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

BAA-18-100-SOL-00003

Amendment 44

June 7, 2023

Biomedical Advanced Research Development Authority (BARDA)

Contracts Management & Acquisition (CMA)

400 7th St., SW

Washington, DC 20024

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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), Administration for Strategic Preparedness and Response (ASPR), Office of Biomedical Advanced Research and Development Authority (BARDA), 400 7th St., SW, Washington, DC, 20024

Issuing Office:

Department of Health and Human Services (HHS), Administration for Strategic Preparedness and Response (ASPR), Biomedical Advanced Research Development Authority (BARDA)/ Contracts Management & Acquisition (CMA), 400 7th St., SW, Washington, DC, 20024

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: 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:

- MedicalCountermeasures.gov[1]
- Public Health Emergency - PHE.gov[2]
- Grants.gov[3]
- SAM.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 encouraged to submit proposals and to join other entities as team members in

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

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:

Contracts Management & Acquisition (CMA) 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 Part VIII: 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 and Advanced Innovation Act of 2019.

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.

The application process is also described in the BARDA BAA Process Flow Chart (Part VIII: Attachment 10) and online on PHE's BARDA Broad Agency Announcement[5].

[5] https://www.phe.gov/about/amcg/BARDA-BAA/Pages/default.aspx

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. The final White Paper submission deadline is September 25, 2023, at 4:30 PM Eastern Time.	A receipt confirmation will be sent within 1 week. A response will be provided within 120 days of the submission deadline.

Proposal Stage	Deadline for Submission*	Government Response
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, or as specified in the invitation for Full Proposal letter in response to a White Paper submission. Full Proposal submission deadline is September 25, 2023, at 4:30 PM Eastern Time, or as specified in the invitation for Full Proposal letter in response to a White Paper submission for open areas of interest.	A receipt confirmation will be sent within 1 week. A response will be provided within 120 days of the submission deadline.

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

Submission Instructions:

All submissions in response to this BARDA BAA must be submitted to the BARDA Digital Resources (BDR) Portal (https://bdr.hhs.gov/) via the process described below.

IMPORTANT: Respondents will be required to apply for a BDR Portal account. This account can be requested by visiting the BDR Portal site and following the applicable prompts.

The account request process is simple but may take several days for approval and access. Account requests will require the Respondent to enter a set of basic information (i.e., first and last name, e-mail address, and phone number). Upon confirmation of a *BDR Portal* account, the Respondent will login using the prescribed two-factor authentication method. Once login is complete, the Respondent will be prompted to enter information about Respondent's organization and to input the submission with other project-specific information.

Failure to submit on-time due to late registration will result in the submission not being considered for award.

Respondents will be provided automated confirmation of successful submission.

Prior to submission of a White Paper, 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.

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 Contracts Management & Acquisition (CMA) 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[6]. Entities with a White 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 Part VIII:

[6] https://www.medicalcountermeasures.gov/Request-BARDA-TechWatch-Meeting/

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 Administration for Strategic Preparedness and Response (ASPR), in 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-Hazards Preparedness and Advanced Innovation Act of 2019 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*[7] (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[8] (August 2010), the *BARDA Strategic Plan 2011-2016*[9] (October 2011), and HHS Pandemic Influenza Plan[10] (June 2017).

Vaccines, therapeutics, diagnostics, 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's priority for influenza vaccines is sustainable, cost effective approaches that improve pandemic influenza preparedness and rapid response capabilities. BARDA's strategy to address this priority includes 1) improve vaccine effectiveness; 2) modernize production processes to decrease response time; 3) increase and diversify the sustainable domestic vaccine manufacturing infrastructure; 4) develop new adjuvants, delivery approaches, and other strategies that can provide a priming and protective response with a single vaccine dose and are more amenable to

[7] https://www.medicalcountermeasures.gov/media/1138/mcmreviewfinalcover-508.pdf
[8] https://www.medicalcountermeasures.gov/BARDA/documents/2010%20pcast-influenza-vaccinology.pdf
[9] https://www.medicalcountermeasures.gov/media/745/bardastrategicplan9-28--508.pdf
[10] https://www.medicalcountermeasures.gov/BARDA/Documents/pan-flu-report-2017v2.pdf

mass vaccinations in a response event. BARDA is also prioritizing broadly reactive immunotherapeutics, such as monoclonal antibodies, that will be effective in treating severely ill, hospitalized patients of all ages who are infected with influenza or in specific cases as described in subsequent sections, 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 older adults, 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 2017-2018 PHEMCE Strategy and Implementation Plan[11]. 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, older adults, 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

[11] https://www.medicalcountermeasures.gov/BARDA/documents/2017-phemce-sip.pdf

product development.

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[12] 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[13], (PAHPRA).
- The Pandemic and All-Hazards Preparedness and Advanced Innovation Act of 2019[14] Public Law 116-22 and 42 USC247d-7e[15]; (PAHPAIA)

Learn more about legal authorities, policies, and committees[16] and strategies and reports[17] for pandemic influenza, Chemical, Biological, Radiological, and Nuclear Medical Countermeasures.

[12] https://www.govinfo.gov/content/pkg/PLAW-109publ417/pdf/PLAW-109publ417.pdf
[13] https://www.govinfo.gov/content/pkg/PLAW-113publ5/pdf/PLAW-113publ5.pdf
[14] https://www.congress.gov/bill/116th-congress/senate-bill/1379
[15] https://uscode.house.gov/view.xhtml?req=42+USC+247d-7e
[16] http://www.phe.gov/preparedness/legal/Pages/default.aspx
[17] 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/BARDA's Contracts Management & Acquisition (CMA).

The final white paper submission deadline is September 25, 2023 at 4:30 PM Eastern Time. The final full proposal submission deadline is September 25, 2023 at 4:30 PM Eastern Time, or as specified in the invitation letter.

Area of Interest #1: CBRN Vaccines

The mission of BARDA's CBRN Vaccine program includes a critical need to develop vaccines to prevent the spread of disease or potentially protect those individuals who may be or who have recently been exposed to a threat agent but are not yet symptomatic. The CBRN Vaccine program seeks to support new vaccines or technologies that can provide flexible approaches to address emerging threats, improve operational logistics, and increase the sustainability of preparedness strategies. Vaccine(s) will be critical to mount an appropriate response to the emergence or spread of a pathogen that poses a significant threat to national security or public health. The current area of interest will focus on Ebola viruses, Marburg virus.

