL have been completed. For a detailed list of TRL definitions for diagnostics development see Attachment 1A of

[21] https://www.niaid.nih.gov/research/influenza-resources
[22] https://www.niaid.nih.gov/research/microbiology-and-infectious-diseases-resources

this BAA. Development programs at lower maturity levels should consider funding opportunities offered by The National Institute of Allergy and Infectious Diseases (NIAID) or other Federal agencies that fund earlier stage R&D projects.

10.1 Development and characterization of improved respiratory protective devices (RPD).

Support for advanced development of improved RPDs such as masks, surgical masks, PAPRs, elastomeric masks, elastomeric half mask, or respirators to reduce transmission of influenza virus and other infectious agents. These RPDs should demonstrate improved features over currently available products. Examples of desirable improvements:

- reduced cost of at least an order of magnitude to acquire and stockpile,
- manufacturing efficiency or speed,
- decontamination and re-use,
- functionality,
- fit flexibility to support a broad population (e.g., pediatric through adult),
- elimination of fit testing,
- usability, comfort.

All proposed products must have a clear path to NIOSH certification and FDA clearance as applicable. Proposed activities should offer beneficial clinical and public health impact with a TRL 4 or greater.

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Area of Interest #11: Ventilators

Technical Readiness Level:

Offerors should propose development projects that have reached a TRL equal to or greater than that specified in each sub-section below. A product can be described as achieving a TRL only if all relevant activities identified in that TRL have been completed. For a detailed list of TRL definitions for diagnostics development see Attachment 1A of this BAA. Development programs at lower maturity levels should consider funding opportunities offered by The National Institute of Allergy and Infectious Diseases (NIAID) or other Federal agencies that fund earlier stage R&D projects

11.1 Advanced development of new or improved ventilators to provide respiratory support in clinical care, transport, and emergency use settings for severe respiratory conditions resulting from influenza infections or All-Hazards incidents. Ideal ventilators should:

- be portable;
- support neonate (≥ 2.5kg) to adult populations;
- be easy to set up, select initial ventilation settings, and troubleshoot by minimally trained care providers;

- be able to use other manufacturers' breathing circuits;
- be low maintenance for ease of stockpiling;
- accommodate/provide accessories typically used in ventilator standard of care;
- consider low resource environments (where power and oxygen may be limited);
- and have a low cost per unit (<$4,000 per fully kitted unit at a quantity of 5,000 units or greater).

Offeror should also be able to accommodate domestic surge production capacity. TRL 4 or greater.

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Area of Interest #12: MCM Production Platform Systems

12.1 Monoclonal Antibody Platform

BARDA is interested in supporting technology platforms for the rapid, cost-effective, discovery, development, manufacturing and regulatory approval of new monoclonal antibodies (mAbs) in response to influenza and/or emerging infectious diseases. Current bottlenecks in antibody development center on the rapid transition from discovery of the antibody to GMP production of clinical trial material along with the necessary regulatory requirements needed for such rapid production and clinical evaluation. The strongest proposals will provide data that demonstrates a rapid antibody discovery platform linked to an equally rapid therapeutic product manufacturing platform. BARDA expects discovery of mAb to production of GMP material to take no more than 6 months. The Offeror should use the screening, optimization, production and regulatory approval of broad-spectrum neutralizing influenza monoclonal antibodies as the proof-of-concept study to demonstrate their platform technology's capabilities and provide a regulatory strategy for the future use of these rapidly produced antibodies against diverse novel pathogens.

In addition to the challenges described above, many of the mAbs currently in development for the treatment of infectious diseases are being tested in the clinic using doses in the gram to multi-gram range, which require intravenous infusion. BARDA seeks proposals to develop platform technologies that can be used to reduce the dose of these types of antibodies by an order of magnitude, to the milligram range, allowing for alternate delivery routes. Such technologies could include novel bi-specific antibodies, alterations to existing antibodies to increase potency, drug conjugation, alternatives to IgG-based mAbs, or novel delivery methods. These are just examples; other technological approaches could be proposed. The ultimate goal is the development of antibodies that are efficacious and easy to deliver during a response effort.

12.2 Vaccine Production Platform

BARDA is interested in supporting the development, assessment and demonstration of "ready to use" rapid response platform technologies for production of vaccines against

infectious disease pathogens on an accelerated timeline and at a lower cost to develop and manufacture compared to current standard vaccine approaches. Of greatest interest are platforms that offer an integrated approach to the full spectrum of vaccine development, from creation of candidate vaccines through testing, selection and regulatory approval to full-scale manufacturing capability, with the fewest adjustments and refinements necessary for each new disease application.

Technologies will be evaluated by criteria that address the rapid response goal (time to human clinical testing, manufacturing scalability and capacity, cost to develop and manufacture, current development and regulatory status), and the applicability of the technology to a range of threats as a platform (categories of pathogens covered, completeness of the technology from candidate generation to full manufacturing, use without variation for each new application). Additional criteria that relate to the use of the technology for public health vaccines as well as the capabilities of the Offeror will also be considered.

Proposals for the development, demonstration and evaluation of vaccine platform technologies that have not yet been proven successful by licensure of an initial vaccine product may be submitted for consideration under this Area of Interest. The proposed scope of work should consist of an application of the technology to the development of a vaccine that will allow for refinement and optimization of the technology, and demonstrate its feasibility to meet the rapid response need. The vaccine proposed for this development work should ideally fit in BARDA's mission space (Biothreats, Pandemic Influenza, and Emerging Infectious Diseases) and be at a stage of development appropriate for BARDA (TRL6 unless otherwise noted). The proposed work should proceed from the current stage of development of the vaccine under consideration and proceed through a verification of the successful production and clinical testing of the product towards regulatory approval (pre-EUA or licensure). Upon completion of a successful platform technology demonstration, application of the technology to a pathogen of BARDA's choice may be requested to provide a real-time demonstration of the flexibility and nimbleness of the vaccine technology in a response scenario.

Offerors who possess platform technologies that have successfully proven their ability to provide rapid and cost-effective vaccine response capability, may also submit proposals under this Area of Interest for establishing an ongoing platform operationalization partnership with BARDA for the development of vaccines of public health interest in a preparedness or response mode. It is anticipated that under this program, BARDA will request the development of vaccines against known threats through at least the initial stage of clinical evaluation and regulatory approval in preparation for their potential use. In case of a newly emerging threat, BARDA may request the development, testing, and deployment of a new vaccine in the shortest time possible in order to mitigate disease consequences. Submissions must include convincing data that demonstrate the utility of the platform for additional applications and how broad that range of applications might be. The proposed scope of work should provide a breakdown of all elements (resources, cost, time, etc.) required for development, manufacturing, and evaluation of a generic new vaccine from scratch using the platform technology.

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Area of Interest #13: Modeling as an Enabling Technology for Influenza, Emerging Infectious Disease, and CBRN Threats

Offerors for Area of Interest #13 should propose activities for tools, analyses, and modeling activities that support the breadth of BARDA's product development work as described in AOI #1-12 for CBRN, pandemic influenza, emerging infectious disease, and integration of rare event response into all-hazards response. These capabilities will be integrated into the suite of capabilities of the BARDA Modeling and Visualization Hub. Proposals that foster innovative development, deployment, or use of medical countermeasure technologies, especially those applicable across multiple technology types described in AOI #1-12, are highly encouraged. A successful proposal will provide and end product that can be shared with other governmental stakeholders and BARDA supported product developers. All models and tools developed will be used on-site at HHS by trained HHS personnel and modularity is highly encouraged to allow for integration with existing capabilities. Additionally, compatibility with current HHS information technology infrastructure, including the BARDA Modeling and Visualization Hub's CAVE2™ which is air gapped and NOT online, is highly encouraged and compliance with federal information security and privacy protection regulations is required.

13.1 Pioneering capabilities to flexibly identify and quantify needs for medical countermeasures.

For new capabilities to identify and quantify need for MCMs, BARDA prefers capabilities that are flexible, rapid, and can assess relative need across a diverse portfolio of threats and countermeasures. Tools and analyses that can assess return on investment for a countermeasure or portfolio of countermeasures, both in the event of an unpredictable disaster and for routine operations, are encouraged. Additionally, BARDA encourages tools and analyses that can improve our capability for data-based identification of when new or updated assessments of medical countermeasure need are merited for emerging or evolving natural threats.

13.2 Adaptable capabilities to target improvements to operationalizing medical countermeasures.

BARDA encourages proposals for capabilities that can be integrated with existing medical countermeasure need models to enable reasonable, data-based assessment of the geographic changing need for countermeasures over time after an incident, especially when an incident has delayed notice or causes mass migration of evacuees. Capabilities are highly encourage that could be leveraged both for planning and during a response to rapidly inform BARDA's vendor managed inventory and other MCM distribution decisions. Capabilities that enable scientifically rigorous assessment of the sustainability of our preparedness posture through supply chain, market force, and manufacturing assessment across a portfolio of countermeasures are encouraged if they provide innovative analytics, novel data sources, and predictive capabilities. Innovative assessments of the types of medical countermeasure advancements that could provide "game changing" improvements to the Government's preparedness posture may be considered.

13.3 Reliable situational awareness to support nimble and effective BARDA response during man-made and naturally occurring public health incidents.

BARDA encourages proposals for capabilities that improve the data-based estimation of potential impacts of ongoing incidents. This includes data streams and capabilities to develop near term forecasts to inform decision-makers of the potential future magnitude of an ongoing outbreak. BARDA also encourages proposals of a test bed environment of real and/or simulated multifaceted data to evaluate analytic performance of existing government and academic forecasting models, especially if the environment leveraged data streams that could be made available for near real time response. Additionally, BARDA encourages capabilities and data streams that can be used to assess in real time the potential or actual impact of medical countermeasures and other public health response activities to guide BARDA decision-making during a public health response. Cross applicability of data streams and capabilities with other AOI sections in this BAA is highly encouraged (e.g., AOI 9.4).

13.4 Robust analytic capabilities to innovatively support improvements in medical countermeasure advanced development, testing, and evaluation.

BARDA encourages proposals for capabilities that harness novel analytic techniques to target medical countermeasure development. Capabilities that can advance the understanding of viral and bacterial evolution and strain emergence to provide intelligent estimation of cross-strain, cross-target efficacy of existing and potential countermeasures against an ever changing threat landscape are highly encouraged. Capabilities that can be used in collaboration with countermeasure developers to exploit advances in computational methodology and distributed computing power to revisit the potential for intelligent drug design to expedite medical countermeasure down-selection during the development process are encouraged, especially if they can be implemented within the HHS information technology infrastructure. Capabilities that enable robust synthesis of the natural history of disease progression data to guide development of animal models and the correlation of human and animal endpoints are encouraged, especially if they have a baseline dataset incorporated. BARDA encourages capabilities for rapid and robust development of, integration of new data in to, and visualization of in vitro absorption, distribution, metabolism, excretion and toxicity data based physiologically based pharmacokinetic (PB/PK) models of threat impact on human health and evaluate drugs developed to counter these threat. BARDA encourages proposals for capabilities that innovatively promote efficient testing of medical countermeasure safety and efficacy, including innovative, novel, and adaptive clinical trial design, analysis structure, and complex multi-injury or disease correlate endpoints to support decision-makers in designing the most cost effective trial for BARDA countermeasures, especially if they can robustly support rapid assessment of medical countermeasure safety and efficacy in both preparedness and during emergency response.

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Area of Interest #14: Visual Analytics an Enabling Technology for Influenza, Emerging Infectious Disease, and CBRN Threats

Offerors for Area of Interest #14 should propose activities for visual analytics capabilities, applications, and tools to support the breadth of BARDA's product development work as described in AOI #1-12 for CBRN, pandemic influenza, emerging

infectious disease, and integration of rare event response into all-hazards response. These capabilities will be integrated into the suite of capabilities of the BARDA Modeling and Visualization Hub. Proposals that foster innovative development, deployment, or use of medical countermeasure technologies, especially those applicable across multiple technology types described in AOI #1-12, are highly encouraged. All proposals should address how the proposed capability will demonstrate a value from visualization and visual analytics over traditional data analytics, including but not limited to decreased time from data to decision, novel insight to trends and features that would not otherwise be observed, and improved confidence in end results. A successful proposal will provide and end product that can be shared with other governmental stakeholders and BARDA supported product developers. All applications, data and tools developed will be used on-site at HHS by trained HHS personnel. Modularity is highly encourage, and compatibility with current HHS information technology infrastructure, including the BARDA Modeling and Visualization Hub's CAVE2™ which is air gapped and NOT online, is highly encouraged and compliance with federal information security and privacy protection regulations is required. Capabilities dependent on access to large and/or frequently updating data sets (e.g., genomic, geospatial) must address the feasibility, mechanism, and frequency of data refresh when used in an offline/air-gapped environment.

14.1 Discovery through data visualization. BARDA seeks proposals for the use of visual analytics for data exploration of large data sets relevant to BARDA's mission, especially capabilities to effectively analyses open source data with non-public, proprietary, and other limited use data without combining the data sets. Proposals for capabilities to use visual analytics to assess drug target interactions, assess potential targets for broad-spectrum products, and estimate the utility of existing products for new applications are especially encouraged.

14.2 Capabilities to enhance medical countermeasure development by leveraging immersive visualization. BARDA encourages proposals for the use of immersive data visualization and visual analytics to enhance medical countermeasure development, deployment, and use.

14.3 Innovative techniques and capabilities for data visualization to support medical countermeasure decision-making during preparedness and in a response. BARDA encourages capabilities to use data visualization and visual analytic to support innovative, collaborative problem-solving and decision-making for medical countermeasure development. Data visualization and visual analytics that can improve BARDA's situational awareness for potential pandemic threats, especially those that integrate human and animal populations when relevant, may be considered if they can directly support countermeasure development decisions. Visualization capabilities that can similarly support medical countermeasure decision-making during response may be considered if they can rapidly identify, assess relevancy and reliability of, and/or exploit emerging or alternative sources of information if they are directly applicable to supporting BARDA's portion of a potential public health emergency response.

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Part II: Development and Technical Objectives

The information in this section is provided to assist and guide Offerors in preparing their White Papers and Full Proposals Statements of Work (SOW). The topics listed below exemplify some of the typical activities undertaken during a drug, biologic, diagnostics or device development effort in the areas of project management, clinical and non-clinical studies, manufacturing, and regulatory strategy. Offerors should address these in the White Paper in sufficient detail (within space limitation) to demonstrate that Offeror understands the scope of work needed. Offerors shall submit a SOW in their Full Proposal that addresses these topics as appropriate. Provide as much detail as may be necessary to fully explain and justify the proposed technical approach or method. In the event that an Offeror's technical approach provides for performance in excess of one year, the SOW must be presented in a manner so that the base segment and option segments are discrete and non- severable. Each segment must contain specific work elements that must be achieved to support go/no-go milestones that predicate execution of each subsequent option segment of the work.

Consequently, contracts awarded under this BAA may contain contract options that may be unilaterally exercised by the Government that either follow or run concurrently with a base period of performance. The length of the base period of the contract is subject to negotiation. Offerors are invited to propose certain discrete stages or areas of work as contract options.

Offerors should propose a SOW consistent with activities for the Technology Readiness Level indicated for each Development Area of Interest in Part I. Development programs at a maturity level less than that indicated for each Development Area of Interest should consider funding opportunities offered by The National Institute of Allergy and Infectious Diseases (NIAID) or other Federal agencies that fund earlier stage research and development projects.

The work statement must be presented in discrete segments that are non-severable in their activity.

Proposal preparation and submission instructions are contained in Part V and VI.

Program Management Approach:

White Papers and Full Proposals for all Areas of Interest must address Program Management. Program Management Activities may include but are not limited to:

a. Identification of and management to, distinct stages of the product development pathway that are gates for Go/No Go decisions for advancing to the next stage of the Integrated Product Development Plan.

b. Establishment of and tracking of milestones and timelines for the initiation conduct, and completion of product development activities for each stage with a budget (in direct costs) linked to each stage.

c. Ongoing evaluation of qualitative and quantitative criteria and accompanying data used to assess the scientific merit and technical feasibility of proceeding to the next stage of product development.

d. Maintaining and managing staff (in-house and contracted) to assure the necessary expertise and dedicated effort to perform the work.

e. Directing and overseeing subcontractors and consultants to assure successful performance of planned activities within the cost and schedule constraints of the contract.

f. Conducting performance measurement that shall include establishing an initial plan; defining measurable parameters; defining how these parameters relate to cost and schedule impacts; their approach in providing a detailed schedule that generates a critical path for the project; and a description of the cost- accounting system used or intended to be used based on budget estimates to monitor all costs related to the contract award for both prime- and sub- contractors on a real time bases.

g. Development of a risk evaluation and mitigation strategy for the overall project.

Regulatory Approach:

White Papers and Full Proposals for all Areas of Interest must address regulatory activities. Regulatory activities, as appropriate for the MCM, may include but are not limited to:

a. A clear and comprehensive regulatory master plan that focuses on the crucial pathway integrating all products, risk evaluation and mitigation at all development stages, non-clinical and clinical testing, and manufacturing activities using the most current and available information, including documented and time-relevant consultation with FDA. Plan should include a tentative schedule for regulatory milestones.

b. Establishment and filing of regulatory submissions to the correct office with the FDA.

c. Maintenance of a plan for additional studies to support future filing for FDA- approval/clearance.

d. Development of a potential Plan for consideration of an Emergency Use Authorization (EUA) of a medical product when appropriate. www.fda.gov/oc/guidance/emergencyuse.html

e. Maintaining all required regulatory documentation (investigator brochure, regulatory binder, etc.) providing periodic updates to the FDA as required and seeking FDA guidance on the conduct of studies that will be used to support approval/licensure/EUA.

f. Conducting site initiation, monitoring, and closeout visits to contract research organizations subcontracted to perform studies.

Development and Manufacturing Approach:

Product development, including clinical/non-clinical studies and manufacturing activities are listed here for Small Molecules and Biologics, including therapeutics), Vaccines, Diagnostics, and Respiratory Protective Devices.

Small Molecules and Biologics, including therapeutics

For Small Molecules and Biologics, the proposed development program should consist of these elements when applicable:

1. Non-Clinical Toxicology, PK and Efficacy
2. Clinical Evaluation
3. Chemistry and Manufacturing Controls (CMC)

1. Non-Clinical Toxicology, PK and Efficacy Research and Development Activities include but are not limited to:

    a. Evaluating the safety, toxicology, pharmacokinetics / pharmacodynamics, bioavailability, solubility, formulation, of the medical countermeasure using both in vitro and animal models following Good Laboratory Practice guidelines (GLP: as defined in the U.S. Code of Federal Regulations - 21 CFR Part § 58), as and when appropriate.

    b. Screening of small molecule libraries for antitoxin / antimicrobial / antiviral activities (for already approved or licensed product).

    c. Expand assessment of antiviral potential for therapeutics previously approved for other indications.

    d. Evaluating the immunogenicity, safety, efficacy, pharmacokinetics / pharmacodynamics, bioavailability, solubility, formulation, dose, route and schedule of the medical countermeasure using both in vitro and animal models following Good Laboratory Practice guidelines (GLP: as defined in the U.S. Code of Federal Regulations, 21 CFR Part § 58), as appropriate.

2. Clinical Evaluation Activities include but are not limited to:

    a. Design and conduct of Phase 1 clinical studies to evaluate the safety and pharmacokinetics of the therapeutic candidate/product in humans in accordance with Good Clinical Practice guidelines (GCP: as defined by 21 CFR §312 and International Council for Harmonization [ICH] Guidelines document E6).

    b. Design and conduct of a Phase 2 and/or Phase 3 clinical studies in accordance with all Federal regulations and GCP guidelines.

    c. Design and conduct of clinical trials to evaluate safety and/or efficacy of candidate products in at-risk populations (e.g., elderly, pediatric, or immunocompromised persons).

    d. Design and conduct clinical trials to evaluate optimal use of influenza antivirals or immunomodulators for informing clinical and public health management decisions.

3. CMC Activities include but are not limited to:

    a. Development of master and working cell banks under GMP guidelines (GMP as defined in the U.S. Code of Federal Regulations 21 CFR § 211).

    b. Process development activities to increase efficiency, yield, quality, and reduce the variability and risk factors in the manufacture of the drug substance and drug product.

    c. Formulation development to evaluate combinations of excipients and their influence on the target product profile and stability.

    d. Manufacture of non-GMP and of GMP pilot lots of candidate product in amounts sufficient to carry out required/proposed non-clinical and Phase 1 and/or Phase 2 clinical trials.

e. Identification of Critical Quality Attributes (CQA) and Critical Process Parameters.

f. Manufacturing scale-up plan to lead to consistency lot manufacturing of the candidate product.

g. Process flow for personnel, material and waste disposal.

h. Proposed packaging design and execution of fill-finish of final drug product.

i. Design of stability testing plan and conduct of stability studies on bulk and final product.

j. Manufacturing/Testing facility plan to support phase I through commercial scale product supply

k. Development of analytical methods and assays appropriate for product characterization and product release, including tests for the identity, purity, potency, and stability of the bulk drug substance and final drug product. Offerors shall identify a stable source and availability of reagents and reference standards for these assays required.

l. Development of Validation Protocol for analytical and assay methods to defining product manufacturing control, performance, potency and product stability indication.

m. Development of processes that would benefit from alternative techniques using CM (e.g. continuous perfusion, continuous synthesis, non-column based chromatography), if applicable.

n. Integration of continuous mode(s) into manufacturing process and the development of in-line process analytical technologies, if applicable.

o. Continuous processing for homogeneous production of final dosage forms (e.g. tableting, strip film manufacturing system, injection molding, and printing) if applicable.

p. Development of Risk Evaluation and Mitigation Strategies or similar risk mitigation strategy proposals

q. Manufacturing/Testing facility plan to support clinical trial lots through commercial scale product supply, including consideration of capacity for surge manufacturing in the event of an influenza pandemic.

Vaccines

For vaccines, the proposed development program should consist of these elements when applicable:

1. Non-Clinical
2. Analytical Assays
3. Clinical Evaluation
4. Chemistry and Manufacturing Controls

1. Non-Clinical Activities include but are not limited to:

   a. Limited evaluation in ancillary nonclinical studies as required to support proposed activities with a maturity of TRL6 or greater.

2. Analytical Assays Activities include but are not limited to:

   a. Development of analytical methods and assays appropriate for product

characterization and product release, including tests for the identity, purity, potency, and stability of the bulk drug substance and final drug product. Offerors shall identify a stable source and availability of reagents and reference standards required for these assays.

b. Development of validation protocols for analytical and assay methods to define product manufacturing control, performance, potency and product stability indication.

3. Clinical Evaluation Activities include but are not limited to:

a. Design and conduct of clinical trials to evaluate candidate medical countermeasure and device products in humans in accordance with Good Clinical Practice guidelines (GCP: as defined by 21 CFR § 312 and ICH Guidelines document E6). Clinical trial activities can be conducted at domestic or international sites, given appropriate justification.
b. Design and conduct of clinical trials to evaluate safety and/or efficacy of candidate products in at-risk populations (e.g., elderly, pediatric, or immunocompromised persons).
c. Evaluation and validation or correlation of clinical and/or immunological endpoints to support the development of broadly reactive ("universal") influenza vaccines, including innate and adaptive immunity, both humoral and cellular.
d. Development of a clinical development plan that outlines key milestones and activities to mature the candidate product through FDA approval/licensure.

4. CMC Activities, include but are not limited to:

a. Development of master and working cell banks under Good Manufacturing Practice guidelines (GMP: as defined in the U.S. Code of Federal Regulations - 21 CFR § 211).

b. Process development activities to increase efficiency, yield, and quality, and to reduce the variability and risk factors in the manufacturing of the drug substance and drug product.

c. Formulation development to evaluate combinations of excipients and their influence on the target product profile and on product stability.

d. Continuous processing for homogeneous production of final dosage forms (e.g., tableting, strip film manufacturing system, injection molding, and printing), if applicable.

e. Manufacture of GMP lots of candidate products in amounts sufficient to carry out required/proposed clinical trials that would seek to enhance the effectiveness of existing biologics and pharmaceuticals.

f. Identification of CQA and Critical Process Parameters.

g. Manufacturing scale-up plan to lead to consistency lot manufacturing of the candidate product.

h. Process flow for personnel, material and waste disposal.

i. Proposed packaging design and execution of fill-finish of final drug product.

j. Design of stability testing plan and conduct of stability studies on bulk and final product.

k. Development of Risk Evaluation and Mitigation Strategies or similar risk mitigation strategy proposals

l. Manufacturing/Testing facility plan to support clinical trial lots through commercial scale product supply, including consideration of capacity for surge manufacturing in the event of an influenza pandemic.

Diagnostics

For Diagnostics, the proposed development program should consist of these elements when applicable:

1. Product Development
2. Clinical Evaluation
3. Manufacturing

1. Product Development Activities include but are not limited to:

   a. Perform natural/case history studies of threat agent(s), if needed.

   b. Review the pathology of human disease related to threat agent(s)

   c. Identification of diagnostic markers of disease for threats of interest, if needed.

   d. Performance of human or non-GLP animal studies to demonstrate the clinical relevance, performance, and/or diagnostic utility of biomarkers.

   e. Performance of appropriate studies to demonstrate acceptable clinical performance of the assay with specimens and specimen volumes relevant to diagnostic intended use.

   f. Development of assays, reagents, devices, instruments, and consumables, or components thereof, necessary to perform diagnostic tests, either manually or with automated means. This includes the development of tooling and processes necessary to produce these products.

   g. Development of verification and validation protocols and execution of these protocols to prove performance of products developed.

   h. Identification of reference standard for use in validation and/or verification.

   i. Development of requirements that incorporates all potential users and environments of use for the product.

   j. Development of design control documents using a FDA compliant Quality Management System (QMS).

   k. Development of a product risk evaluation and mitigation strategy.

   l. Production of non-GMP compliant prototypes and reagent lots at laboratory scale.

2. Manufacturing Development Activities include but are not limited to:

   a. Identifying/developing pilot scale manufacturing facilities capable of producing diagnostic systems, assays, reagents, and consumables in compliance with Good Manufacturing Practice guidelines (GMP: as defined in the U.S. Code of Federal Regulations – 21 CFR §211).

   b. Development of full-scale manufacturing processes and procedures.

c. Development of tooling to manufacture products appropriate for pilot scale manufacturing.

d. Process development activities to increase efficiency, yield, quality, and reduce the variability and risk factors in the manufacture of diagnostic devices, assays, reagents, and consumables.

e. Manufacture of non-GMP and of GMP pilot lots of candidate product in amounts sufficient to carry out required/proposed integration, verification, validation, animal studies, or clinical trials.

f. Manufacturing scale-up plan to lead to consistent lot manufacturing of the candidate product.

g. Process flow for personnel, material and waste disposal.

h. Design of stability testing plan and conduct of stability studies assays and reagents.

i. Development of a manufacturing risk evaluation and mitigation strategy or similar risk mitigation strategy proposal.

j. Development of procedures and equipment/components for quality acceptance or quality assurance of manufactured products under QMS.

k. Performance of Installation Qualifications (IQ) or Process qualifications (PQ).

3. Clinical Evaluation Activities include but are not limited to:

a. Design and execution of clinical studies/trials to evaluate the efficacy, safety, sensitivity and specificity of Diagnostic Systems in humans in accordance with FDA requirements and, where applicable, with Good Clinical Practice guidelines (GCP: as defined by 21 CFR §312 and ICH Guidelines document E6).

Respiratory Protective Devices (Masks & Respirators) and Ventilators

The proposed development program should consist of these elements when applicable:

1. Product Development
2. Clinical Evaluation
3. Manufacturing

1. Product Development Activities include but are not limited to:

a. Perform natural/case history studies of threat agent(s), if needed.

b. Performance of animal studies to demonstrate the clinical performance of ventilator, as needed.

c. Performance of appropriate studies to demonstrate acceptable clinical performance of the assay with specimens and specimen volumes relevant to diagnostic intended use.

d. Development of devices, RPDs, and consumables, or components thereof, necessary to perform verification tests, either manually or with automated means. This includes the development of tooling and processes necessary to produce these products.

e. Development of verification and validation protocols and execution of these protocols to prove performance of products developed.

f. Identification of reference standard for use in validation and/or verification.

g. Development of requirements that incorporates all potential users and environments of use for the product.

h. Development of design control documents using a FDA compliant Quality Management System (QMS).

i. Development of a product risk evaluation and mitigation strategy.

j. Production of non-GMP compliant prototypes.

k. Performance of usability studies.

2. Manufacturing Development Activities include but are not limited to:

a. Identifying/developing pilot scale manufacturing facilities capable of producing RPDs or ventilators and consumables in compliance with Good Manufacturing Practice guidelines (GMP: as defined in the U.S. Code of Federal Regulations – 21 CFR § 211).

b. Development of full-scale manufacturing processes and procedures.

c. Development of tooling to manufacture products appropriate for pilot scale manufacturing.

d. Process development activities to increase efficiency, yield, quality, and reduce the variability and risk factors in the manufacture of RPDs or ventilators and consumables.

e. Manufacture of non-GMP and of GMP pilot lots of candidate product in amounts sufficient to carry out required/proposed integration, verification, validation, animal studies, or clinical trials.

f. Manufacturing scale-up plan to lead to consistent lot manufacturing of the candidate product.

g. Process flow for personnel, material and waste disposal.

h. Design of stability/durability testing plan and conduct of stability/durability studies assays and reagents.

i. Development of a manufacturing risk evaluation and mitigation strategy or similar risk mitigation strategy proposal.

j. Development of procedures and equipment/components for quality acceptance or quality assurance of manufactured products under QMS.

k. Performance of Installation Qualifications (IQ) or Process qualifications (PQ).

3. Clinical Evaluation Activities include but are not limited to:

b. Design and execution of clinical studies/trials to evaluate the efficacy and safety of RPDs or ventilators in humans in accordance with FDA requirements and, where applicable, with Good Clinical Practice guidelines (GCP: as defined by 21 CFR §312 and ICH Guidelines document E6).

Part III: Reporting Requirements and Deliverables

Some reports and other deliverables are relevant to specific activities that may or may not be performed during the contract period of performance. The Offeror and the Government will agree during final contract negotiations on which reports and other deliverables are relevant and will be required as deliverables as determined in the negotiated SOW.

As part of the work to be performed under this BAA, the Contractor will prepare and deliver the following reports throughout the period of performance. Each document should be submitted electronically in Microsoft Word, Microsoft Excel, Microsoft Project, and/or Adobe Acrobat PDF file.

The following reports are not elements of the Full Proposal submission. They may be required as deliverables during the period of performance of a contract.

Reports:

1. **Technical Progress Reports**
   The frequency of Technical Progress Reporting will be determined by the Government during negotiation of the contract. Typically, on the 15th day of each month, the Contractor must submit to the Contracting Officer and the Contracting Officer's Representative (COR) a Technical Progress Report describing activities performed during the previous calendar month. The appropriate formats for the Technical Progress Report and Executive Summary will be provided by the Government. The Technical Progress Reports will include project timelines and summaries of product manufacturing, testing, and clinical evaluation activities. A Technical Progress Report will not be required for the month in which the Final Report is due. The Contractor will be required to submit one paper copy of the Technical Progress Report to the Contracting Officer and an electronic copy to the Contracting Officer and COR. The Contractor should inform the Contracting Officer and the COR in advance if the delivery of a Technical Progress Report will be delayed.

2. **Final Report**
   By the expiration date of the contract, the Contractor will submit a comprehensive Final Report that details, documents, and summarizes the results of all work performed under the contract. A draft Final Report will be submitted to the Contracting Officer and COR for review and comment, after which the Final Report will be submitted. The Contractor must submit one paper copy to the Contracting Officer and an electronic copy to the Contracting Officer and COR.

There may be additional reports, deliverables, and submission requirements for the final negotiated contract.