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 Ebola and Marburg virus. BARDA is interested in advanced development projects for monovalent vaccines against Sudan ebolavirus and Marburg virus, as these viruses represent urgent, unmet needs in terms of vaccine preparedness. The proposed vaccine candidate must have demonstrated protection from lethal challenge in non-human primate studies. The suggested animal model will utilize an acceptable intramuscular challenge model, with the Gulu strain (for Sudan ebolavirus) and/or the Angola strain (for Marburg virus). While not required, preference will be given to candidate products with Phase 1 clinical data, an active Investigational New Drug (IND) with the FDA, safety toxicity data, and demonstrated manufacturing process to support use in clinical trials. The objective of this program is to advance projects through the end of Phase 2 clinical development. The scope of work may include late preclinical development as long as IND submission is expected within one year of submission. Multivalent candidates will be considered only upon completion of phase 2 clinical study with clear guidance from FDA on regulatory pathway.

Alternative administration approaches and technologies that may reduce or eliminate bottlenecks related to ancillary supplies and distribution are of high interest. In the case of Sudan and Marburg vaccines, any such approaches should be evaluated early in the development program. For example, approaches that may be amenable to administration of the vaccine without needles, or distributed manufacturing of the vaccine, would potentially reduce bottlenecks related to syringe and needle availability and manufacturing scale up.

BARDA is interested in advanced development projects for licensed vaccines against Zaire ebolavirus that may meet key program goals in terms of improving the operational use of late-stage products. BARDA's goals in this area are focused on 1) expanding label indication to include special populations and/or 2) generating data to support a potential boosting strategy, if needed. Projects in this area will be limited to vaccine candidates for which phase 2 clinical trials have been completed.

Technical Point of Contact: Daniel Wolfe; Daniel.Wolfe2@hhs.gov

Contracting Point of Contact: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI 1 (CBRN Vaccine): <brief description>"

Area of Interest #2: CBRN Antivirals and Antitoxins

BARDA is seeking therapeutics that will improve preparedness and response against toxins and viruses that pose a threat to the American public. Candidates must demonstrate efficacy against anthrax, botulism, smallpox or filoviruses as summarized in 2.1-2.4. BARDA is also interested in such candidates that have potential for broad activity against multiple toxins, toxin classes, viruses, virus genera or virus families. BARDA's strategy is to develop products that are sustainable, improve operational logistics or capabilities, and reduce risk through diversification of countermeasures. Candidates for funding under this area should be at TRL-5 (lead identified) or higher, as indicated below. However, candidates earlier in development may be considered if it is anticipated they will significantly improve existing capabilities. Competitive products will expand current response capabilities either through:

1. Product type (e.g., mAbs or mAb cocktails, peptides, small molecules or novel compounds, etc.)
2. Mechanism of action
3. A significant change in operational use and/or total life cycle cost (e.g., route of administration, shelf-life >10 years, significant reduction in cost of goods, etc.)

Additional considerations for Offerors preparing white papers or full proposals can be found in *Part II: Development and Technical Objectives* of this BAA.

2.1 Anthrax Antitoxins. Candidates for funding under this BAA must advance or expand current response capabilities against the threat of inhalational anthrax. The Department of Homeland Security issued Material Threat Determinations for *Bacillus anthracis* (*B. anthracis*) in 2004 and multi-drug resistant (MDR) *B. anthracis* in 2006. *B. anthracis* is considered a serious bioterrorism agent due to the ability of the spores to persist in the environment, the ability of aerosolized spores to readily cause infection, and the high mortality of inhalation anthrax.

HHS is pursuing a comprehensive strategy to address the threat of anthrax, including the procurement of antimicrobial drugs, vaccines, and therapeutics to the Strategic National Stockpile. A competitive product will encompass some or all of the characteristics below to maximize and diversify the capabilities of the United States Government to launch an effective response to a public health emergency caused by anthrax:

- Non-intravenous route of delivery;
- A minimum of three-year shelf life with the potential for extension to 10-years;
- Product form not requiring cold-chain;
- Equivalent or improved efficacy in comparison to currently licensed products;
- Different product class and/or mechanism of action relative to FDA-approved anthrax antitoxins;
- Compatibility with, and mechanism of action that complements, antibiotic treatment;
- Potential for efficacy against toxins produced by MDR or engineered *B. anthracis*.

2.2 Botulism Antitoxins. Candidates for funding under this BAA must advance or expand current response capabilities against the threat of botulinum intoxication. In 2004, the Department of Homeland Security (DHS) determined that *Clostridium botulinum* (*C. botulinum*) presents a material threat to national security. Based on this Material Threat Determination and the subsequent Material Threat Assessment, HHS has identified a requirement for a botulinum antitoxin with efficacy against botulinum neurotoxin serotypes A-G.

To improve upon and diversify the United States Government's preparedness against this priority threat, BARDA aims to support the development of improved next-generation botulism antitoxins. A competitive antitoxin product will encompass some or all of the characteristics below to maximize and diversify the capabilities of the United States Government to launch an effective response to a public health emergency caused by botulinum:

- A single heptavalent product or a combination of antitoxins that covers serotypes A-G;
- Non-intravenous route of delivery;
- A minimum of three-year shelf life with the potential for extension to 10-years;
- Product form not requiring cold-chain;
- Equivalent or improved efficacy in comparison to currently licensed products;
- Different product class and/or mechanism of action relative to FDA-approved botulinum antitoxins.

2.3 Smallpox Antiviral. The Department of Homeland Security (DHS) issued a Material Threat Determination for smallpox in 2004, establishing it as a threat to national security. Periodic smallpox outbreaks were common prior to the twentieth century with fatality rates of greater than thirty percent. Although smallpox was eliminated as an endemic disease by 1980, the potential re-emergence of the virus via natural sources or a bioterrorist act remain a possibility.

A competitive therapeutic candidate will encompass the characteristics below to build upon existing capabilities of the United States Government:

- TRL-6 or higher;
- Demonstrated preclinical efficacy against orthopoxviruses in appropriate animal models;
- Different product class and/or mechanism of action relative to existing FDA-approved smallpox therapeutics;
- Potential to complement existing FDA-approved smallpox therapeutics;
- Offers potential for a substantial improvement in or expansion of current response capabilities; products that offer minimal or incremental gains are not a current priority.

2.4 Filovirus Therapeutics. In 2006, the Department of Homeland Security determined that Ebola virus and Marburg virus are material threats to national health security. Medical countermeasures that can be deployed in the event of a filovirus outbreak are a crucial component to the United States Government's outbreak response plan. BARDA is seeking to augment response capabilities with therapeutics targeting species of *Ebolavirus* and *Marburgvirus* with potential to cause disease in humans.

A competitive therapeutic candidate will encompass some or all of the characteristics below to build upon existing capabilities of the United States Government:

- Demonstrated preclinical efficacy for at least one filovirus species in a relevant animal model, with strong preference for efficacy when administered after onset of symptoms and for demonstrated or anticipated efficacy against multiple filovirus species;
- A minimum of three-year shelf life with the potential for extension to 10-years;
- Product form not requiring cold-chain;
- Non-intravenous route of delivery;
- A product type other than a monoclonal antibody or antibody cocktail.