Meetings:

The Contractor will participate in regular meetings to coordinate and oversee the contract effort as directed by the Contracting Officer and COR. Such meetings may include, but are not limited to, all Contractors and subcontractors to discuss clinical manufacturing progress, product development, product assay development, scale-up manufacturing development, clinical sample assay development, preclinical/clinical study designs and regulatory issues, or other relevant activities; meetings with individual Contractors and other HHS officials to discuss the technical, regulatory, and ethical aspects of the program; and meeting with Government technical consultants to discuss technical data provided by the Contractor.

Bi-weekly and/or Monthly teleconference between the Contractor and subcontractors and the Government will be held to review technical progress. The Government reserves the right to request more frequent teleconferences and face-to-face meetings depending on the nature and importance of the work being performed. The Contractor will receive feedback from the Government during the teleconference regarding contract performance. The Contractor will have an opportunity to respond and recommend corrective actions.

The only contractual relationship will be between the Government and the prime Contractor. No business obligation exists between the Government and any subcontractors unless a teaming arrangement is established.

Regulatory and Quality Management:

FDA submissions and meetings:

a. The Contractor will forward the dates and times of any meeting with the FDA to the Contracting Officer and COR and arrange for BARDA staff to attend.

b. The Contractor will provide BARDA the opportunity to review and comment on any documents prior to submission to the FDA. The contractor should provide BARDA with a minimum of five business days to provide comments back to the Contractor.

c. The Contractor will forward the initial draft minutes and final draft minutes of any formal meeting with the FDA to the Contracting Officer and COR.

d. The Contractor will provide the Contracting Officer and COR with the final draft minutes of any informal meeting with the FDA.

e. The Contractor will forward copies of any relevant Standard Operating Procedures upon request from the Government.

f. The Contractor will provide upon request animal study and/or other data packages developed under this contract. Packages shall include complete protocols and information on critical reagents for animal models developed and/or improved with contract funding.

g. The Contractor will provide upon request raw data and/or specific analysis of data generated with Government funds.

Audits / Site Visits:

FDA Audits

Within 30 calendar days of an FDA audit of Contractor or subcontractor facilities, the Contractor shall provide copies of the audit findings, final report, and a plan for addressing areas of nonconformance to FDA regulations and guidance for GLP, GMP, or GCP guidelines as identified in the final audit report.

Other U.S. Government Audits

The Government reserves the right to conduct an audit of the Contractor with 48 hours' notice. The Government reserves the right to accompany the Contractor on routine and for-cause site visits and audits of subcontractors. At the discretion of the Government and independent of testing conducted by the Contractor, the Government reserves the right to conduct site visits and audits and collect samples of product held by the Contractor and subcontractors.

Program Management Plans and Documentation:

1. **Integrated Master Schedule**: An Integrated Master Schedule (IMS), also known by its graphical representation as a Gantt chart, will be submitted by the Offeror as part of their Full Proposal and will be incorporated into the contract. The IMS shall include the key contract progress milestones and Go/No-Go decision criteria. The IMS for the period of performance will be negotiated prior to award.

2. **Integrated Product Development Plan**: Within 14 calendar days of the effective date of an award, the successful Offeror (or Contractor) shall submit an updated Integrated Product Development Plan (IPDP), which shall be approved by the COR and the Contracting Officer prior to initiation of any activities related to their implementation.

   During the course of contract performance, in response to a need to change the IPDP, the successful Offeror (or Contractor) shall submit a Deviation Report. This plan shall request a change in the agreed-upon Plan and timelines. This plan shall include:

   a. Discussion of the justification/rationale for the proposed change.

   b. Options for addressing the needed changes from the approved timelines, including a cost-benefit analysis of each option.

   c. Recommendations for the preferred option that includes a full analysis and discussion of the effect of the change on the entire product development program, timelines, and budget.

3. **Risk Management Plan**: The Offeror will propose a risk management plan to identify potential risks that may arise during the life of the contract and the impact of these risks on cost, schedule, and performance, and appropriate remediation plans. This plan should reference relevant WBS elements where appropriate. The format for such a plan and timeline for submission will be

determined during contract negotiations.

Learn more about ASPR Business Toolkit[23] for additional program management information and templates.

Project Progress Management:

Project monitoring tools (e.g., Gantt chart with associated cost for identified activities) will be required. The metrics will be used to track and monitor cost and schedule of the project under each contract.

Note: Earned Value Management Systems (EVMS) may be required based on the Contracting Officer's determination.

[23] http://www.phe.gov/about/amcg/contracts/Pages/toolkit.aspx

Part IV: Special Considerations

Special Instructions will be posted as amendments to the BAA on FedBizOpps when they become apparent. Please monitor this solicitation for future special instructions. In addition, please consider the following:

A. Contractor Responsibility Regarding Sensitive Information:

- The Contractor will investigate violations to determine the cause, extent, loss or compromise of sensitive program information, and corrective actions taken to prevent future violations. The Contracting Officer in coordination with the COR will determine the severity of the violation. Any contractual actions resulting from the violation will be determined by the Contracting Officer.

B. Security Plan:

- In the event a security plan is needed for this requirement, the Contracting Officer will make a determination and inform the Offeror of the need for a security plan. Should a security plan be requested, all pertinent documents for the creation of one will be provided to the Offeror by the Contracting Officer.

C. Identification and Disposition of Data:

- The Contractor will be required to provide certain data generated under this contract to the HHS. HHS reserves the right to review any other data determined by HHS to be relevant to this contract. The contractor shall keep copies of all data required by the FDA relevant to this contract for the time specified by the FDA.

D. Confidentiality of Information:

- The following information is covered by HHSAR Clause 352.224-71 Confidential Information (December 18, 2015).

E. Publications:

- Any manuscript or scientific meeting abstract or presentation containing data generated under this contract must be submitted to the Contracting Officer and COR for review no less than 30 calendar days for manuscripts and 15 calendar days for abstracts before submission for public presentation or publication. Contract support shall be acknowledged in all such publications. A "publication" is defined as an issue of printed material offered for distribution or any communication or oral presentation of information.

F. Press Releases:

- The Contractor agrees to accurately and factually represent the work

conducted under this contract in all press releases. Misrepresenting contract results or releasing information that is injurious to the integrity of the Government may be construed as improper conduct. Press releases shall be considered to include the public release of information to any medium, excluding peer-reviewed scientific publications. The contractor shall ensure that the Contracting officer and COR have received an advance copy of any press release related to the contract not less than four working days prior to the issuance of the press release.

G. Export Control Notification:

- Offerors are responsible for ensuring compliance with all export control laws and regulations that maybe 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) (22 CRF Parts 120-130) and /or the Department of Commerce regarding the Export Administration Regulations (15 CRF Parts 730-774).

H. Manufacturing Standards:

- The Good Manufacturing Practice (GMP) Regulations (21 CFR Parts 210-211) and regulations pertaining to biological products (21 CFR Part 600) and regulations pertaining to diagnostic products (21 CFR Part 860) will be the standard to be applied for manufacturing, processing, packaging, storage and delivery of this product.

- If at any time during the life of the contract, the Contractor fails to comply with GMP in the manufacturing, processing, packaging, storage, stability and other testing of the manufactured drug substance or product and delivery of this product and such failure results in a material adverse effect on the safety, purity or potency of the product (a material failure) as identified by the FDA , the Offeror shall have 30 calendar days from the time such material failure is identified to cure such material failure. If the Offeror fails to take such an action to the satisfaction of the Contracting Officer within the 30 calendar day period, then the contract may be terminated.

I. Prohibition on Contractor Involvement with Terrorist Activities:

- The Contractor acknowledges that U.S. Executive Orders and Laws, including but not limited to Executive Order 13224 and Public Law 107-56, prohibit transactions with, and the provision of resources and support to, individuals and organizations associated with terrorism. It is the legal responsibility of the contractor to ensure compliance with these Executive Orders and Laws. This clause must be included in all subcontracts issued under this contract.

J. Invoices:

- The Contracting Officer and Contractor will discuss the Contract Type

during contract negotiations. Regardless of contract type, a successful contractor should expect requirements similar to the following invoicing requirements:

1. The contractor agrees to provide a detailed breakdown on invoices of the categories similar, but not limited to, the following:

    a. Direct Labor - List individuals by name, title/position, hourly/annual rate, level of effort (actual hours), and amount claimed.

    b. Fringe Benefits - Cite rate and amount.

    c. Overhead - Cite rate and amount.

    d. Materials & Supplies - Include detailed breakdown when total amount is over $1,500.

    e. Travel - Identify travelers, dates, destination (e.g., city and state), purpose of trip, transportation, and total amount. Cite COA, if appropriate. List separately, domestic travel, general scientific meeting travel, and foreign travel.

    f. Consultant Fees - Identify individuals, activities, and amounts. Cite appropriate COA.

    g. Subcontracts - Attach subcontractor invoice(s). Cite appropriate COA.

    h. Equipment - Cite authorization and amount. Cite appropriate COA.

    i. General and Administrative (G&A) - Cite rate and amount.

    j. Total Cost.

    k. Fixed Fee (if applicable).

    l. Total CPFF (if applicable).

2. Monthly invoices must include the cumulative total expenses to date, adjusted (as applicable) to show any amounts suspended by the Government. In order to verify allowability, further breakdown of costs may be requested at the Government's discretion.

3. The contractor agrees to immediately notify the Contracting Officer in writing if there is an anticipated overrun (any amount) or unexpended balance (greater than 10 percent) of the amount allotted to the contract, and the reasons for the variance. Also refer to the requirements of the Limitation of Cost (FAR 52.232-20) clause in the contract.

Part V: Quad Chart/White Paper Instructions (Stage 1)

The application process is in two stages as follows:

- **Quad Chart/White Paper (Stage 1)**
- Full Proposal (Stage 2)
    - Volume I - Technical Proposal
    - Volume I – Technical Proposal Attachments
    - Volume II - Cost Proposal
    - Volume II – Cost Proposal Attachments

Stage 1: Quad Chart and White Paper Preparation

Recommendation: It is strongly recommended that potential Offerors request and conduct a TechWatch (see TechWatch Program section) prior to submitting a White Paper.

Interested Offerors shall submit a Quad Chart and White Paper, which expands on the information provided in the Quad Chart. The initial submission is limited to a cover page, one-page Quad Chart, White Paper not to exceed 10 pages, and an addendum (not to exceed two pages) as discussed below. **This results in a submission packet not to exceed 14 pages.** If submissions exceed these limitations, only those pages previously defined will be reviewed.

Combine all files and forms into a single searchable PDF file before submitting.

Quad Chart, White Paper, and a Rough Order of Magnitude (ROM) estimate of costs must be submitted in accordance with the preparation guidance below. The Quad Chart and White Paper should describe the effort in sufficient detail to allow evaluation of the concept's technical merit and its potential contribution to the BARDA mission. Offerors whose Quad Chart and White Paper receive a favorable evaluation will be invited by email to submit a Full Proposal (Stage 2). Offerors whose Quad Chart and White Paper did not receive a favorable evaluation will be notified as well by email. Note that an Offeror who receives an unfavorable rating is not precluded from submitting a Full Proposal; however, it is strongly recommended the Offeror resubmit a revised White Paper.

As a White Paper is not considered a “proposal,” no debriefing per the procedures in FAR Subpart 15.5 will be provided.

Quad Chart Format: The format, information and sample, template is located in Attachment #5. All Quad Charts should be laid out in landscape format.

1. Heading: Title, BAA #, Development Area of Interest, Technical/Administrative point of contact (Name, Email, Phone), Company’s Name & Address.

2. Upper left: Objective, description of effort.

3. Lower left: Benefits of proposed technology, challenges, maturity of technology research area addressed as indicated by the TRL (see Attachment 1).

4. Upper right: Picture or graphic.

5. Lower Right: Milestones, period of performance, ROM cost estimate.

White Paper Format

1. The White Paper should provide a brief technical discussion of the Offeror's objective, approach, level of effort, and the nature and extent of the anticipated results. Specifically, the White Paper should include, at a minimum, the following core elements:

   a. A brief discussion on how the proposed countermeasure aligns with the objectives of the PHEMCE Implementation Plan and the BAA area of interest to which the submission is responding.

   b. Sufficient data to justify the proposed Technology Readiness Level (TRL) maturity of the candidate product or device. Appropriate supporting information could include summary data from preclinical studies and clinical trials, process development and manufacturing milestones, and regulatory status.

   c. A clear and concise plan for meeting product development objectives that includes all key activities (e.g., non-clinical, clinical, manufacturing, and regulatory activities).

   d. A high-level Gantt chart showing an overview of the proposed activities and timelines.

   e. A brief description of the Offeror's intellectual property ownership of the proposed countermeasure. If intellectual property impediments may affect the Offeror's ability to develop the proposed technology. Offerors should briefly outline their strategy for addressing such impediments.

   f. An overview of the Offeror's capabilities and experience (past and current) as they relate to the proposed development activities.

2. The cost portion of the White Paper shall contain a brief cost estimate revealing all the component parts of the proposal.

3. As an addendum to the White Paper, include biographical sketches (two pages) of the key personnel who will perform the research or management of project activities, highlighting their relevant qualifications and experience.

4. Any applicable references should also be cited if they are relevant to the proposed work plan.

5. Restrictive markings: Submissions will be protected from unauthorized disclosure in accordance with 41 U.S.C. § 2102 and applicable regulations. **Please note that any White Paper submitted under this solicitation may be shared with other government agencies for non-BARDA funding considerations and evaluation.**

6. IMPORTANT NOTE: The Government may reject White Paper submissions that are deemed non-compliant. Non-compliant is defined in this context as a White Paper that significantly deviates from the instructions in this BAA.

7. Furthermore, White Papers that are outside the scope of the BAA may be returned to the Offeror. In addition, if the White Paper does not meet the required TRLs for submission, it may be returned to the Offeror without review.

Rough Order of Magnitude Preparation:

A ROM cost estimate is required with the Quad Chart and White Paper submission. The ROM cost estimate is based on the top-level task(s) or objective(s) set forth in the White Paper. It uses a top down estimating approach based on expert knowledge and/or previous experience. For the White Paper, each task (or objective) needs to have a ROM cost estimate. A total ROM cost (i.e., sum of all the tasks or objectives) should also be provided.

Quad Chart and White Paper Submission

Quad Charts and White Papers WILL NOT BE ACCEPTED after 4:30 PM (Eastern Standard Time) on October 31, 2019.

Offerors must email Quad Charts and White Papers directly to the following email address: BARDA-BAA@hhs.gov. Do not mail paper copies of Quad Charts and White Papers.

IMPORTANT: The subject line of the email should consist of the announcement number, area of interest number, and purpose of the email (e.g., BAA-18-100-SOL-00003 AOI #3 Quad Chart & White Paper Submission). White Papers do not require any special forms, but must be submitted in the following format:

- Single PDF file as an email attachment
- Page Size: 8 ½ x 11" with 1" Margins
- Spacing – single
- Font – Arial, 11 point (use of Arial or another readable font and readable smaller size point in tables and captions will be accepted)

The file should not exceed 10 Megabytes of storage space. Movie and sound file attachments, URL Links, or other additional files, will not be accepted.

Classification: All Quad Chart and White Paper submissions must be UNCLASSIFIED.

Chart and White Paper Review

Quad Chart and White Paper submissions will be reviewed by a panel with primary focus on the submission's technical merit and relevance to BARDA programmatic priorities. Offerors should expect to receive a response within 90 calendar days of the next interim or final deadline following submission. Technical feedback will be provided in the response, and the response will express whether a Full Proposal is recommended or

not. Offerors may receive a response sooner than 90 calendar days depending on the number of White Papers submitted to BARDA**.** Offerors who submit White Papers after a given submission deadline may not have their materials reviewed until after the next submission date. **Debriefings prescribed under FAR Part 15 for Quad Chart and White Paper will not be provided, however, technical feedback will be provided in the response letter from BARDA.**

IMPORTANT NOTE: Titles given to the White Papers and Full Proposals should be descriptive of the work proposed and not be merely a copy of the title of this solicitation.