Specifically for candidate products with preclinical efficacy only for the *Zaire ebolavirus*, candidates must be TRL-6 or higher and have at least one of the following:

- Non-intravenous route of delivery;
- Different product class and/or mechanism of action relative to existing FDA-approved Ebola virus therapeutics;
- Potential to complement existing FDA-approved Ebola virus therapeutics via demonstrable efficacy in immune privileged sites, including the reproductive tract and central nervous system; efficacy against persistent infection; beneficial impact on long term sequelae associated with Ebola virus infection; or efficacy in severe acute infection.

Technical Point of Contact: Dr. Karen Martins; Karen.Martins@hhs.gov

Contracting Point of Contact: BARDA-BAA@hhs.gov with the subject line “Contracting questions: AOI 2 (CBRN Antitoxin): <brief description>”

Area of Interest #3: Antibacterials

The mission of BARDA's Antibacterials Program is to minimize the morbidity and mortality caused by multidrug-resistant organisms (MDROs) and biothreat pathogens.

Critical to national preparedness is the availability of safe and effective antimicrobial drugs for all patient populations. During routine medical practice, public health emergencies, and mass casualty events, hospital-associated and community-acquired infections caused by MDROs can complicate patient care and recovery. Antimicrobial resistance also poses a risk to our ability to respond to biothreat infections due to limited treatment options, particularly for special populations including pediatrics. Antimicrobial resistance places a substantial health and economic burden on society and will continue to do so if not adequately addressed.

The Antibacterials Program seeks to accelerate innovation and product development through public-private partnerships that support the advanced research, development, manufacture, regulatory approval, and availability of novel antimicrobial candidates against MDROs. Of particular interest to the Government are proposals which aim to:

3.1 Develop products for treatment of MDROs and biothreat pathogens.

Drug candidates with activity against bacterial pathogens identified by the Centers for Disease Control and Prevention (CDC) as "urgent" or "serious" threats[18] as well as multiple strains of one or more biothreat pathogens (*Bacillus anthracis*, *Yersinia pestis*, *Francisella tularensis*, *Burkholderia mallei*, and *Burkholderia pseudomallei*) will be prioritized. Though candidates with aforementioned dual activity are favored, candidates with activity only against CDC priority bacterial pathogens (no biothreat activity) will also be considered.

Priority will also be given to drug candidates that:

1. Address hospital-associated and community-acquired drug-resistant infections as well as secondary or opportunistic infections;
2. Are clinically differentiated from approved antimicrobials (e.g. respiratory or bloodstream infections);
3. Have an improved formulation or alternate delivery regimen (e.g. oral, once daily intravenous or intramuscular dose);
4. Offer therapeutic benefit to all segments of the American population, including but not limited to pediatric subjects, older adults, and pregnant women.
5. Have an activity profile (MIC_{50} and MIC_{90}) and propose a development path that will generate data that could support a pre-Emergency Use Authorization for a biothreat pathogen (e.g. animal efficacy studies and potentially a clinical trial for respiratory infections);

All aspects of advanced clinical stage drug development are considered permissible for funding, including nonclinical studies, safety, toxicology, microbiological studies, pharmacokinetics (PK)/pharmacodynamics (PD), manufacturing, analytical assay development and validation, clinical studies including pediatric studies, regulatory submission preparation, development of diagnostics to enhance clinical trial enrollment or inform product use in the target patient population (e.g. susceptibility testing or

[18] https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

therapeutic drug monitoring), and post-approval requirements.

3.2 Treatment of MDR fungal infections.

BARDA is seeking to support the development of broad-spectrum antifungal drug candidates with novel mechanisms of action that target *Candida* species*,* including *Candida auris*, and *Aspergillus* species. Candidates that also demonstrate activity against rare molds, such as Mucorales, are of interest. Drug candidates must be TRL6 or higher.

Priority will be given to drug candidates with the following characteristics:

- Represent a first-in-class antifungal with a novel mechanism of action (including novel targets). Candidates within existing classes (e.g., azoles, echinocandins, polyenes, pyrimidines) may be considered though they must demonstrate a significant improvement over FDA approved products (e.g., reduced toxicity, effectiveness against resistant strains, acceptable dosing schedule, expanded spectrum of activity, potential for use in pediatrics or other special populations);
- Have an improved formulation or alternate delivery regimen (e.g., oral and intravenous) with limited duration of therapy

Qualities that strengthen the competitiveness of a proposal

A well-conceived proposal should summarize key concepts that demonstrate the product developer's knowledge and understanding of the market need and development pathway for the drug candidate. The proposal should provide sufficient detail on the candidate's current state of development (nonclinical and clinical), manufacturing scale, the direction for future development, and the current regulatory status and plan to obtain product approval.

- Innovation: Candidates demonstrating substantial improvements over existing antimicrobial products are of greatest priority, including first-in-class compounds with novel mechanisms of action as well as non-traditional modalities and compounds (e.g. bacteriophage, host-directed immunotherapeutics, etc.). If a candidate belongs to an existing antimicrobial class (same/similar chemistry and molecular target), it must demonstrate a significantly meaningful improvement over other similarly marketed products or products in development (e.g. broader spectrum of activity, reduced toxicity, utility in special populations, etc.). Beta-lactam/beta-lactamase inhibitor combinations are restricted to candidates that are broad spectrum (candidate needs to address both serine and metallo-beta-lactamases).

- Biodefense: If biothreat development is proposed, *in vitro* activity (MIC_{50} and MIC_{90}) against the proposed biothreat pathogen(s) must be demonstrated. *In vivo* efficacy in relevant animal models of infection will strengthen the proposal. Post-exposure prophylaxis will only be considered in the context of a biothreat pathogen. If the drug candidate will not be developed for a biothreat pathogen the proposal must describe how the candidate will be used as part of a response during a public health emergency (e.g. secondary bacterial infections following a CBRN event, a flu pandemic, or outbreak of an emerging infectious disease).

- Optimized development: Programs demonstrating novel approaches that improve

upon traditional drug development (e.g. novel clinical trial designs that optimize limited patient resources, continuous manufacturing) are of greater interest.

- Development stage of the drug candidate: In general, drug candidates in more advanced stages of development will be prioritized over those in earlier stages. Candidates should minimally have an open IND. More advanced candidates that have progressed into and completed some clinical development studies (i.e., Phase 1 or 2) and have achieved manufacturing at a scale greater than benchtop are preferred. Offeror's seeking consideration for an Other Transaction Agreement must propose multiple candidates with at least one in Phase 3 clinical development.

- Regulatory feasibility: Because it is BARDA's mission to support U.S. Food and Drug Administration (FDA) approval of the prioritized drug candidate, evidence of regulatory correspondence from the FDA that indicates support for the development plan and a feasible path toward approval of the candidate should be presented in the appendix of the proposal.

- 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 encouraged.

BARDA requests that Offerors provide a summary of their commercialization strategy for the proposed product and a corporate sustainability strategy. This information will help BARDA understand the commercial landscape for the product and how the company and product will be sustained. The summary can be provided in an appendix that will not count against the proposal page count.

Learn more about Antibacterials[19].

Technical Point of Contact: Dr. Mark Albrecht; Mark.Albrecht@hhs.gov

Contracting Point of Contact: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI 3 (Antibacterials): <brief description>"

[19] https://www.medicalcountermeasures.gov/barda/cbrn/antibacterials/

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

Radiological/Nuclear threats include accidental or intentional incidents resulting in exposure to ionizing radiation, such as the use of a radiological dispersal device or nuclear detonation. The priority focus is on medical consequences from a nuclear detonation as it is a higher impact threat. Injuries resulting from nuclear detonations include radiation exposure, mechanical trauma, and thermal burns (see AOI6). All injuries are likely to be complex and could include combined injuries from radiation exposure concomitant with mechanical trauma or thermal burns.

Radiation exposure causes severe injury at the cellular level (*e.g.* DNA damage and reactive oxygen species production) that results in systemic cellular apoptosis, loss of progenitor cells, endothelial cell damage, and altered cell metabolism. These injuries lead to the clinical manifestation of Acute Radiation Syndrome (ARS). ARS involves systemic disruption of vascular and immune homeostasis and integrity, which can include endotheliopathy, coagulopathy, inflammation, bone marrow depletion, and pancytopenia and subsequently lead to hemorrhage, ischemia, multi-organ failure, and/or infection/sepsis. Several of these are shared pathophysiologies with the systemic effects of mechanical trauma.

Mechanical trauma sustained during a radiological/nuclear event may be due to blast forces, projectile debris, or thermal radiation. MCMs that address systemic dysregulation of vascular and immune homeostasis, which may include hemorrhage, coagulopathy, inflammation, and sepsis, due to radiation injury and/or mechanical trauma should be submitted under Area of Interest (AOI) #4 Radiological/Nuclear Threat MCMs. MCMs that address detection, mitigation, or management of the consequences of mechanical trauma related to disruption of the structural integrity of body organ tissue, bones, and blood vessels should be submitted to AOI #6 Burn and Blast MCMs. Both programs reserve the right to cross-reference or swap submissions as they fit programmatic priorities.

BARDA Area of Interest #4 focuses on the development of MCMs to treat radiation injury, mechanical trauma, and/or combined injury that results from a radiological/nuclear event. Offerors proposing work in this area of interest should be at a TRL 5 or higher for ARS, mechanical trauma, or related indications. 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 FDA meeting minutes, if requested. Offerors should plan to address the needs of special populations (see Background).

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

Emergency response to a radiological/nuclear event will likely follow two general phases of treatment: field care and definitive care. The field (or pre-hospital) care phase generally includes the first 72 hours of the emergency response. During this time resources and trained personnel are expected to be exceedingly scarce, thus delaying

and limiting access to advanced medical care and treatments. The definitive care phase is administered at medical centers or hospitals and generally extends beyond the initial 72 hours of the emergency response. Definitive care includes the full range of medical support and treatments necessary to manage a patient's condition. Desirable MCM characteristics should improve flexibility and usability in a mass casualty incident including favorable storage conditions (e.g., storage at room temperature), ease of use (e.g. favorable deployment and route of administration), and sufficient efficacy when administered a minimum of 24 hours or later after injury. Efficacy should be assessed based on improved survival outcome or mitigation of relevant clinical endpoints. Priorities for the field (pre-hospital) and definitive care phases include next generation blood products, cellular therapies, and products that enhance the engraftment and/or activity of these therapies, among others.

b) Repurposing Commercially Available Products

Familiarity with MCM products and procedures as part of routine medical care by practitioners could greatly improve capabilities in the event of a radiological/nuclear mass casualty incident. 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. For either licensed or novel products, the proposed development plan could include parallel activities for additional commercially relevant indications. A clear business strategy should be included in the plan for establishing a self-sustainable commercial market space to allow use of a Vendor-Managed Inventory (VMI) for emergency use by the USG, if feasible.

c) Addressing Multiple Relevant Indications or Multiple Threat Areas

BARDA prioritizes host-based MCMs that have the potential to treat multiple relevant indications or multiple threat areas, as similar clinical manifestations may result from a variety of potential injuries or exposures. Threat agents may have similar underlying mechanisms that disrupt homeostasis or result in similar conditions. For example, coagulopathy is observed as a result of exposure to ionizing radiation, mechanical trauma, and viral hemorrhagic fevers; in this example, MCMs that treat coagulopathy could be prioritized. Examples of other common pathophysiologies requiring host-directed therapeutics include vascular injury, inflammation, and endotheliopathy.

Please note that while host-based MCMs are prioritized, submissions to Area Interest #4 must include an indication for an injury that results from a radiological/nuclear incident.

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

b) Novel and repurposed therapeutics to address microvascular and macrovascular injuries and endotheliopathy, including therapeutics to address vascular permeability and repair, hemorrhage, coagulopathy, ischemia, or resultant multi-

organ failure.

c) Novel and repurposed therapeutics to address systemic inflammatory and immune responses resulting from acute exposure to ionizing radiation.

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. BARDA could support advanced development of next generation blood products that will enhance our ability to respond to mass casualty events and meet blood product treatment gaps. The proposed indication should be an injury or condition that results from radiation exposure, mechanical trauma, or both (see considerations above) sustained during a radiological/nuclear event. Products and technologies should minimize immunological barriers associated with transfusions and other transplantations (e.g., ABO and HLA typing).

Potential areas of development include, but are not limited to:

a) Technologies that improve the safety and availability of blood products in a mass casualty event. This may include pathogen reduction technologies and next generation blood products that have improved storage characteristics that will allow them to be stockpiled or available for use in a field care/prehospital setting (e.g., extended shelf life or storage at elevated temperatures).

b) Pharmaceuticals that could be used in lieu of blood products to treat hemorrhage. Candidates will improve patient outcome, reduce the need for transfusions, be fast acting, and/or be available in a field care/prehospital space.

c) Next generation blood products derived from stem and progenitor cells to produce safe and non-alloimmunizing human red blood cell, platelet, or white blood cell products for use in transfusing humans.

d) Technologies for reliably producing hematopoietic stem cells and their progenitors, including optimization of directed differentiation and engraftment of functional and safe hematopoietic cells. Programs can include activities to improve cell processing, optimize 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 (preferred; seeks intracellular or distributed depots) chelators of radionuclides of high threat potential. Development of decorporation agents with additional commercial utility (e.g. lead, gadolinium) are of particular interest as are formulations appropriate for all age populations, especially for children under the age of two years and others who may have difficulty swallowing solid oral dosage forms.