Part VI: Full Proposal Instructions (Stage 2)

The application process is in two stages as follows:

- Quad Chart/White Paper (Stage 1)
- **Full Proposal (Stage 2)**
    - Volume I - Technical Proposal
    - Volume I – Technical Proposal Attachments
    - Volume II - Cost Proposal
    - Volume II – Cost Proposal Attachments

Stage 2: Full Proposal Instructions

With a successful review of the Offeror's White Paper, the Offeror will be invited to submit a Full Proposal. Offerors may also submit a Full Proposal in the absence of a White Paper submission. Offerors must ensure that the Full Proposal is valid for at least 120 days from the submission date. Offerors invited to submit a Full Proposal are advised to schedule a teleconference with technical and contracting staff to address the written administrative and technical feedback contained in the invitation for Full Proposal. The Full Proposal must be prepared in two separate Volumes as follows: Volume I Technical Proposal and Volume II Cost Proposal. Each Volume will have its separate related Attachments. Additional applicable forms will be provided in the letter of invitation to submit a Full Proposal.

Volume I – Technical Proposal

Offerors shall not include any cost information in the Technical Proposal. The technical proposal page limit is 50 pages of technical volume (excluding items A-C) and 70 pages of appended material *unless otherwise specified* in the invitation letter, including figures, tables, and graphs**. This results in a Technical Proposal package not to exceed 120 pages.** If the proposal exceeds the number of pages specified, only the pages up to the limit will be reviewed. A page is defined as 8.5 X 11 inches, single-spaced, with one-inch margins in type not smaller than 11 point Arial font. This should include the following items:

A. Cover Page:

- The follow information shall be provided on the first page of the technical proposal:

1. The words "Volume I: Technical Proposal;"
2. BAA number;
3. Title of proposal (descriptive of the work proposed and not a copy of the title of the solicitation);
4. Research and Development Area of Interest;

5. Date of submission;

6. Offeror and complete list of subcontractors, if applicable;

7. Technical contact (name, address, phone, electronic mail address);

8. Administrative/business contact (name, address, phone, electronic mail address); and

9. Proposed period of performance.

B. Official Transmittal Letter:

- This is an official transmittal letter including:

1. The name, title, mailing address, and telephone number of the company or organization;

2. The name, title, mailing address, telephone number, and e-mail address of the division point of contact regarding decisions made with respect to the Offeror and who can obligate the proposal contractually;

3. The name, title, mailing address, telephone number, and e-mail address and those individual(s) authorized to negotiate with the Government; and

4. A statement indicating you are submitting a final Full Proposal for consideration.

C. Table of contents:

- An alphabetical/numerical listing of the sections within the proposal, including corresponding page numbers.

D. Executive Summary:

- An abstract or synopsis of the proposed project. The Government recommends that the length of the summary remain within one to two pages.

E. Introduction:

- Provide a brief description (one to two paragraphs) of the overall project and objectives in broad terms that indicates the size and magnitude of the proposed effort.

F. Statement of Work:

- **NOTE TO OFFEROR: The Technical Requirements shall begin with the following introductory paragraph:**

  "Independently, and not as an agent of the Government, the Contractor shall furnish all necessary services, qualified professional, technical, and administrative personnel, material, equipment and facilities, not otherwise provided by the Government under the terms of this contract, as needed to perform the tasks set

forth below."

- The SOW should clearly detail the scope and objectives of the effort and the technical approach. It is anticipated that the proposed SOW will be incorporated as an attachment to the potential award instrument. To that end, the proposal should be specific, non-severable, discrete work segments, and be written as a self-standing document without any proprietary restrictions. The SOW should include a detailed listing of the technical tasks/subtasks organized by discrete work periods (base and option periods) including appropriate Work Breakdown Structure references for each task.

- Visit ASPR Business Toolkit[24] (for template).

G. Development Approach:

- A detailed description of the experimental design, including the rationale for experimental approaches, acceptance criteria and measurable objectives, and a description of alternative approaches to be employed if these methods do not achieve the defined goals. Previous results and data should be included as necessary to justify the proposed development activities.

H. Gantt Chart/Integrated Master Schedule (IMS), Work Breakdown Structure (WBS) and Contract Go/No-Go Milestones:

- A detailed Gantt Chart/IMS with associated WBS and Contract Go/No – Go Milestones for each phase (base and options) will be provided as part of the technical submission. The break points of different phases proposed in the contract should be indicated. Learn more about the ASPR Business Toolkit[25] for additional program management information and templates.

I. Deliverables:

- A detailed description of the results and products to be delivered inclusive of the timeframe in which they will be delivered.

J. Key Personnel:

- A listing of key personnel (including proposed consultants) who possess the necessary education, training, and experience to successfully perform the work identified in the technical proposal (resumes to be included in the Appended material). A summary of related activities must also be provided for key personnel; instructions are provided in Attachment 4.

K. Organizational Chart:

- An organizational chart for the project with affiliations (who will report to whom).

L. Contractor provided Facilities, Infrastructure and other Resources

[24] http://www.phe.gov/about/amcg/contracts/Pages/toolkit.aspx
[25] http://www.phe.gov/about/amcg/contracts/Pages/toolkit.aspx

Representative Activities.

- If applicable or specifically requested by the Government this may include but is not limited to:

1. Current facility design including quality control labs for testing & release, laboratory areas supporting formulation and assay development, manufacturing process flow, and animal studies.

2. Major equipment and layout (e.g., preliminary piping and instrumentation drawing).

3. Manufacturing capacity expansion plans to match the proposed manufacturing scale up.

4. Overview of the management of Quality Systems at the facility.

5. List of capabilities for clinical activities conducted in house and at contract research organizations. List of clinical sites engaged for product evaluations.

6. Qualified animal facilities where GLP studies would be conducted and appropriate certifications for humane care and use of vertebrate animals.

7. The handling, storing and shipping of potentially dangerous biological and chemical agents, including Select Agents, under biosafety levels required for working with the biological agents under study.

8. Validation master plan for key equipment, analytical methods, and manufacturing process.

9. Commercial capabilities of the Offeror, including current products, and marketing, distribution and customer support capabilities (as applicable).

10. List of key vendors or service providers, locations, and brief description of their expertise/experience.

M. BARDA Intramural Core Services:

- Offerors are hereby informed that BARDA maintains a comprehensive set of medical countermeasure product development core services and manufacturing technology capabilities [e.g., Centers for Innovation in Advanced Development and Manufacturing (CIADM), Nonclinical Development Network (NDN)]. Offerors may be given the opportunity to utilize these core services and are encouraged to evaluate their potential application in their proposed work plan. Learn more about BARDA Core Services[26].

N. Past Performance Information:

- The Offeror shall provide a list of the last three Government contracts during the past three years and all contracts currently being performed that are similar in nature to the proposed project. Contracts listed may include those entered into by

[26] https://www.medicalcountermeasures.gov/barda/core-services/

the Federal Government, agencies of state and local Governments and commercial concerns. Offerors may also submit past performance information regarding predecessor companies, key personnel who have relevant experience or subcontractors that will perform major or critical aspects of the requirement when such information is relevant to the instant acquisition. For the purposes of this BAA, a "major subcontract" is defined as a subcontract that exceeds $25,000.

- Include the following information for each contract or subcontract listed:

    1. Name of Contracting Organization
    2. Contract Number (for subcontracts, provide the prime contract number and the subcontract number)
    3. Contract Type
    4. Total Contract Value
    5. Description of Requirement
    6. Contracting Officer's Name and Telephone Number
    7. Program Manager's Name and Telephone Number
    8. North American Industry Classification System Code

- The Offeror may provide information on problems encountered on the identified contracts and the Offeror's corrective actions.

O. Additional Requirements:

The Offeror must also represent that they have adequately addressed the following requirements:

1. Research involving Human Subjects/Anatomical Substances (if proposed).
2. Research involving Animals (if proposed).
3. Evidence of GLP Compliance (if appropriate).
4. Evidence of GMP Compliance (if appropriate).
5. Evidence of GCP Compliance (if appropriate).
6. Evidence of Laboratory Licensure Requirements (if appropriate)
7. Compliant Use of Select Agents (if appropriate)
8. All required Representations and Certifications are completed and on file.

P. Deviation Report:

During the course of contract performance, in response to a need to change the SOW

or IPDP, the Offeror shall submit a Deviation Report. This report shall request a change in the agreed-upon Plan and timelines. This report shall include:

1. Discussion of the justification/rationale for the proposed change.

2. Options for addressing the needed changes from the approved timelines, including a cost-benefit analysis of each option.

3. Recommendations for the preferred option that includes a full analysis and discussion of the effect of the change on the entire product development program, timelines, and budget

Q. Prior Approval Notification:

- The Offeror shall carry out activities within the contract SOW only as requested and approved by the Contracting Officer, and must not conduct work on the contract without prior approval from the Contracting Officer, including initiating work that deviates from the agreed-upon IPDP.

Volume I - Technical Proposal Attachments

Attachments should contain supplemental data that accompanies the technical proposal. The combined page total of Attachments in Volume I will be specified in the Full Proposal invitation letter. Additional specific information to be included is referenced below. If a particular item in not relevant to the proposed effort, state that it is not applicable along with any supporting justification. See Special Considerations Section for additional information on any of the Items listed below.

Table 2: Technical Proposal Attachments

	Item	Required	Reference & Document Type
1	Updated Quad Chart	Yes	Template in Attachment #5. Please note any differences with the original Quad Chart.
2	Protection of Human Subjects	If Applicable	Human Subject Research (45 CFR 46)[27]
3	Animal Welfare	If Applicable	Office of laboratory Animal Welfare (OLAW)[28]
4	Intellectual Property	Yes	
5	Biographical Sketches	Yes	
6	Use of Select Agents	If Applicable	Federal Select Agent Program[29] Agriculture Select Agent Service[30]

[27] http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html
[28] http://grants.nih.gov/grants/olaw/olaw.htm
[29] http://www.selectagents.gov/
[30] www.aphis.usda.gov/wps/portal/aphis/ourfocus/animalhealth/sa_import_into_us/sa_ag_select_agent

	Item	Required	Reference & Document Type
7	Laboratory License Requirements	If Applicable	
8	Target Product Profile (TPP)	Yes, except for Diagnostics, Ventilators, Respiratory Protective Devices, Platforms, Modeling, and Visual Analytics	Template in Attachment #2
9	Supporting Data	No	Any additional product development data referenced in Volume I may be included here, provided that the Attachments remain within the page limit.
11	FDA Communication	Yes	Provide all relevant official communication with FDA regarding product with BAA submission (e.g., Complete pre-IND minutes, Type C minutes, etc). This is independent of page limit. Submission of any products in clinical hold may result in the proposal not being reviewed. [At discretion of BARDA]

1. Quad Chart

- Offerors will need to include a revised Quad Chart showing differences from the original Quad Chart submitted during Stage 1 - Quad Chart/White Paper.

2. Protection of Human Subjects

- All research under this BAA must address the involvement of human subjects and protections from research risk related to their participation in the proposed research plan and comply with 42 U.S.C. 300v-1(b), 32 CFR 219, and, as applicable, 21 CFR Parts 11, 50, 54, 56, 312)(45 CFR Part 46) and the ICH as well as other applicable federal and state regulations. HHS Policy also requires that women and members of minority groups and their subpopulations: children and the elderly (pediatric and geriatric) must be included in the study population of research involving human subjects, unless a clear and compelling rationale and justification is provided with respect to the health of the subjects or the purpose of the research. Learn more about HHS policy on studies that involved human subjects[31].

[31] http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html

- Research projects involving humans and/or human specimens can only be initiated with written approval by the BARDA Project Officer.

- The Good Clinical Practice Regulations (GCP)(21 CFR Parts 50, 54, 56 312)(45 CFR Part 46)(ICH E6) as well as other applicable federal and state regulations will be standards that apply for use of human subject and/or human specimens in clinical studies.

- If at any time during the life of the contract, the Contractor fails to comply with GCP as identified by regulations outline above , the Offeror shall have thirty (30) calendar days from the time such material failure is identified to cure such or initiate cure to the satisfaction of the Government Project Officer. If the Offeror fails to take such an action within the 30 calendar-day period, then the contract may be terminated.

3. Animal Welfare

- If the Offeror proposes to use contract funds to conduct animal studies, the Offeror must demonstrate its understanding and ability to comply with the Public Health Services (PHS) Policy on Humane Care and Use of Laboratory Animals http://grants.nih.gov/grants/olaw/olaw.htm). If the Offeror has an Animal Welfare Assurance on file with the Office of Extramural Research (OER), Office of Laboratory Animal Welfare (OLAW), provide the Assurance number with the proposal. If the Offeror proposes animal studies, the Offeror must submit a plan that describes how the Offeror will comply with the PHS Policy and addresses the five points listed below:

  a. Provide a detailed description of the proposed use of the animals in the work outlined in the experimental design and methods section. Identify the species, strains, ages, sex, and numbers of animals to be used in the proposed work.

  b. Justify the use of animals, the choice of species, and the numbers used. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and their numbers.

  c. Provide information on the veterinary care of the animals involved.

  d. Describe the procedures for ensuring that discomfort, distress, pain, and injury will be limited to that which is unavoidable in the conduct of scientifically sound research. Describe the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices where appropriate to minimize comfort, distress, pain, and injury.

  e. Describe any euthanasia method to be used and the reasons for its selection.

  f. State whether this method is consistent with the recommendations of the Panel on Euthanasia of the American Veterinary Medical Association. If not, present a justification for not following the recommendations. Learn more about AVMA Guidelines for the Euthanasia of Animals[32].

[32] https://www.avma.org/KB/Policies/Pages/Euthanasia-Guidelines.aspx

4. Intellectual Property

- Offerors must describe any limitations on any intellectual property (patents, inventions, trade secrets, copyrights, technical data, or trademarks) that will impact the Offeror's performance of the contract or impact the Government's subsequent use of any deliverable under the contract. Offerors must describe how the Government can accomplish the stated objectives of this BAA with the limitations described or proposed by the Offeror. Offerors must include this information in Volume I – Attachments.

- For issued patents or published patent applications that will be used in the performance of the contract, 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 the Offeror is licensing the candidate drug for the proposed work, Offeror is required to provide copies of any licensing agreements, or portions thereof, applicable to the candidate drug before a potential contract can be entered into.

5. Biographical Sketches

- This Section shall contain the biographical sketches for only the key personnel from both the contractor and subcontractor(s): The Full Proposal must list the names and proposed duties of the professional personnel, consultants, and key subcontractor employees assigned to the project. Their resumes should be included in the attachments in Volume I of the Full Proposal. The resumes should contain information on education, background, recent experience, and specific or technical accomplishments as they pertain to their ability to support the objectives of this project. The approximate percentage of time each individual will be available for this project must be stated. The proposed staff hours of each individual should be allocated against each project task or subtask.

- Offerors must also include a list of those individuals authorized to contractually obligate the entity, as well as a list of those individuals authorized to negotiate with the Government on behalf of the entity.

6. Use of Select Agents

- An HHS chaired committee of contracting, security, safety and scientific program management will assess the applicability of the facilities, regulations, policies, and procedures for meeting the U.S. requirements described in 42 CFR part 73, 7 CFR part 331, and/or 9 CFR part 121.

7. Laboratory License Requirements

- The Contractor shall comply with all applicable requirements of Section 353 of the Public Health Service Act (Clinical Laboratory Improvement Act as amended). This requirement shall also be included in any subcontract for services under the contract.

8. Target Product Profile (TPP)

- Offerors should use the template in Attachment #2 to develop the Target Product Profile (TPP) to discuss the TPP of proposed candidate medical countermeasures, except for Diagnostics, Ventilators, Respiratory Protective Devices, Platforms, Modeling, and Visual Analytics.

a. The intended use or indication of the proposed medical countermeasure.

b. The intended product profile (strength, quality, purity and identity) noting the performance specifications and features of the medical countermeasure that provide benefit.

c. A description of the medical countermeasure as it is currently configured.

d. A description of the manufacturing process including expected formulation (configuration) of the final product.

e. A description and developmental status of the assays for product release which provide characterization, strength, identity, and purity, as well as any needed assays for product activity and efficacy.

f. Discussions with appropriate FDA reviewers that is relevant to development activities for the proposed medical countermeasure, including plans for generating data to support an Investigational New Drug (IND), Biologics License Application (BLA) or New Drug Application (NDA), Pre-Market Approval and/or 510(k) application: summary of any prior, time-relevant communication with FDA relevant to the product development for the indication noted; summary of audits and inspections relative to the current development or proposed manufacturing (Including at key sub-contractors) of the intended product.