4.4 Enabling Technologies: BARDA is seeking technologies that help elucidate the natural history of injuries that result from radiological/nuclear events that also have forward looking applications for MCM development. Technologies could also enable:

identification of novel therapeutic targets; development of assays for diagnosis or prognosis; and/or improvement of MCM testing and screening. BARDA may support development and use of new technologies for**:**

a) Development of 3-D microphysiological systems to help elucidate the natural history of radiation injury and aid in new therapeutic target identification.

b) Development of assays for key radiation injury biomarkers to aid in product development; circulatory biomarkers and non-invasive imaging assays are of particular interest for assessing vascular permeability, hemorrhage, coagulopathy, systemic inflammatory and immune responses, ischemia, or resultant multi-organ failure.

BARDA encourages innovation. For Area of Interest #4:, innovations could range from pre-clinical through licensure development plans or strategies. For example, product development plans might include a systems biology approach, use of microphysiological systems, 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[20].

Technical Point of Contact: Dr. Mary J. Homer; Mary.Homer@hhs.gov

Contracting Point of Contact: BARDA-BAA@hhs.gov with the subject line “Contracting questions: AOI4 (Rad/Nuc MCM): <brief description>”

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

Area of Interest #5: Chemical Threat Medical Countermeasures

The mission of BARDA's Chemical Medical Countermeasures program is to develop MCMs that treat the acute and chronic health effects of chemical threats, are easy to administer in a mass-casualty situation, and are rapidly effective as post-exposure therapies. The specific injuries caused by exposure to chemicals are often similar or identical to conditions observed in clinical practice; therefore, Offerors should propose a relevant commercial indication for their candidate as applicable. Proposals that contemplate expansion of indications of already approved/authorized drugs are preferred. All Chemical MCMs should be safe and effective for the entire population, including infants, children, adolescents, older adults, pregnant women and immunocompromised individuals.

The Chemical MCM Program seeks to accelerate innovation and product development through public-private partnerships that support the advanced research, development, manufacture, regulatory approval, and availability of effective and novel MCMs against chemical threats. The following thrust areas are prioritized:

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

5.2 Opioids: Development of MCMs to treat life-threatening respiratory depression caused by opioid overdose. These post-exposure treatments should be fast-acting and effective against a variety of opioids, including synthetic opioids such as Fentanyl and derivatives, and must be amenable to emergency use in the field. Candidates should have a mechanism of action different from existing opioid receptor antagonists. *Note that the remit of the Chemical MCM program is the emergency treatment of overdose rather than prevention or treatment of opioid use disorder.*

5.3 Vesicants: Development of MCMs that limit harmful aspects of exposure to vesicating agents such as sulfur mustard and lewisite. Particular preference is given to drugs with the potential to prevent or ameliorate the chronic effects of vesicant exposure

5.4 Blood/Metabolic Agents: Development of MCMs to treat acute poisoning from metabolic agents (e.g. cyanides). Treatments should be easily administered by first responders in personal protective equipment. Preference is given to those treatments that are also effective against smoke inhalation-related exposure.

5.5 Nerve Agents and Organophosphorus (OP) Pesticides: Development of label-expansion indications of already FDA-approved medications that can be used to treat the muscarinic, nicotinic, or seizure-causing effects of nerve agent and pesticide exposure. An additional focus is the treatment of benzodiazepine refractory seizures.

5.6. Novel MCM Delivery Mechanisms: Development of improved methods and/or routes 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.

Under Area of Interest #5, all aspects of advanced clinical stage drug development are considered permissible for funding, including nonclinical studies, safety, toxicology, pharmacokinetics (PK)/pharmacodynamics (PD), manufacturing, analytical assay

development and validation, clinical studies including pediatric studies, regulatory submission preparation, and post-approval requirements.

5.7 Innovative Approaches to Understanding Chemical Injury in Humans: Creative solutions including but not limited to *in vitro* humanized systems (such as organoids/organ chips/microphysiological systems) and human-relevant animal models to better characterize the human response to toxic chemical exposure. Developers are expected to establish a link between their models and real-world evidence. The goal of these efforts is to identify therapeutic targets and support development of new treatment candidates.

Qualities that strengthen the competitiveness of a proposal

A well-conceived proposal should summarize key concepts that demonstrate the product developer's knowledge and understanding of the market need and development pathway for the drug candidate. The proposal should provide sufficient detail on the candidate's current state of development (nonclinical and clinical), manufacturing scale, the direction for future development, and the current regulatory status and regulatory approach. Factors to be considered include (but are not limited to):

- Development stage of the drug candidate: In general, drug candidates in more advanced stages of development will be prioritized over those in earlier stages. The minimum technology readiness level (TRL) for Chemical MCM candidates should be at TRL 4 or higher for the relevant indication; *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. More advanced candidates that have progressed into and completed some clinical development studies (i.e., Phase 1 or 2) and have achieved manufacturing at a scale greater than benchtop are preferred. Strong preference will be given to drug candidates that are already approved or are in late-stage clinical development for a conventional indication which has similar symptomology to that arising from exposure to a chemical agent.

- Regulatory feasibility: Because it is BARDA's mission to support U.S. Food and Drug Administration (FDA) approval of the prioritized drug candidate, evidence of supportive regulatory correspondences from the FDA concerning the development plan of the candidate and a feasible path toward approval should be in place and presented in the proposal. 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.

- Relevant Concept of Operations: All MCMs should have a treatment window consistent with civilian response. There will most likely be a significant delay (>30 minutes) in the administration of even emergency MCMs after exposure. The proposed route of delivery should be consistent with the timing or setting for use: for instance, IV administration would be acceptable for a treatment to be used in the hospital but not for an emergency treatment in the field.

- Multifunctional Treatments: The Chemical MCM program prioritizes broad-spectrum treatments that can address multiple threats that have similar effects (e.g., lung injury resulting from both sulfur mustard and chlorine exposure). As

previously stated, all MCMs developed by the program should have a conventional clinical indication. Proposed development plans can include parallel tracks for clinical and MCM indications.

- 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 encouraged.

BARDA requests that Offerors provide a summary of their commercialization strategy for the proposed product and a corporate sustainability strategy. This information will help BARDA understand the commercial landscape for the product and how the company and product will be sustained. The summary can be provided in an appendix that will not count against the proposal page count.