9. Supporting Data

- Any additional product development data referenced in Volume I may be included here, provided that the Attachments remain within the page limit.

Volume II – Cost Proposal

The cost proposal shall contain sufficient information for meaningful evaluation. Additionally, a cost summary (not to exceed two pages) must be prepared and submitted in conjunction with the detailed cost proposal. The detailed costs must readily track back to the cost presented in the summary and the WBS, IMS, and SOW. The Offeror must also provide a narrative to support the requirements in each cost element. The cost breakdown by tasks should reference the WBS task in the Technical Proposal. Statement of Work Options should be priced separately.

A. Cover Page:

- The following information shall be provided on the first page of the cost proposal:

    1. The words “Volume II: Cost Proposal”;
    2. BAA Number;
    3. Title of proposal (descriptive of the work proposed and not a copy of the title of the solicitation):
    4. Development Area of Interest:
    5. Offeror (name, address, telephone number, and email address);
    6. Technical contact (name, telephone number, email address);
    7. Administrative contact (name, address, telephone number, and email address) (if available);
    8. Audit Office (name, address, telephone number, and email address) (if available);
    9. Proposed cost and/or price; profit or fee (as applicable); and total;
    10. The following statement: “By submitting this proposal, the Offeror, if selected for discussions, grants the Contracting Officer or an authorized representative the right to examine, at any time before award, any of those books, records, documents, or other records directly pertinent to the information requested or submitted.”
    11. Date of submission; and
    12. Authorized representative (name, title, and signature).
    13. DUNS number and CAGE code.

- This cover sheet information is for use by Offerors to submit information to the Government when cost or pricing data are not required but information to help establish price reasonableness or cost realism is necessary. Such information is not considered cost or pricing data, and shall not be certified in accordance with FAR 15.406-2.

B. Basic Cost/Price Information:

- The final cost proposal with a full cost proposal shall contain sufficient information to allow the Government to perform a basic analysis of the proposed cost or price of the work. This information shall include the amounts of the line items of the proposed cost or price. These elements will include the following elements by milestone event and/or proposed period as applicable:

    1. Direct Labor – Individual labor category or person, with associated labor hours and unburdened direct labor rates;

    2. Indirect Costs – Fringe Benefits, Overhead, (G&A), etc. (Must show base amount and rate). Offerors must submit a copy of their most recent indirect cost rate agreement negotiated with any federal audit agency, if applicable;

    3. Travel – Separate by destinations and include number of trips, durations - number of days, number of travelers, per diem (hotel and meals in accordance with the Federal Travel Regulations), airfare, car rental, if additional miscellaneous expense is included, list description and estimated amount, etc.;

    4. Subcontract – A cost proposal shall be submitted by each subcontractor proposed under the contract. The subcontractor's cost proposal should include on company letterhead the following:

        a. Complete company name and mailing address, technical and administrative/business point of contacts, email address, and telephone number.

        b. Include the DUNS number and CAGE code.

        c. A commitment letter from the proposed subcontractor's business official that includes:

            1) Willingness to perform as a subcontractor for specific duties (list duties) or a SOW;

            2) Proposed period of performance;

            3) Supporting documentation for proposed costs (personnel documents to verify salaries, vendor quotes for equipment, negotiated indirect cost rate agreement; and

            4) Quotes from two other potential subcontractors for similar services (see FAR 44.202(a)(5)).

        If the subcontractor's work entails any unpredictable aspects (e.g., includes experimentation, process development, etc.), a cost proposal conforming to all requirements of this section shall be provided, and shall reference the WBS of the prime contractor's proposal.

        If the subcontractor/vendor is providing commercially available, routine

services/products (e.g. facilities audits, manufacturing from a defined protocol, off-the-shelf reagents, hardware, or software, etc.), then a less detailed price quote is allowable. In each case where the latter level of detail is provided, the Offeror should assign subcontractor/vendor costs to the WBS, and should be prepared to document multiple competitive quotes for the service/product.

5. Consultants – For consultant subcontract arrangement, provide draft consulting agreement or other document which verifies the proposed loaded daily/hourly rate and labor category;

    a. Written verification from the consultant of their proposed rate, along with a statement that it is their usual and customary rate charged to other customers;

    b. Description of the work to be performed by the consultant and direct relevance to the contract work. Include information on why this expertise is not available in-house; and

    c. Verification that costs for the consultant are available within the total estimate cost of the contract and quotes from two other consultants for similar services (see FAR 44.202(a)(5).

6. Materials & Supplies – Should be specifically itemized with costs or estimated costs. Where the total cost is greater than $3,500, indicate pricing method (e.g., competition, historical costs, market survey, etc.). Include supporting documentation, i.e. vendor quotes, catalog price lists, and past invoices of similar purchases.

7. Other Direct Costs – Especially any proposed items of equipment. Equipment generally must be furnished by the Offeror. Justifications must be provided when Government funding for such items is sought.

8. Fee/profit (if applicable), including percentages.

C. Salary Rate Limitation:

- Pursuant to current and applicable prior HHS appropriations acts, it is anticipated that Offerors submitting Full Proposals under this BAA will be subject to a salary rate limitation on funds used to pay the direct salary of individuals. The applicability of this mandate will be confirmed at the time a Full Proposal is requested and is subject to the appropriations used to fund the effort.

    1. Congress has stipulated in the HHS appropriations act that, under applicable extramural contracts appropriated funds cannot be used to pay the direct salary of an individual at a rate in excess of the Federal Executive Schedule Level II.

    2. For purposes of the salary rate limitation, the terms ``direct salary,'' ``salary", and ``institutional base salary'', have the same meaning and are collectively referred to as ``direct salary'', in this clause. An individual's direct salary is the annual compensation that the Contractor pays for an individual's direct effort (costs) under the contract. Direct salary excludes any income that an

individual may be permitted to earn outside of duties to the Contractor. Direct salary also excludes fringe benefits, overhead, and G&A expenses (also referred to as indirect costs or facilities and administrative [F&A] costs). Note: The salary rate limitation does not restrict the salary that an organization may pay an individual working under an HHS contract or order; it merely limits the portion of that salary that may be paid with Federal funds.

3. The salary rate limitation also applies to individuals under subcontracts.

4. See the salaries and wages pay tables on the U.S. Office of Personnel Management Web site for Federal Executive Schedule salary levels that apply to the current and prior periods.

D. Travel:

- Identify as separate items and provide uniform cost assumptions for each travel requirement, e.g., contract initiation meeting, annual progress review meetings, periodic meetings with the Contracting Officer and COR, travel associated with training requirements and clinical site monitoring visits. Include the number of trips per year, location, number of days, and the number of Contractor/subcontract staff, as well as any external advisory group members for who travel expenses will be provided by the Contractor.

Volume II - Cost Proposal Attachments

Attachments to Volume II contain supplemental data of a cost and non-cost nature that should accompany the cost proposal. The combined total of all attachments should not exceed the page limitation specified in the Full Proposal invitation letter. Additional specific information to be included is referenced below. If a particular item in not relevant to the proposed effort, state that it is not applicable along with any supporting justification.

Table 3: Cost Proposal Attachments

	Item	Required	Reference & Document Type
1	DUNS, TIN, CAGE, and NAICS	Yes	Full Proposal Volume II – Cost Proposal
2	Representations and Certifications	Yes	System for Award Management[33] (SAM)
3	Breakdown of Proposed Estimated Cost (Plus Fee) and	Yes	Part VIII: Attachment #7 ASPR Business Toolkit[34] (for template)
4	SF-424 (for grant)	If applicable	Required: SF-424, SF-424A, SF-424B, SF-LLL For grant: Additional resources and templates are available in the ASPR Business Toolkit[35] and [36]
5	HHS Small Business Subcontracting	If applicable	Small Business SubContracting Plan[37]
6	Summary of Related Activities	Yes	Part VIII: Attachment #4 (for template)
7	Lobbying Activities	Yes	For Grant: SF-LLL: Disclosure of Lobbying Activities[38] For Contract: HHSAR 352.203-70[39]
8	Report of Government-Owned, Contractor-Held Property	If applicable	ASPR Business Toolkit[40] (for template)
9	Financial Capacity and Annual Financial Report	Yes	

[33] https://www.sam.gov/
[34] http://www.phe.gov/about/amcg/contracts/Pages/toolkit.aspx
[35] http://www.phe.gov/about/amcg/contracts/Pages/toolkit.aspx
[36] http://www.grants.gov/web/grants/forms.html
[37] https://www.hhs.gov/grants/contracts/contract-policies-regulations/subcontractplan/index.html
[38] https://apply07.grants.gov/apply/forms/sample/SFLLL_1_2-V1.2.pdf
[39] http://www.hhs.gov/grants/contracts/contract-policies-regulations/hhsar/subpart352/
[40] http://www.phe.gov/about/amcg/contracts/Pages/toolkit.aspx

	Item	Required	Reference & Document Type
10	Past Performance Contact Information	Yes	Part VI, Section 10
11	The Reason for the proposed Award Type	If applicable	Overview Information, Type of Award

1. **DUNS[41], TIN, CAGE, and NAICS[42]:**

   - These identification numbers or codes are required for companies to work with the Government.

2. **Representations and Certifications:**

   - In accordance with FAR 4.1201, prospective Contractors shall complete and update the annual representations and certifications at System for Award Management (SAM). Learn more about System for Award Management[43] (SAM) for completion of annual Representations and Certifications.

3. **Breakdown of Proposed Estimated Cost (Plus Fee) and Labor Hours:**

   - Complete the template to provide a breakdown of the proposed estimated cost (plus fee) and labor hours.

4. **SF-424:**

   - The SF-424, SF-424A, SF-424B, and SF-LLL forms are required to be completed for grants and cooperative agreements. Refer to the letter of invitation to submit a Full Proposal for additional details and form requirements.

5. **HHS Small Business Subcontracting Plan:**

   - Successful contract proposals that exceed $700,000, submitted by all but small business concerns, will be required to submit a Small Business Subcontracting Plan in accordance with FAR 19.704.

6. **Summary of Related Activities:**

   - This specific information must be provided by the Offeror pertaining to the Project Director, Principal Investigator, and each of any other proposed key professional individuals designated for performance under any resulting contract.

7. **Lobbying Activities:**

   - In accordance with Prohibition on the Use of Appropriated Funds for Lobbying Activities [HHSAR 352.203-7], the following clause shall be inserted: “Pursuant to

[41] http://www.dnb.com/
[42] http://www.census.gov/eos/www/naics/index.html
[43] https://www.sam.gov/

the HHS annual appropriations acts, except for normal and recognized executive-legislative relationships, the Contractor shall not use any HHS contract funds for: (a) Publicity or propaganda purposes; (b) The preparation, distribution, or use of any kit, pamphlet, booklet, publication, electronic communication, radio, television, or video presentation designed to support or defeat the enactment of legislation before the Congress or any State or local legislature or legislative body, except in presentation to the Congress or any state or local legislature itself; or designed to support or defeat any proposed or pending regulation, administrative action, or order issued by the executive branch of any state or local government, except in presentation to the executive branch of any state or local government itself; or (c) Payment of salary or expenses of the Contractor, or any agent acting for the Contractor, related to any activity designed to influence the enactment of legislation, appropriations, regulation, administrative action, or Executive order proposed or pending before the Congress or any state government, state legislature or local legislature or legislative body, other than for normal and recognized executive-legislative relationships or participation by an agency or officer of a state, local, or tribal government in policymaking and administrative processes within the executive branch of that government. (d) The prohibitions in subsections (a), (b), and (c) above shall include any activity to advocate or promote any proposed, pending, or future federal, state, or local tax increase, or any proposed, pending, or future requirement for, or restriction on, any legal consumer product, including its sale or marketing, including, but not limited to, the advocacy or promotion of gun control."

8. Report of Government-Owned, Contractor-Held Property:

- Complete the spreadsheet available at the ASPR Business Toolkit[44], if Government Furnished Property (GFP) is a part of the proposal. Additionally, include a business case justification for review that outlines that providing GFP is in the Government's best interest and that there is no other commercial alternative other than GFP. Additionally, justify how any proposed costs of GFP are "fair and reasonable". Include the completed spreadsheet with your cost proposal.

9. Financial Capacity & Annual Financial Report:

- The Offeror shall indicate if it has the necessary financial capacity, working capital, and other resources to perform the contract without assistance from any outside source. If not, indicate the amount required and the anticipated source. The Offeror may also be asked to submit a copy of the organization's most recent annual report in the cost proposal attachment.

10. Past Performance:

- The Offeror shall provide a list of the last three Government contracts during the past 3 years and all contracts currently being performed that are similar in nature to the BAA scope. Contracts listed may include those entered into by the Federal Government, agencies of state and local governments and commercial concerns. Offerors may also submit past performance information regarding predecessor

[44] http://www.phe.gov/about/amcg/contracts/Pages/toolkit.aspx

companies, key personnel who have relevant experience or subcontractors that will perform major or critical aspects of the requirement when such information is relevant to the instant acquisition. For the purposes of this BAA, a "major subcontract" is defined as a subcontract that exceeds the simplified acquisition threshold.

- Include the following information for each contract or subcontract listed:

    1. Name of Contracting Organization
    2. Contract Number (for subcontracts, provide the prime contract number and the subcontract number)
    3. Contract Type
    4. Total Contract Value
    5. Description of Requirement
    6. Contracting Officer's Name and Telephone Number
    7. Program Manager's Name and Telephone Number
    8. North American Industry Classification System Code

- The Offeror may provide information on problems encountered on the identified contracts and the Offeror's corrective actions.

Stage 2: Full Proposal Submission

Unless otherwise directed by the Contracting Officer, offerors must mail one paper copy of the Full Proposal to one of the addresses listed below or to the Contracting Officer identified in the Full Proposal Invitation Letter. Additional copies may be requested in the Full Proposal Invitation Letter. Offerors who submit a Full Proposal in the absence of a White Paper submission are required to mail one paper copy of the Full Proposal to one of the addresses listed below. Additionally, Offerors must submit an electronic copy of the Full Proposal via email, to an email address to be provided in the invitation letter, or to BARDA-BAA@hhs.gov in the absence of a White Paper submission. Offerors should provide the Contracting Officer, either directly or through the email address above, with mail tracking number for the paper copy of the Full Proposal. For submission deadlines purposes, the electronic copy takes precedence over the paper copy.

IMPORTANT: The subject line of the email should consist of the announcement number, area of interest number, and purpose of the email (e.g., BAA-18-100-SOL-00003 AOI #4 Full Proposal Submission).

Note: Do not staple, laminate, punch holes in, or semi-permanent bind the paper copy.

United States Postal Service (USPS) First Class Mail/United Parcel Service (UPS)/Federal Express (FedEx):

Contracting Officer
ASPR/Office of Acquisitions Management, Contracts, and Grants (AMCG)
Second Floor - O'Neill House Office Building
Washington, DC 20515

Note: Due to mail screening process, delivery of first class mails can take four to six additional working days.

Expedited Courier Services:

Contracting Officer
ASPR/Office of Acquisitions Management, Contracts, and Grants (AMCG)
160 D St. NE
Washington, DC 20510

Offerors shall include in the Full Proposal cover sheet:

- The name, title, mailing address and telephone number of the company or organization;
- The name, title, mailing address, telephone number, and e-mail address of the division point of contact regarding decisions made with respect to the Offeror and who can obligate the proposal contractually;
- The name, title, mailing address, telephone number, and e-mail address and those individual(s) authorized to negotiate with the Government; and
- A statement indicating you are submitting a final Full Proposal for consideration.

Submission file format for the electronic copy: Each volume of the proposal must be submitted as a separate and searchable Portable Document File (PDF) compatible with Adobe Acrobat version 11 or earlier. Each individual file shall not exceed 10 megabytes of storage space.

Notification to Offerors: All Offerors will receive an email acknowledging receipt of their Quad Chart/White Paper and Full Proposal.

Information to be requested from Offerors: Offerors whose proposals are selected for potential award may be contacted to provide additional clarification and technical information if required for award.