Learn more about Chemical Medical Countermeasures[21].

Technical Point of Contact: Dr. Judith Wolfe Laney; Judith.Laney@hhs.gov

Contracting Point of Contact: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI5 (Chem MCM): <brief description>"

[21] https://www.medicalcountermeasures.gov/barda/cbrn/chemical-medical-countermeasures.aspx

Area of Interest #6: Burn and Blast Medical Countermeasures

BARDA has a responsibility to effectively diagnose, treat, and prevent exacerbation of injuries and medical consequences from burn and blast trauma in the civilian population resulting from various threats. Detonation of a nuclear device is among the largest challenges under consideration for mitigation under this BAA. Our strategic priorities include the development of MCMs across the entire continuum of care for burn and blast trauma and ensuring their sustainability and adoption for timely availability. This BAA covers detection and determination of injury severity, triage and proper interventional treatment for management of injuries, and delivery of definitive care.

BARDA actively collaborates with the medical community to address the range of injuries associated with burn and blast trauma. We strive to identify critical procedures and technologies that may address bottlenecks and improve the efficiency in delivery of care, especially in an MCI. The paradigm in delivery of care requires consideration of the treatment window and the need for urgent intervention as well as delivery of more permanent treatments. The two temporal aspects have been denoted as **'initial care**' and '**definitive care**.'

Initial care typically covers the first 72 hours of the emergency response. The primary goal is to provide early life-saving interventions and stabilize patients in order to transfer them to definitive care medical facilities. Initial care treatments could be administered at or near the incident site as part of the triage and evacuation process. Resources and trained personnel are anticipated to be scarce. MCMs should have an intuitive and easy to use functionality and be integrated into routine care to ensure caregivers have expertise for their use. Offerors are referred to guidance on MCM compatibility with the published RTR medical response system (Prehosp Disaster Med. 2009 May-Jun; 24(3):167-78).

Definitive care typically covers advanced diagnoses, evaluations, treatments and procedures after patients are transferred to a medical facility. Products are initially screened for their potential impact on the resultant cost effectiveness as a critical measure of their value proposition as an MCM. The type of MCMs envisioned to provide definitive care range from devices to biologics and therapeutics. Such products should provide detection, evaluation and decision-assist capabilities in acute care as well as contributing to faster recovery and a shortened hospital length of stay. The MCMS may also aid convalescence, restorative, or rehabilitative medical care.

Guidelines for Advanced Development of Burn and Blast MCMs: Mechanical trauma sustained during a radiological/nuclear event may be due to blast forces, projectile debris, or thermal radiation. MCMs that address detection, mitigation, or management of the consequences of mechanical trauma related to disruption of the structural integrity of body organ tissue, bones, and blood vessels should be submitted to Area of Interest (AOI) #6 Burn and Blast MCMs. MCMs that address systemic dysregulation of vascular and immune homeostasis, which may include hemorrhage, coagulopathy, inflammation, and sepsis, due to radiation injury and/or mechanical trauma should be submitted under AOI #4 Radiological/Nuclear Threat MCMs. Both programs reserve the right to cross-reference or swap submissions as they fit programmatic priorities.

Under this BAA, proposed MCMs should have demonstrated the proof-of-concept for the intended use. Data from key parameters such as sensitivity, specificity, effectiveness to

mitigate injury in a reliable model or evaluation should be presented. The MCMs should have the ability to address one or more challenges or bottlenecks in delivery of care as well morbidity associated with injuries from burn or blast trauma. Products are of significant interest if they already have a commercial presence and/or are currently marketed for other indications and have the potential to expand the indication for use to be of value as an MCM.

- **Goals:** proposals for MCM products should have a reasonable approach to address the two goals listed below:

  1) List the types of traumatic injuries a product will help mitigate and provide a strong rationale to address one or more critical bottlenecks in delivery of routine care such that its value is especially evident for use in an MCI; and 2) Have a reasonable path including cost effectiveness which will enable integration into the treatment care paradigm over the long term. Ultimately, we seek products which can become the standard of care and achieve market sustainability while also being an MCM for use in an MCI.

- **Attributes:** The proposed MCMs should have one or more attributes amenable for their integration into routine care as well as show value in reducing bottlenecks in an MCI. The product should not impede the effectiveness of current standards of care in other downstream procedures.

  - Ease of administration and high therapeutic index
  - Robust stability and ease of storage and deployment
  - Ability to accelerate healing, prevent injury exacerbation, or act with specificity in order to directly impact reduction in the length of hospital stay
  - Reduction in resource needs such as surgical needs, time and facilities
  - Enable faster triage and decision assistance for treatment strategy
  - Stabilize patients to expand the timeframe so a delay in definitive care could be managed without complications via temporary interventions or wound coverage

- **Data and FDA Input:** Offerors are required to provide reasonable supporting data that the proposed MCMs offer a clinically meaningful benefit to the patient. This includes proof-of-concept data with justifiable and specific endpoints for their eventual clinical use. It is required that Offerors have sought at least initial guidance from the FDA on a regulatory strategy and clinical development strategy for the proposed MCM. Such data may include testing, treatment goals or study endpoints, and indications for use to outline the path for clearance or approval. Such guidance sought from the FDA should be part of a White Paper or proposal submission for consideration. BARDA may request additional documentation to support FDA input.

- **The Technology Readiness Level (TRL):** The technology would be expected to be TRL 5 or higher (i.e. completed all activities for TRL 5 as described in Attachment 1). Offerors should have held a pre-IND, pre-IDE, or pre-submission meeting with FDA to discuss licensure, clearance and approval as an MCM prior to the submission of a White Paper to the BARDA BAA.

- **Market Sustainability:** All submissions shall include a section outlining a plan for establishing market sustainability for the proposed MCM. Such plans may include having broader clinical indications in conventional care or providing better value proposition for an unmet need in routine care. The Offeror should clearly demonstrate the anticipated benefits as well as objectively analyze potential limitations of their proposed MCM compared with current standard of care (SOC) for the same indication.

Product Areas of Specific Interest in Initial Care and Definitive Care:

6.1 Enabling Technologies to Address General Burn & Blast Traumatic Injuries: The goal for products developed under this category is the ability to demonstrate a substantive reduction of morbidity and mortality due to complications resulting from burn and blast trauma. Types of injuries which may be addressed include extremity fractures, hematomas, severe lacerations and penetrating trauma, and crush injuries. Consistent with the guidelines above, for a product to be considered, Offerors must demonstrate preliminary data on detection capability and/or effectiveness. Specifically, data supporting the rationale for the mode of action or capability should reasonably extrapolate the value of the MCM, such as faster triage or reduction in morbidity and mortality compared to the current standard of care or procedures. Products in this category may include advanced imaging devices, non-invasive fracture fixation devices, or devices enabling minimally invasive vital signs monitoring and enabling continuity of tracking patient data and telemedicine. Products may also include patient-centric device improvements which have a proven efficacy in reducing infections. Products may be independent or may involve concomitant administration of drugs and biologics. Ultimately, the products must meet the broader goals described in the guideline sections above, should address a specific gap in the burn or trauma care continuum, and show a reasonable path to adoption in routine care.