Offerors that are not responsive in a timely manner to Government requests for information (defined as meeting Government deadlines established and communicated with the request) may be removed from award consideration. Offerors that request significant revisions to their proposal subsequent to their selection for potential award 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 time.

Part VII: Quad Chart/White Paper and Full Proposal Evaluation

A. Quad Chart/White Paper Evaluation Criteria

The decision to invite an Offeror to submit a Full Proposal will be based on an evaluation of each Offeror's White Paper and Quad Chart. The White Paper and Quad Chart will be evaluated by a scientific review process based on the following criteria that are listed in descending order of importance pursuant to FAR 35.016(e). The sub-criteria listed under each criterion are of equal importance to each other.

1. Program Relevance

a. Medical countermeasures that address the priorities outlined in the Development Areas of Interest;

b. Medical countermeasures, devices, diagnostics, and supporting analytics that align with the objectives outlined in the HHS Pandemic Influenza Plan, PHEMCE Strategy and Implementation Plan, or other Federal Government strategy documents;

c. Medical countermeasures that are readily administered/used during a public health emergency;

d. The maturity level of the proposed product as determined by applicable TRL criteria. Technological maturity should be justified by the inclusion of relevant data;

e. Medical Countermeasures that are suitable for use with pediatric and other special populations;

f. The extent to which the proposed effort fills an unmet programmatic need;

g. Medical countermeasures as specified in the areas of interest that focus on diagnosis, event/outbreak prophylaxis, treatment and/or mitigation, and are also effective when administered within the treatment window for that agent/event;

h. The Offeror has proposed a product with a sustainable commercial value to ensure long term access to the medical countermeasure; and

i. For Areas of Interest 13 and 14: Analyses that are complementary to and address more than one medical countermeasure and/or type of threat detailed in Areas of Interest 1-12.

2. Overall Scientific and Technical Merits of the Proposal

a. The degree of innovation and potential to offer a revolutionary increase in capability or a significant reduction in cost commensurate with the potential risks of the innovative approach;

b. The soundness, feasibility, and validity of the proposed plans, methods, techniques, and procedures of the technical proposal;

c. The Offeror's understanding of the scope of the proposed work and the technical effort needed to complete it;

d. The reasonableness of the proposed schedule;

e. The Offeror's understanding of the statutory and regulatory requirements for FDA licensure or approval status of the proposed work;

f. The Offeror's freedom to operate given the intellectual property status of the proposed technology;

g. The degree of development of the technology and its readiness for the marketplace; and

h. The Offeror has proposed a product with a feasible technical approach that optimizes the product in a way that reduces the cost for the proposed countermeasure throughout the products life cycle.

3. Offeror's Capabilities and Related Experience, including the Qualifications, Capabilities, and Experiences of the Proposed Key Personnel

a. The expertise of technical personnel proposed;

b. The Offeror's experience in relevant efforts with similar resources;

c. The reasonableness of the proposed project management approach and expertise of the project management personnel proposed;

d. The necessary facilities and infrastructure to carry out the proposed effort. (The Offeror may identify specific subcontractors and other partners); and

e. An organizational chart of the Offeror's personnel that demonstrates the Offeror has relevant infrastructure to support the project.

B. Full Proposal Evaluation Criteria

The selection of one or more sources for award will be based on an evaluation of each Full Proposal. Full Proposals will be evaluated by a Peer or Scientific Review process and will be evaluated based on the following criteria that are listed in descending order of importance. The sub-criteria listed under a particular criterion are of equal importance to each other. Pursuant to FAR 35.016(e), the primary basis for selecting proposals for acceptance shall be technical, importance to agency programs, and fund availability. Therefore, when together non-cost related evaluation criteria significantly outweigh cost-related evaluation criteria.

1. Program Relevance

a. Medical countermeasures that address the priorities outlined in the Development Areas of Interest;

b. Medical countermeasures, devices, diagnostics, and supporting analytics that align with the objectives outlined in the HHS Pandemic Influenza Plan, PHEMCE

Strategy and Implementation Plan, or other Federal Government strategy documents;

c. Medical countermeasures that are readily administered/used during a public health emergency;

d. The maturity level of the proposed product as determined by applicable TRL criteria. Technological maturity should be justified by the inclusion of relevant data;

e. Medical Countermeasures that are suitable for use with pediatric and other special populations;

f. The extent to which the proposed effort fills an unmet programmatic need;

g. Medical countermeasures as specified in the areas of interest that focus on diagnosis, event/outbreak prophylaxis, treatment and/or mitigation, and are also effective when administered within the treatment window for that agent/event;

h. The Offeror has proposed a product with a sustainable commercial value to ensure long term access to the medical countermeasure; and

i. For Areas of Interest 13 and 14: Analyses that are complementary to and address more than one medical countermeasure and/or type of threat detailed in Areas of Interest 1-12.

2. Overall Scientific and Technical Merits of the Proposal

a. The degree of innovation and potential to offer a revolutionary increase in capability or a significant reduction in cost commensurate with the potential risks of the innovative approach;

b. The soundness, feasibility, and validity of the proposed plans, methods, techniques, and procedures of the technical proposal;

c. The Offeror's understanding of the scope of the proposed work and the technical effort needed to complete it;

d. The reasonableness of the proposed schedule;

e. The Offeror's understanding of the statutory and regulatory requirements for FDA licensure or approval status of the proposed work;

f. The Offeror's freedom to operate given the intellectual property status of the proposed technology;

g. The degree of development of the technology and its readiness for the marketplace; and

h. The Offeror has proposed a product with a feasible technical approach that optimizes the product in a way that reduces the cost for the proposed countermeasure throughout the products life cycle.

3. Offeror's Capabilities and Related Experience, including the Qualifications, Capabilities, and Experiences of the Proposed Key Personnel

a. The expertise of technical personnel proposed;

b. The Offeror's experience in relevant efforts with similar resources;

c. The reasonableness of the proposed project management approach and expertise of the project management personnel proposed;

d. The necessary facilities and infrastructure to carry out the proposed effort. (The Offeror may identify specific subcontractors and other partners); and

e. An organizational chart of the Offeror's personnel that demonstrates the Offeror has relevant infrastructure to support the project.

C. Other Evaluation Factors and Considerations

In accordance with FAR 35.016 (e), the primary basis for selecting proposals for acceptance shall be technical, importance to agency programs, and fund availability. Cost realism and reasonableness shall also be considered to the extent appropriate.

1. Cost/Price

Each price / cost response will be reviewed for price / cost realism, reasonableness, and overall best value to the Government. Proposals will be reviewed to determine if the costs proposed are based on realistic assumptions, reflect a sufficient understanding of the technical goals and the objectives of the BAA and are consistent with the Offeror's technical approach. For proposals with a likelihood of commercial application, cost-sharing may be positively evaluated under this criterion.

2. Past Performance

Past performance information will be evaluated to the extent of determining the Offeror's ability to perform the contract successfully. Offerors shall submit the following information as part of their proposal.

The Government is not required to contact all references provided by the Offeror. Also, references other than those identified by the Offeror may be contacted by the Government to obtain additional information that will be used in the evaluation of the Offeror's past performance.

The Government will use the Past Performance Information Retrieval System (PPIRS) to help assess Offeror past performance.

3. Subcontracting Program Evaluation

For contract awards to be made to large businesses, the socio-economic merits of each proposal will be evaluated, but not scored, based on the extent of the Offeror's commitment in providing meaningful subcontracting opportunities for small businesses, small disadvantaged businesses, woman-owned businesses, service disabled veteran- owned small businesses, Hub-zone small business concerns,

historically black colleges and universities, and minority institutions.

4. Requested Proof of Concept Studies

Full Proposals, which were requested to provide Proof of Concept (POC) studies, will be evaluated in regards to the POC design, power of the studies, budget, and timelines. If the technical evaluation does not result in a favorable decision, the Offeror may be asked to perform additional work on the product's development at their cost and resubmit. A successful review of the POC design will result in a negotiation for a contract to perform the POC (or a negotiated POC) as a base contract with or without Options, all subject to availability of funds.

The final evaluation will be based on an assessment of the overall best value to the Government based on these criteria. Awards, if any, will be made based on proposal evaluation and funds availability.

D. Evaluation Rating

The Full Proposal will be evaluated and categorized as follows:

Acceptable: The proposal has been evaluated and deemed appropriate for additional consideration and discussion. The proposal is generally considered well-conceived, scientifically, and technically sound and important to program goals and objectives. Proposal submissions given this designation may proceed into negotiations.

Note: An acceptable rating does not guarantee contract award. The following will be taken into consideration: program priorities, negotiations, and availability of funds.

Unacceptable: The proposal has been evaluated and deemed inappropriate for additional consideration and discussion at this time. Proposals given this designation are not technically sound or do not meet program priorities and will be rejected.

E. Additional Information

Offerors selected for negotiations may be subject to inspections of their facilities and Quality Assurance/Quality Control (QA/QC) capabilities. The decision to inspect specific facilities will be made by the Contracting Officer in coordination with the COR. If inspections are performed during the negotiations, the results of the inspection will be considered in final selection for award of a contract. Offerors, including proposed subcontractors, will be requested to make all non-proprietary records, including previous regulatory inspection records, and staff available in response to a pre-award site visit or audit by BARDA or its designee. Pre- award site visits may be made with short notice. Offerors are expected to guarantee the availability of key staff or other staff determined by the Government as essential for purposes of this site visit.

Offerors are hereby notified that the Government intends to use a Technical Evaluation Panel (TEP), in determining which initiatives should be funded. The TEP may consist of Government personnel and technical contract support personnel.

All personnel assigned to a TEP have signed a Nondisclosure Agreement, Conflict of Interest Disclosure, and will be made aware that proposals shall not be duplicated, used, or disclosed in whole or in part for any purpose other than to evaluate the proposal. Any

Offeror who states in writing that they are unwilling to allow contractor members of the TEP to review their proposal shall have their proposal returned without evaluation.

Offerors whose Full Proposals are issued an "Unacceptable" letter and are not invited to negotiations may request a debriefing. See 41 U.S.C. § 3705. Offerors may request a preaward debriefing by submitting a written request for debriefing to the Contracting Officer within three days after receipt of the notice of exclusion from negotiations. If the Offeror does not submit a timely request, the Offeror need not be given either a preaward or a postaward debriefing. Offerors are entitled to no more than one debriefing.

Part VIII: Attachments

Attachment 1: Technology Readiness Level Criteria

Minimum Technology Readiness Level (TRL) criteria have been identified for each Development Areas of Interest. Offerors must identify in their Quad Chart and White Paper that such criteria have been met for the proposed medical countermeasure product. Two different Technology Readiness Level (TRL) criteria are provided here.

Attachment 1A: Diagnostic and Medical Devices TRLs adapted from Q-TRLs

For use with:

- Area of Interest #7: Diagnostics
- Area of Interest #10: Respiratory Protective Devices
- Area of Interest #11: Ventilators

Attachment 1B: Technology Readiness Level for Medical Countermeasure Products (Drugs and Biologics)

For use with:

- Area of Interest #1: CBRN Vaccines
- Area of Interest #2: Antitoxins and Therapeutics Proteins
- Area of Interest #3: Antibacterials
- Area of Interest #4: Radiological/Nuclear Threat Medical Countermeasures
- Area of Interest #5: Chemical Threat Medical Countermeasures
- Area of Interest #6: Burn Medical Countermeasures
- Area of Interest #8: IEID Vaccines
- Area of Interest #9: IEID Therapeutics
- Area of Interest #12: MCM Production Platform Systems

Attachment 1A: Diagnostics and Medical Devices TRLs adapted from Q-TRLs (For Use with Areas of Interest #7, 10, 11)

Table 4: Technical Readiness Level and Description for Areas of Interest 7, 10, 11

TRL Level	TRL Description *A product can be described as achieving a TRL only if all relevant activities identified in that TRL have been completed.*
1	**Review of Scientific Knowledge.** Active monitoring of scientific knowledge base to identify clinical pathological markers for diagnostic countermeasure candidates. Scientific findings are reviewed and assessed as a foundation for characterizing approaches to intervene in disease. Basic research needs identified.
2	**Concept Generation and Development of Experimental Designs** Develop research plans to answer specific questions and experimental designs for addressing the related scientific issues and to establish feasibility. Focus on practical applications based on basic principles.
3	**Characterization of Preliminary Candidates(s) and Feasibility Demonstration** Begin R&D, data collection, and analysis in order to verify feasibility. Explore alternative concepts, identify and evaluate critical technologies and components, and begin characterizing specifications required. Demonstrate the performance of candidate diagnostic targets and high risk components. Develop a business case for the proposed product.
4	**Optimization and Preparation for Assay, Component, and Instrument Development** Prepare for test system development. Finalize diagnostic target(s) and methods for detecting or quantitating target(s). Develop detailed plans and finalize critical design requirements. Execute commercial agreements with key external development partners. Identify manufacturing resources, vendor sourcing, and experimental designs
5	**Product Development – Reagents, components, subsystems and modules** Develop reagents and buffers. Build and test non-GLP prototypes of components and subsystems. Code and unit test software. Begin pilot scale manufacturing preparations. Develop protocols for assay and integration testing Initiate reagent stability testing. Hold pre-IDE meeting with FDA. Initiate Design History file.
6	**System integration & testing** Integrate and test alpha and beta instruments/devices, software and assays, evaluating performance and updating specifications. Implement design improvements to address defects discovered during testing. Produce and evaluate pilot lots of reagents and beta (pilot) instruments. Increase the maturity of software. Prepare for clinical testing. Complete short term stability testing of reagents.
7	**Analytical Verification and Preparation for Clinical Studies** Evaluate assay and integrated diagnostic system performance utilizing contrived, retrospective human and animal samples. Make preparations for clinical evaluation. Begin preparation for full scale production of instruments and assays.
8	**Clinical Studies and/or evaluation with Animal Studies, FDA Clearance or Approval, Finalize GMP manufacturing preparations.** Complete clinical evaluations. Prepare and submit FDA filing. **End of TRL8:** Acquire FDA approval, or clearance.

Attachment 1B: Technology Readiness Level for Medical Countermeasure Products (Drugs and Biologics)[45,46] (For Use with Areas of Interest 1-6 and 8-9)

For Areas of Interest 1-6, 8-9, and 12, Offerors must identify in their Quad Chart and White Paper that the criteria for TRL 6 have been met for the proposed product and for the proposed influenza indication, using the *Technology Readiness Levels for Medical Countermeasure Products (Drugs and Biologics)* as shown below. Please note that all activities within a TRL (or sublevel) must be completed to have achieved that TRL status. These TRL criteria can also be found at: MedicalCountermeasures.Gov

FOR USE WITH AREAS OF INTEREST 1-6, 8-9, AND 12

Note: *When using these criteria, a medical countermeasure product should be rated at a particular level only after the sponsor has completed all activities listed in that level (e.g., a product is rated at TRL 4 once it completes all of the activities listed in TRL 4).*

Table 5: Technology Readiness Level and Description for Areas of Interest 1-6 and 8-9

Level	Description
TRL 1	**Review of Scientific Knowledge Base** Active monitoring of scientific knowledge base. Scientific findings are reviewed and assessed as a foundation for characterizing new technologies.
TRL 2	**Development of Hypotheses and Experimental Designs** Scientific "paper studies" to generate research ideas, hypotheses, and experimental designs for addressing the related scientific issues. Focus on practical applications based on basic principles observed. Use of computer simulation or other virtual platforms to test hypotheses.
TRL 3	**Target/Candidate Identification and Characterization of Preliminary Candidate(s)** Begin research, data collection, and analysis in order to test hypothesis. Explore alternative concepts, identify and evaluate critical technologies and components, and begin characterization of candidate(s). Preliminary efficacy demonstrated *in vivo*. **3A** Identify target and/or candidate. **3B** Demonstrate *in vitro* activity of candidate(s) to counteract the effects of the threat agent. **3C** Generate preliminary *in vivo* proof-of-concept efficacy data (non-GLP (Good Laboratory Practice)).

[45] This document is designed for evaluating the maturity of medical countermeasure development programs. For a detailed description of development processes for assays and animal models, please consult the Technology Readiness Levels for Product Development Tools (PDTs), developed by the PDT Working Group of the HHS Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) and available at: https://www.medicalcountermeasures.gov/

[46] This document does not serve as official FDA Guidance nor does it represent FDA's current thinking on this topic. For the purposes of a regulatory application seeking licensure or approval for a specific medical product, additional data may be required by FDA.

Level	Description
TRL 4	**Candidate Optimization and Non-GLP In Vivo Demonstration of Activity and Efficacy** Integration of critical technologies for candidate development. Initiation of animal model development. Non-GLP *in vivo* toxicity and efficacy demonstration in accordance with the product's intended use. Initiation of experiments to identify markers, correlates of protection, assays, and endpoints for further non-clinical and clinical studies. **Animal Models:** Initiate development of appropriate and relevant animal model(s) for the desired indications. **Assays**: Initiate development of appropriate and relevant assays and associated reagents for the desired indications. **Manufacturing:** Manufacture laboratory-scale (i.e. non-GMP (Good Manufacturing Practice)) quantities of bulk product and proposed formulated product. **4A** Demonstrate non-GLP *in vivo* activity and potential for efficacy consistent with the product's intended use (i.e. dose, schedule, duration, route of administration, and route of threat agent challenge). **4B** Conduct initial non-GLP toxicity studies and determine pharmacodynamics and pharmacokinetics and/or immune response in appropriate animal models (as applicable). **4C** Initiate experiments to determine assays, parameters, surrogate markers, correlates of protection, and endpoints to be used during non-clinical and clinical studies to further evaluate and characterize candidate(s).
TRL 5	**Advanced Characterization of Candidate and Initiation of GMP Process Development** Continue non-GLP *in vivo* studies, and animal model and assay development. Establish draft Target Product Profiles. Develop a scalable and reproducible manufacturing process amenable to GMP. **Animal Models:** Continue development of animal models for efficacy and dose-ranging studies. **Assays:** Initiate development of in-process assays and analytical methods for product characterization and release, including assessments of potency, purity, identity, strength, sterility, and quality as appropriate. **Manufacturing:** Initiate process development for small-scale manufacturing amenable to GMP. **Target Product Profile:** Draft preliminary Target Product Profile. Questions of shelf life, storage conditions, and packaging should be considered to ensure that anticipated use of the product is consistent with the intended use for which approval will be sought from FDA. **5A** Demonstrate acceptable Absorption, Distribution, Metabolism and Elimination characteristics and/or immune responses in non-GLP animal studies as necessary for IND filing. **5B** Continue establishing correlates of protection, endpoints, and/or surrogate markers for efficacy for use in future GLP studies in animal models. Identify minimally effective dose to facilitate determination of "humanized" dose once clinical data are obtained.

Level	Description
TRL 6	**GMP Pilot Lot Production, IND Submission, and Phase 1 Clinical Trial(s)** Manufacture GMP-compliant pilot lots. Prepare and submit Investigational New Drug (IND) package to FDA and conduct Phase 1 clinical trial(s) to determine the safety and pharmacokinetics of the clinical test article. **Animal Models:** Continue animal model development via toxicology, pharmacology, and immunogenicity studies. **Assays:** Qualify assays for manufacturing quality control and immunogenicity, if applicable. **Manufacturing:** Manufacture, release and conduct stability testing of GMP-compliant bulk and formulated product in support of the IND and clinical trial(s). **Target Product Profile:** Update Target Product Profile as appropriate. **6A** Conduct GLP non-clinical studies for toxicology, pharmacology, and immunogenicity as appropriate. **6B** Prepare and submit full IND package to FDA to support initial clinical trial(s). **6C** Complete Phase 1 clinical trial(s) that establish an initial safety, pharmacokinetics and immunogenicity assessment as appropriate.
TRL 7	**Scale-up, Initiation of GMP Process Validation, and Phase 2 Clinical Trial(s)**[47] Scale-up and initiate validation of GMP manufacturing process. Conduct animal efficacy studies as appropriate.[48] Conduct Phase 2 clinical trial(s).[47] **Animal Models:** Refine animal model development in preparation for pivotal GLP animal efficacy studies. **Assays:** Validate assays for manufacturing quality control and immunogenicity if applicable. **Manufacturing:** Scale-up and validate GMP manufacturing process at a scale compatible with USG requirements. Begin stability studies of the GMP product in a formulation, dosage form, and container consistent with Target Product Profile. Initiate manufacturing process validation and consistency lot production. **Target Product Profile:** Update Target Product Profile as appropriate. **7A** Conduct GLP animal efficacy studies as appropriate for the product at this stage.[48]

[47] Identification of later regulatory stages of clinical development in this document (e.g., Phase 2, Phase 3) may not apply to some products being developed under the "Animal Rule". Other than human safety studies, no additional clinical data may be feasible or ethical to obtain. For additional information on the "Animal Rule", please see: http://www.fda.gov/OHRMS/DOCKETS/98fr/053102a.htm

[48] These could include GLP animal efficacy studies required by FDA at this stage in support of an Emergency Use Authorization (EUA). The scientific evidence required for issuance of an EUA will be handled on a case-by-case basis and will depend on, among other things, the nature and extent of the threat at any point during the product development timeline, from the initiation of Phase 1 studies through licensure or approval. GLP animal efficacy study requirements may also vary by product type (e.g., vaccine, therapeutic, prophylactic) and U.S. government agency program office.

Level	Description
	7B Complete expanded clinical safety trials as appropriate for the product (e.g., Phase 2).[47]
TRL 8	**Completion of GMP Validation and Consistency Lot Manufacturing, Pivotal Animal Efficacy Studies or Clinical Trials[47], and FDA Approval or Licensure** Finalize GMP manufacturing process. Complete pivotal animal efficacy studies or clinical trials (e.g., Phase 3), and/or expanded clinical safety trials as appropriate. Prepare and submit NDA/BLA. **Manufacturing:** Complete validation and manufacturing of consistency lots at a scale compatible with USG requirements. Complete stability studies in support of label expiry dating. **Target Product Profile:** Finalize Target Product Profile in preparation for FDA approval. **8A** Complete pivotal GLP animal efficacy studies or pivotal clinical trials (e.g., Phase 3), and any additional expanded clinical safety trials as appropriate for the product.[47] **8B** Prepare and submit New Drug Application (NDA) or Biologics Licensing Application (BLA) to the FDA. **8C** Obtain FDA approval or licensure.
TRL 9	**Post-Licensure and Post-Approval Activities** **9A** Commence post-licensure/post-approval and Phase 4 studies (post-marketing commitments), such as safety surveillance, studies to support use in special populations, and clinical trials to confirm safety and efficacy as feasible and appropriate.[49] **9B** Maintain manufacturing capability as appropriate.

[49] For products approved under the "Animal Rule", confirmatory efficacy data are required, if such studies are feasible and ethical, and may be obtained from use during an event.

Attachment 2: Target Product Profile Template

The success of a product development program requires a relentless focus on the desired characteristics of the resulting medical countermeasure product. During Stage 2, in addition to the Full Proposal, Offerors are requested to provide a Target Product Profile. The template immediately below is as a tool for Offerors to describe the objectives of their advanced research and development activities, and to update dynamically as supporting data about their product is obtained. All Offerors are encouraged to submit a Target Product Profile for the proposed medical countermeasure, with a particular focus on elements 1-4. For those products for which the Target Product Profile format is not applicable, appropriate equivalent information regarding the development objectives should be provided.

Target Product Profile Template
Target Product Profile: ***Drug Name***
(may be modified for use with devices)

Table 6: Target Product Profile: Drug Name

Milestone (meeting or submission)	Date	*TPP Submitted? Y/N	TPP Version Date	TPP Discussed? Y/N
Pre-IND				
IND Submission				
EOP1				
EOP2A				
EOP2/Pre-Phase 3				
Pre-NDA/BLA				
Other (specify)				
Pre-IDE				
IDE Submission				
510(k) or PMA				
Other (specify)				

1 Indications and Usage

Target	Annotations
A statement that the drug is indicated in the treatment, prevention, or diagnosis of a recognized disease or condition, OR *A statement that the drug is indicated for the treatment, prevention, or diagnosis of an important manifestation of a disease or condition, OR* *A statement that the drug is indicated for the relief of symptoms associated with a disease or syndrome, OR* *A statement that the drug is indicated for a particular indication only in conjunction with a primary mode of therapy*	*Summary information regarding completed or planned studies to support the target:* *Protocol #, Serial #, Submission date* *When listing studies, consider:* *The intent to develop evidence to support safety and efficacy in selected subgroups (i.e., limitations of use)* *Tests needed for selection or monitoring of patients (i.e., susceptibility tests)* *Whether safety considerations require the drug to be reserved for certain situations (i.e., in refractory patients)* *Whether the drug is to be used on a chronic basis* *What evidence will be developed to support comparator statements regarding safety or effectiveness*

Comments:

2 Dosage and Administration

Target	Annotations
For each indication, state the following: *Route of administration* *Recommended usual dose* *Dose range shown to be safe and effective* *Exposure (dose- or blood level-response relationship, if any)* *Dosage intervals or titration schedule* *Usual duration of treatment course when treatment is not chronic* *Dosage adjustments (e.g., in specific genotypes, pediatric patients, geriatric patients, or patients with renal or hepatic disease)* *Tests for guiding dosing (e.g., target plasma drug levels, therapeutic range, response biomarkers)*	*Summary information regarding completed or planned studies to support the safety and effectiveness of the proposed dosage and route of administration:* *Protocol #, Serial #, Submission date*

Comments:

3 Dosage Forms and Strengths

Target	Annotations
Include information on the available dosage forms, including strength or potency of dosage	*Summary information regarding completed or planned studies to support the dosage forms*

form in metric system and a description of identifying characteristics of dosage forms	*and strengths:* *Protocol #, Serial #, Submission date*

Comments:

4 Contraindications

Target	**Annotations**
List situations in which the drug might be contraindicated, including: *Increased risk of harm because of age, sex, concomitant therapy, disease state* *Adverse reactions which would limit use* *Known, not theoretical, hazards*	*Summary information regarding completed or planned studies to support the target:* *Protocol #, Serial #, Submission date* *Or, literature references describing contraindication for drug class.*
Comments:	

5 Warnings and Precautions

Target	**Annotations**
Include a description of clinically significant adverse reactions and potential safety hazards and limitations of use because of safety considerations, as reasonable evidence of these issues is established or suspected during the drug development program. A causal relationship need not be demonstrated. *Include information regarding any special care to be exercised for safe use, including precautions that are not required under any other section of the label.* *Identify any laboratory tests helpful in following the patient's response or in identifying possible adverse reactions.*	*Summary information regarding completed or planned studies to support the target:* *Protocol #, Serial #, Submission date* *Or, literature references describing significant adverse reactions shared by the drug class of the new drug.*
Comments:	

6 Adverse Reactions

Target	**Annotations**
Describe overall adverse reaction profile of the drug based on entire safety database. List adverse reactions that occur with the drug and with drugs in the same pharmacologically active and chemically related class, if applicable. *Within a listing, adverse reactions should be categorized by body system, severity of the reaction, or in order of decreasing frequency, or by a combination of these, as appropriate.* *Within a category, adverse reactions should be listed in decreasing order of frequency.* *Include the studies in the development program*	*Summary information regarding completed or planned studies to support the target:* *Protocol #, Serial #, Submission date*

that will address adverse reactions associated with a particular drug class.	

Comments:

7 Drug Interactions

Target	Annotations
Describe clinically significant interactions, either observed or predicted (i.e., other prescription drugs or over-the-counter drugs, class of drugs, or foods such as grapefruit juice or dietary supplements); practical advice on how to prevent drug-drug interactions; (description of results from studies conducted or observations from the integrated safety summary); drug-laboratory test interactions (known interference of drug with lab test outcome).	*Summary information regarding completed or planned studies to support the target: Protocol #, Serial #, Submission date*

Comments:

8 Use in Specific Populations

Target	Annotations
Consider the following: Limitations, need for monitoring, specific hazards, differences in response, or other information pertinent to the population.	*Summary information regarding completed or planned studies to support the target: Protocol #, Serial #, Submission date If there are no plans to study the drug in a specific population, include rationale.*

Comments:

8.1 Pregnancy** (This subsection can be omitted if the drug is not absorbed systemically)**:
Teratogenic effects: Pregnancy Categories: A, B, C, D, X
Non-teratogenic effects: Other effects on reproduction, the fetus, or newborn.
***8.2 Labor and Delivery:** Use during labor or delivery, effects on mother, fetus, duration of labor, delivery, and effects on later growth of newborn.*
***8.3 Nursing Mothers:** If the drug is absorbed systemically, information about excretion of drug in human milk and effects on the nursing infant. Describe pertinent adverse events in animal offspring or tumorigenicity potential if it is detected or suspected.*
***8.4 Pediatric Use:** Statements relevant to the use of the drug product in the pediatric population (birth to 16 years of age). Cite any limitations, need for monitoring, specific hazards, differences in response, or other information pertinent to the pediatric population.*
***8.5 Geriatric Use:** Statements relevant to the use of the drug product in the geriatric population (age 65 and older). Cite any limitations, need for monitoring, specific hazards, differences in response, or other information pertinent to the referenced population.*
***8.6 Additional Subsections:** Use of drug in other specified populations (e.g., those with renal or hepatic impairment).*

9 Drug Abuse and Dependence

Target	Annotations
Include the following subsections, as appropriate for the drug:	*Summary information regarding completed or planned studies to support the target: Protocol #, Serial #, Submission date*

Comments:

9.1 Controlled Substance: *Anticipated DEA schedule.*
9.2 Abuse: *Identify types of abuse and adverse reactions pertinent to them. Identify particularly susceptible patient populations.*
9.3 Dependence**:** *Discuss potential for dependence and describe the characteristic effects resulting from psychological or physical dependence.*

10 Overdosage

Target	Annotations
Provide specific information about: *Signs, symptoms, and lab findings associated with an overdosage of the drug* *Complications that can occur with overdose of the drug (e.g., organ toxicity)* *Concentrations of the drug in biofluids associated with toxicity or death* *The amount of the drug in a single overdose that is ordinarily associated with symptoms, and the amount of the drug in a single overdose that is likely to be life-threatening* *Whether the drug is dialyzable* *Recommended general treatment procedures*	*Summary information regarding completed or planned studies to support the target: Protocol #, Serial #, Submission date* *Update with human data, if available.*

Comments:

11 Description

Target	Annotations
Include the proprietary name and established name, dosage form and route of administration, qualitative and quantitative ingredients, pharmacologic or therapeutic class, and any other important physical and chemical characteristics.	*Summary information regarding completed or planned studies to support the target: Protocol #, Serial #, Submission date*

Comments:

12 Clinical Pharmacology

Target	Annotations
Include a concise factual summary of the clinical pharmacology and actions of the drug in humans. Data that describe the drug's pharmacologic activity can be included in this section, including biochemical or physiological mechanism of action, pharmacokinetic information, degree of absorption, pathway for biotransformation, percent dose unchanged, metabolites, rate of half-lives including elimination concentration in body fluids at therapeutic and toxic levels, degree of binding to plasma, degree of uptake by a particular organ or fetus, and passage across the blood-brain barrier. Include the following subsections:	*Summary information regarding completed or planned studies to support the target: Protocol #, Serial #, Submission date* *If applicable, a subsection (e.g., 12.4 Microbiology) can be created under this section heading and all of the microbiology information for antimicrobial products consolidated into that subsection.*

Comments:

12.1 Mechanism of Action: *Summarize **established** mechanisms of action in humans at various levels (e.g., receptor membrane, tissue, organ, whole body). Do not include theorized mechanisms of action.*

12.2 Pharmacodynamics: *Include a description of any biochemical or physiologic pharmacologic effects of the drug or active metabolites related to the drug's clinical effect or those related to adverse effects or toxicity. Include data on exposure-response relationship and time course of pharmacodynamic response.*

12.3 Pharmacokinetics: *Describe clinically significant pharmacokinetics of a drug or active metabolites (i.e., pertinent absorption, distribution, metabolism, and excretion parameters). Include results of pharmacokinetic studies that establish the absence of an effect, including pertinent human studies and in vitro data.*