- **6.2 Head & Neck Injuries in Trauma:** The goal for product development under this category must address a specific gap in the current care continuum and show a reasonable path to adoption in routine care. Products could address detection of neurotrauma or moderate to severe acute traumatic brain injuries (TBI) either non-invasively or in a minimally-invasively manner to provide initial treatment. Conditions typically seen in such injuries, such as internal brain hemorrhage, elevated intracranial pressure (ICP), or cervical spine injury fall within this category. Products could also enable or provide minimally invasive therapeutic value to ultimately reduce morbidity and mortality of patients with TBI. For a product to be considered, Offerors must demonstrate preliminary data and supporting rationale for the technology to enable diagnostic triage of traumatic injuries to the head and neck (primarily brain and cervical spine) region.

<u>Desirable attributes for products that address traumatic injuries to the head and neck as described above should include:</u>

1) Provides easy to interpret imaging or output which supports decision assist capability for care providers to detect internal brain hemorrhage and/or elevated intracranial pressure; 2) Rapid, easy and portable (ideally non-invasive) use by trauma specialists and emergency care physicians in a hospital setting; 3) Devices

which demonstrate specificity and sensitivity equivalent or better than the current standard of care for assessment of comprehensive brain injury; 4) Ability to provide rapid monitoring, controls and/or stabilization for TBI to provide decision assist or expand the treatment window, improve patient outcomes, survivability and reduce secondary effects or more permanent damage to brain function; 5) Work as minimally invasive or non-invasive product that is easy to use and rapidly reduces brain edema and/or ICP; Enables earlier detection/triage of cervical spine injury; and 6) Improves upon current standard of care cervical spine stabilization.

- **6.3 Detection and Management of Internal or External Hemorrhage from Non-Compressible Trauma Wounds:** The goal for product development under this area is to detect, locate even when at low levels, and/or provide rapid control of hemorrhage in body areas where compression is not feasible. For products to be considered, Offerors must demonstrate preliminary data and supporting rationale on its ability and feasibility for the above outlined application. Products which address internal or external non-compressible hemorrhage from junctional wounds such as in the neck area, axilla and groin, as well as in the torso are of special interest.

The Offeror should clearly define the intended clinical window of opportunity for use of the product which should exert rapid control during initial trauma management.

Products for hemorrhage control intended to treat injuries to extremities are out of scope as they can be effectively managed with tourniquets. Similarly, products that control hemorrhage through systemic mechanisms of action to establish hemostasis, may be explored for submission under Area of Interest 4.

Desirable attributes for products that control internal/external non-compressible hemorrhage should include:

1) Allow rapid control and stabilization of hemorrhage; 2) Ability to extend the duration of patient survivability and enable management of patients when definitive care access is delayed (i.e. extends the “golden hour”); 3) Easy and rapid use by first responders with minimal need for other ancillary products; 4) Lower the resource needs on first responders; 5) Has minimal or no systemic effect on thrombotic mechanism; 6) Amenable for storage at room temperature and transport; 7) Potential to integrate into routine use on ambulances and/or field medical kits; and 8) Does not impede with other treatments and procedures in definitive care by trauma specialists (for example, should be easy to remove).

Desirable attributes for products that detect and locate internal hemorrhage should include:

1) Enable decision assist capability for care providers to detect and locate internal hemorrhage though easy to interpret data outputs (ideally visual); 2) Require quick set up and easy to use (ideally non-invasive) for use in trauma and emergency care; and 3) and Require minimal resource and operational needs (low footprint, power, ancillary products, training, maintenance).

- **6.4 Detection and Management of Airway Access Complications in Trauma:** The goal for development of products in this category is to simplify or improve upper airway access for use in patients with impaired oxygenation in

acute trauma. Products also include technologies which could improve management of airway access in difficult to implement or rescue situations or complement failed intubations (for example, due to body habitus, pediatric use). Preliminary data demonstrating the rationale and the value of the technology to achieve reduced times to rectify/ improve impaired oxygenation or to overcome challenges in particularly complicated situations with difficult airway access should be included.

Products in this category of interest may include the following capabilities:

1) Products addressing management of difficult or failed intubations; 2) Products demonstrating improved oxygenation; 3) Products that can be used in the field, by less trained providers, such as EMTs, or in an MCI to provide a secure airway and oxygenation until such injured are transported to definitive care; 4) Products may ideally have a universal size or "one-size-fits-most" approach; 5) Products that can assist EMTs in the field to determine / triage which patients are in imminent need of an airway for oxygenation; and 6) Products that improve visualization of the vocal cords.

- **6.5 Non-autologous topical products to prevent or reduce burn wound conversion (defined as a worsening of a burn wound from its original depth):** The goal for product development in this category is to promote novel solutions that can serve to reduce the severity of burn wounds by using a synthetic and/or non-autologous product. Products with demonstrated clinical data from proof of concept studies to prevent or reduce burn wound conversion from a partial-thickness (2nd degree) to a full-thickness (3rd degree) burn. Products should have the potential for supporting an indication for use which may include tangible clinical benefits to the patient, specifically, reduction in need for autografting and wound progression. Products should demonstrate a mechanism of action at the wound level, not as a systemic treatment (e.g. affects homeostasis). Novel technologies that mitigate burn wound conversion and/or optimize complete wound closure as a permanent, autograft sparing skin substitute will be considered.

Product attributes should include the following:

1) Non-autologous source material; 2) Demonstrated capability for rapid product availability, consistency, and scalability; 3) Manageable temperature requirements (example, room temperature); 4) Long shelf-life (at least 2-3 years); 5) Ease-of-application to large surface areas with mixed depth burns; 6) No preclusion from being applied to full-thickness burns; 7) Minimal re-applications and dressing changes; 8) Ability to administer in multiple settings (e.g. operating room, treatment room, bedside, outpatient, etc.); 9) Amenable for clinical observation of the wound without the need for removal and replacement; 10) Ability to prevent or reduce burn wound infections; and 11) Potential to temporize burn wounds in order to delay the need for surgical intervention beyond the normal standard of care.

Learn more about Burn and Blast Medical Countermeasures[22].