13 Nonclinical Toxicology

Target	Annotations
Include the following subsections, as appropriate:	*Summary information regarding completed or planned studies to support the target: Protocol #, Serial #, Submission date*

Comments:

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility:

Results of long-term carcinogenicity studies — species identified

Mutagenesis results

Reproduction study results

13.2 Animal Toxicology and/or Pharmacology: *Ordinarily, significant animal data necessary for safe and effective use of the drug in humans should be included in other sections of the labeling, as appropriate. If the pertinent animal data cannot be appropriately incorporated into other sections of the labeling, this subsection can be used.*

14 Clinical Studies

Target	Annotations
Provide a description of studies that support statements about the efficacy or safety benefits. Consider including a description of supporting tables and graphs.	*Summary information about completed or planned studies regarding the intent to develop evidence to support benefits of treatment (i.e., safety or efficacy benefits of primary or secondary endpoints in the selected population):* *Protocol #, Serial #, Submission date* *Measurement instruments (e.g., patient-reported outcomes instrument) and references to supporting development and validation documentation* *Also consider including where the studies will be (or have been) run (i.e., geographical area).*
Comments:	

15 References — *Can include when labeling must summarize or otherwise rely on recommendation by authoritative scientific body, or a standardized methodology, scale, or technique, because information is necessary for safe and effective use.*

16 How Supplied/Storage and Handling

Target	Annotations
Include information about the available dosage forms to which the labeling will apply and for which the manufacturer or distributor will be responsible. For example: *Strength of the dosage form* *Units in which the dosage form ordinarily is available* *Information to facilitate identification of dosage forms* *Special handling and storage conditions*	*Summary information regarding completed or planned studies to support the target:* *Protocol #, Serial #, Submission date*
Comments:	

17 Patient Counseling Information

Target	Annotations
Include information for prescribers to convey to patients to use the drug safely and effectively. *For example:* *Precautions concerning driving* *Concomitant use of other substances that may have harmful additive effects* *Proper use and disposal of syringes and needles* *Adverse reactions reasonably associated with use of the drug* *Lab tests and monitoring required* *Indicate whether a Patient Package Insert or MedGuide are planned.*	*Summary information regarding completed or planned studies to support the target:* *Protocol #, Serial #, Submission date*
Comments:	

1. This guidance has been prepared by the Office of New Drugs in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.
2. For the purposes of this guidance, all references to *drug* include both human drugs and therapeutic biological products unless otherwise noted. All references to another product including *in vitro diagnostic* and other devices.
3. We update guidance periodically. To make sure you have the most recent version of a guidance, check the following web pages at:
   - http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/default.htm
   - http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm.
   - http://www.fda.gov/MedicalDevices/default.htm
4. See the guidance for industry *Fast Track Drug Development Programs — Designation, Development, and Application Review*
5. A clean copy of the Target Product Profile Template can be found at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm080593.pdf
6. Critical Path Initiative: http://www.fda.gov/ScienceResearch/SpecialTopics/CriticalPathInitiative/default.htm

Attachment 3: Regulatory Guidance for Devices Including Diagnostics

Overview of Device Regulation[50]

Introduction

FDA's Center for Devices and Radiological Health (CDRH) is responsible for regulating firms who manufacture, repackage, relabel, and/or import medical devices (including *in vitro* diagnostics [IVD]) sold in the United States.

In addition, CDRH regulates radiation-emitting electronic products (medical and non-medical) such as lasers, x-ray systems, ultrasound equipment, microwave ovens and color televisions.

Medical devices are classified into Class I, II, and III. Regulatory control increases from Class I to Class III. The device classification regulation defines the regulatory requirements for a general device type. Most Class I devices are exempt from Premarket Notification 510(k); most Class II devices require Premarket Notification 510(k); and most Class III devices require Premarket Approval. A description of device classification and a link to the Product Classification Database is available at "Classification of Medical Devices."

The basic regulatory requirements that manufacturers of medical devices distributed in the U.S. must comply with Medical Device Regulation, including all components below:

Establishment Registration - 21 CFR Part 807

Manufacturers (both domestic and foreign) and initial distributors (importers) of medical devices must register their establishments with the FDA. All establishment registrations must be submitted electronically unless a waiver has been granted by FDA. All registration information must be verified annually between October 1st and December 31st of each year. In addition to registration, foreign manufacturers must also designate a U.S. Agent. Beginning October 1, 2007, most establishments are required to pay an establishment registration fee.

Medical Device Listing - 21CFR Part 807

Manufacturers must list their devices with the FDA. Establishments required to list their devices include:

- manufacturers
- contract manufacturers that commecially distribute the device
- contract sterilizers that commercially distribute the device
- repackagers and relabelers
- specification developers

[50] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/default.htm

- reprocessors single-use devices
- remanufacturer
- manufacturers of accessories and components sold directly to the end user
- U.S. manufacturers of "export only" devices
- Medical Device Listing

Premarket Notification 510(k) - 21 CFR Part 807 Subpart E

If your device requires the submission of a Premarket Notification 510(k), you cannot commercially distribute the device until you receive a letter of substantial equivalence from FDA authorizing you to do so. A 510(k) must demonstrate that the device is substantially equivalent to one legally in commercial distribution in the United States: (1) before May 28, 1976; or (2) to a device that has been determined by FDA to be substantially equivalent.

On October 26, 2002 the Medical Device User Fee and Modernization Act of 2002 became law. It authorizes FDA to charge a fee for medical device Premarket Notifcation 510(k) reviews. A small business may pay a reduced fee. The application fee applies to Traditional, Abbreviated, and Special 510(k)s. The payment of a premarket review fee is not related in any way to FDA's final decision on a submissi

Most Class I devices and some Class II devices are exempt from the Premarket Notification 510(k) submission. A list of 501(k) exempt devices is located at:

If you plan to send a 510(k) application to FDA for a Class I or Class II device, you may find 510(k) review by an Accredited Persons beneficial. FDA accredited 12 organizations to conduct a primary review of 670 types of devices. By law, FDA must issue a final determination within 30 days after receiving a recommendation from an Accredited Person. Please note that 510(k) review by an Accredited Person is exempt from any FDA fee; however, the third-party may charge a fee for its review.

Premarket Approval (PMA) - 21 CFR Part 814

Product requiring PMAs are Class III devices are high risk devices that pose a significant risk of illness or injury, or devices found not substantially equivalent to Class I and II predicate through the 510(k) process. The PMA process is more involved and includes the submission of clinical data to support claims made for the device

Beginning fiscal year 2003 (October 1, 2002 through September 30, 2003), medical device user fees apply to original PMAs and certain types of PMA supplements. Small businesses are eligible for reduced or waived fees.

Investigational Device Exemption (IDE) - 21CFR Part 812

An investigational device exemption (IDE) allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support a Premarket Approval (PMA) application or a Premarket Notification 510(k) submission to FDA. Clinical studies with devices of significant risk must be approved by FDA and by an

Institutional Review Board (IRB) before the study can begin. Studies with devices of nonsignificant risk must be approved by the IRB only before the study can begin.

Quality System Regulation (QS)/Good Manufacturing Practices (GMP) - 21 CFR Part 820

The quality system regulation includes requirements related to the methods used in and the facilities and controls used for: designing, purchasing, manufacturing, packaging, labeling, storing, installing and servicing of medical devices. Manufacturing facilities undergo FDA inspections to assure compliance with the QS requirements.

Labeling - 21 CFR Part 801

Labeling includes labels on the device as well as descriptive and informational literature that accompanies the device.

Medical Device Reporting - 21 CFR Part 803

Incidents in which a device may have caused or contributed to a death or serious injury must to be reported to FDA under the Medical Device Reporting program. In addition, certain malfunctions must also be reported. The MDR regulation is a mechanism for FDA and manufacturers to identify and monitor significant adverse events involving medical devices. The goals of the regulation are to detect and correct problems in a timely manner.

Attachment 4: Summary of Related Activities

The following specific information must be provided by the Offeror pertaining to the Project Director, Principal Investigator, and each of any other proposed key professional individuals designated for performance under any resulting contract.

During negotiations, the Offeror has a continuing obligation to update the Government regarding changes to the information provided below.

a. Identify the total amount of all presently active federal contracts/cooperative agreements/grants and commercial agreements citing the committed levels of effort for those projects for each of the key individuals***** in this proposal.

Professional's Name and Title/Position:

Identifying Number	Agency	Total Effort Committed
1.		
2.		
3.		
4.		

*****If an individual has no obligation(s), so state.

b. Provide the total number of outstanding proposals, exclusive of the instant proposal, having been submitted by your organization, not presently accepted but in an anticipatory stage, which will commit levels of effort by the proposed professional individuals*****.

Professional's Name and Title/Position:

Identifying Number	Agency	Total Effort Committed
1.		
2.		
3.		
4.		

*****If no commitment of effort is intended, so state.

c. Provide a statement of the level of effort to be dedicated to any resultant contract awarded to your organization for those individuals designated and cited in this proposal.

Name	Title/Position	Total Proposed Effort
1.		
2.		

Attachment 5: Quad Chart Format Template

A quad chart must contain the following information and be positioned in a landscape view. Any quad chart submitted that exceeds the one-page limit will not be read or evaluated. Please note that the Title of the Project should be different than that of the Area of Interest.

TITLE OF PROJECT, BAA#, DEVELOPMENT AREA OF INTEREST, TECHNICAL/ADMINISTRATIVE POINT OF CONTACT (NAME, EMAIL, PHONE), COMPANY NAME & ADDRESS

Objective: Clear, concise (two to three sentences) description of the objectives and methodologies of the effort. Description of effort: A bullet list (2-3) of the primary scientific challenges being addressed	Picture or Graphic that Illustrates the research or concept (e.g. data figures, molecule illustrations or processes)
Benefits of Proposed Technology: Challenges: Maturity of Technology:	Bullet list of the major goals/milestones by Project Year Proposed Funding Base year cost plus each option year (Rough Order of Magnitude Estimate)

Attachment 6: Government Notice for Handling and Submitting Proposals

Note: This Notice is for the Technical Evaluation Review Panel who will be reviewing the proposals submitted in response to this BAA. THE OFFEROR SHALL PLACE A COPY OF THIS NOTICE BEHIND THE TITLE PAGE OF EACH COPY OF THE TECHNICAL PROPOSAL.

This proposal shall be used and disclosed for evaluation purposes only, and a copy of this Government notice shall be applied to any reproduction or abstract thereof. Any authorized restrictive notices, which the submitter places on this proposal shall be strictly complied with. Disclosure of this proposal outside the Government for evaluation purposes shall be made only to the extent authorized by, and in accordance with, the procedures in HHSAR 352.215-1 (Instructions to Offerors—competitive acquisition).

(a) If authorized in agency implementing regulations, agencies may release proposals outside the Government for evaluation, consistent with the following:

(1) Decisions to release proposals outside the Government for evaluation purposes shall be made by the agency head or designee;

(2) Written agreement must be obtained from the evaluator that the information (data) contained in the proposal will be used only for evaluation purposes and will not be further disclosed;

(3) Any authorized restrictive legends placed on the proposal by the prospective Contractor or subcontractor or by the Government shall be applied to any reproduction or abstracted information made by the evaluator;

(4) Upon completing the evaluation, all copies of the proposal, as well as any abstracts thereof, shall be returned to the Government office which initially furnished them for evaluation; and

(5) All determinations to release the proposal outside the Government take into consideration requirements for avoiding organizational conflicts of interest and the competitive relationship, if any, between the prospective Contractor or subcontractor and the prospective outside evaluator.

(b) The submitter of any proposal shall be provided notice adequate to afford an opportunity to take appropriate action before release of any information (data) contained therein pursuant to a request under the Freedom of Information Act (5 U.S.C. 552); and, time permitting, the submitter should be consulted to obtain assistance in determining the eligibility of the information (data) in question as an exemption under the Act. (See also Subpart 24.2, Freedom of Information Act.)

Attachment 7: Breakdown of Proposed Estimated Cost (Plus Fee) and Labor Hours (For Cost Proposal)

Refer to the ASPR Business Toolkit[51] for additional supplemental guidance and templates.

INSTRUCTIONS FOR USE OF THE FORMAT

1. This format has been prepared as a guideline. It may require amending to meet the specific requirements of this BAA. If the proposal is structured using options, identify each period independently. Each period should then be broken out into sub-elements.

2. This format shall be used to submit the breakdown of all proposed estimated cost elements. List each cost element and sub-element for direct costs, indirect costs and fee, if applicable. In addition, provide detailed calculations for all items. For example:

    a. For all personnel, list the skill / labor category, rate per hour and number of hours proposed. If a pool of personnel is proposed, list the composition of the pool and how the cost proposed was calculated. List the factor used for prorating base period and the escalation rate applied between periods.
    Offeror's proposal should be stated in the same terms as will be used to account for and record the effort under a contract. If percentages of effort are used, the basis to which such percentages are applied must also be submitted by the Offeror. The attached format should be revised to accommodate direct labor proposed as a percentage of effort.

    b. For all materials, supplies, and other direct costs, list all unit prices, etc., to detail how the calculations were made.

    c. For all indirect costs, list the rates applied and the base the rate is applied to.

    d. For all travel, list the specifics for each trip.

    e. For any subcontract proposed, submit a separate breakdown format.

    f. Justification for the need of some cost elements may be listed as an attachment, i.e., special equipment, above average consultant fees, etc.

3. If the Government has provided "uniform pricing assumptions" for this BAA, the Offeror must comply with and identify each item.

4. It is requested that you use the spreadsheet that is provided below (or to be provided with the Full Proposal invitation letter or prior to entering into negotiation) to prepare your cost proposal. Please submit a hard copy of the completed spreadsheet by mail and the electronic file (or diskette) by email (or by mail).

[51] http://www.phe.gov/about/amcg/contracts/Pages/toolkit.aspx

BREAKDOWN OF PROPOSED ESTIMATED COST (PLUS FEE, IF APPLICABLE) AND LABOR HOURS

Table 7: Breakdown (consisting of summary tab and separate tabs for each cost element) of Proposed Estimated Cost (Plus Fee, if applicable; insert as necessary: Contractor Cost-Share; Government Total Estimated Cost) and Labor Hours

COST ELEMENT	Period 1	Period 2	Period 3	Period 4	Period 5	
Labor Category	(Rate / Hours)	(Rate / Hours)	(Rate / Hours)	(Rate / Hours)	(Rate / Hours)	Total
DIRECT LABOR COST:	$	$	$	$	$	$
MATERIAL COST:	$	$	$	$	$	$
TRAVEL COST:	$	$	$	$	$	$
OTHER (Specify)	$	$	$	$	$	$
OTHER (Specify)	$	$	$	$	$	$
TOTAL DIRECT COST:	$	$	$	$	$	$
FRINGE BENEFIT COST: (if applicable) % of Direct Labor Cost	$	$	$	$	$	$
INDIRECT COST: % of Total Direct Cost	$	$	$	$	$	$
TOTAL COST:	$	$	$	$	$	$
FIXED FEE: (if applicable) % of Total Est. Cost	$	$	$	$	$	$
GRAND TOTAL ESTIMATED CPFF)	$	$	$	$	$	$

Attachment 8: Cost Certification

CERTIFICATE OF CURRENT COST OR PRICING DATA

This is to certify that, to the best of my knowledge and belief, the cost or pricing data (as defined in section 2.101 of the Federal Acquisition Regulation (FAR) and required under FAR subsection 15.403-4) submitted, either actually or by specific identification in writing, to the Contracting Officer or to the Contracting Officer's representative in support of _____* are accurate, complete, and current as of _____**. This certification includes the cost or pricing data supporting any advance agreements and forward pricing rate agreements between the offeror and the Government that are part of the proposal.

Firm _____

Signature _____

Name _____

Title _____

Date of execution***_____

* Identify the proposal, request for price adjustment, or other submission involved, giving the appropriate identifying number (e.g., RFP No.).

** Insert the day, month, and year when price negotiations were concluded and price agreement was reached or, if applicable, an earlier date agreed upon between the parties that is as close as practicable to the date of agreement on price.

*** Insert the day, month, and year of signing, which should be as close as practicable to the date when the price negotiations were concluded and the contract price was agreed to.