[22] https://www.medicalcountermeasures.gov/barda/cbrn/thermal-burn.aspx

Technical Point of Contact: Dr. Narayan V. Iyer; Narayan.Iyer@hhs.gov

Contracting Point of Contact: BARDA-BAA@hhs.gov with the subject line “Contracting questions: AOI6 (Burn and Blast MCMs): <brief description>”

Area of Interest #7: Diagnostics

The clinical diagnostics AOI #7 consists of the following: 7.1 Innovations, 7.2 Biothreats, 7.3 Antibiotic resistance, 7.4 Radiation exposure/biodosimetry, 7.5 Chemical threat exposure, 7.6 Influenza, 7.7 Emerging diseases, 7.8 Sequencing system development, 7.9 Threat agnostic diagnostics, and 7.10 Diagnostics for effective therapy utilization.

Definitions for the purpose of this AOI:

- Diagnostic is defined as an assay and, if required, a platform that together are FDA-cleared or -approved.
- Point-of-care 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, preferably CLIA-waivable, and provide results in less than 30 minutes.
- Home-use is defined as a test that achieves regulatory authorization, clearance, or approval for use in an Over-the-Counter (OTC) setting.
- Molecular assays are defined as tests with high specificity and sensitivity that detect nucleic acids (e.g., nucleic acid amplification tests [NAAT]).
- Platform is defined as instrumentation plus consumables capable of performing more than one assay.

Technology Readiness Level (TRL):

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

Development of Instrumentation:

In general, assays for BARDA priority biothreats, antibiotic resistant priority bacterial pathogens, or pandemic influenza and emerging infectious disease that can be performed using existing diagnostic instrument platforms that have a large number of

U.S. placements (clinical laboratory, point-of-care, or home-use settings) that are/will be readily available to inform routine patient care are preferred.

Proposals for new platforms must describe development of at least one assay relevant to BARDA priorities. BARDA prefers platforms with potential for sustained commercial marketability. The proposed technology must demonstrate significant improvements over existing technology and must meet TRL 4 or greater (unless otherwise specified).

Preference will be given to POC/ Home-use Instruments that offer these elements:

a. Small footprint, easily portable
b. Lightweight – less than 5 lbs. preferred
c. Rapid results - sample to answer in under 30 minutes (less than 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; wireless is preferred
h. Able to operate in non-temperature/humidity-controlled environments.
i. Low cost

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

Design, manufacture, labeling, and packaging of all 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 or OTC settings.

7.1 [SUSPENDED] Diagnostic Innovations

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

7.2 Biothreat Agent Diagnostics

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

7.2.1 Biothreat Agent Diagnostics: Point-of-Care

Advanced development, clinical evaluation, and FDA clearance/approval of rapid, accurate point-of-care diagnostic systems for biothreats defined above. Home-use indication is not currently supported in this AOI. 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. TRL 4 or greater required.

7.2.2 Biothreat Agent Diagnostics: Laboratory

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

- It is highly preferred that these assays are developed and optimized for use with existing diagnostic instrument platforms that have a large number of U.S. clinical laboratory placements, and that are FDA-cleared for other “routine healthcare” 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.
- Single threat and multiplex biothreat assays will be considered. TRL 4 or greater required.

7.2.3 Biothreat Agent Diagnostics: Filovirus Point-of-Care and Remote Settings

Advanced development, clinical evaluation, and FDA clearance/approval of rapid, accurate, point-of-care, field-useable, CLIA-waivable, molecular diagnostic systems for filoviruses that can, at minimum, detect Ebola Zaire, Ebola Sudan, Ebola Bundibugyo, and Marburg virus. The ability to differentiate between these viruses is desirable. Assays must detect viral targets at clinically relevant concentrations present during the early stages of disease in whole blood, plasma, and serum for living patients and after death in oral fluids for cadavers.

Preference will be given to tests that are low cost and provide results in 30 minutes or less (15 minutes is preferred). GFM animal studies may be provided, if needed. The product must be at TRL 3 or greater, with anticipation of achieving TRL 4 within one month of award, FDA EUA submission within four months of award, and ultimately 510(k) submission and clearance.

If an instrument is part of this test, preference will be given to instruments that offer:

- Mobile, portable platform for use in resource limited environments and/or remote locations:
    - Small footprint, easily portable
    - Lightweight instrument– less than 3 pounds preferred
    - Able to operate in non-temperature/non-humidity-controlled environments
    - Ability to operate from batteries and/or solar power sources
    - Ability to electronically transmit data when in range of Wi-Fi/cellular transceivers is preferred

7.3 Antibiotic Resistance Diagnostics for priority bacterial pathogens

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

detect drug-resistant priority public health bacterial pathogens* and to characterize their resistance profiles for biological threats and/or routine clinical use. Assays must support clinical decision points.

Refer to the latest CDC report on "Antibiotic Resistance Threats in the United States."

7.3.1 Bacterial AMR Testing Direct from Specimen

Advanced development, clinical evaluation, and FDA clearance/approval of direct-specimen diagnostic tests for priority bacterial pathogens that identify the pathogen(s) and their resistance or susceptibility to relevant antibiotics within 24 hours and without additional sample preparation (positive blood culture is not an acceptable starting material). The assay must have clinically relevant sensitivity and specificity, and useful for multiple specimen types (e.g., blood, sputum, CSF, and nasal secretions). Molecular or phenotypic tests are acceptable.

It is highly preferred that pathogen identification be available in less than 30 minutes from time of sample collection. Priority will be given to AST solutions with reduced time to results, a small footprint, and fully automated compared to current standard of care. TRL 4 or greater required.

7.3.2 Bacterial vs. Viral Infections: Point-of-Care

Advanced development, clinical evaluation, and FDA clearance/approval of CLIA-waivable/waived, rapid platforms and assays for use in point-of-care settings that will reliably distinguish between Viral and Bacterial infections 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). Preference will be made for tests with results available in less than 30 minutes. Priority will be given to solutions on platforms that are FDA-cleared for other routine healthcare applications. TRL 4 or greater required.

7.3.3 AMR Sequencing Solutions

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/or novel resistance determinants directly from a broad range of clinical specimen types (e.g., blood, sputum, CSF, and nasal secretions). Priority will be given to solutions on platforms that are FDA-cleared for other routine healthcare applications. TRL 4 or greater required.

7.4 [SUSPENDED] Radiation Exposure (Biodosimetry) Diagnostics

Submissions for Radiation Exposure (Biodosimetry) Diagnostics will not be considered during the open period of this BAA, unless specifically announced through amendments or special instructions.

7.5 [SUSPENDED] 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 must include evaluation of reactivity to emerging, novel avian and swine influenza viruses.

7.6.1 Influenza Home-Use Testing (for OTC)

Advanced development, clinical evaluation and FDA clearance/approval of home-use molecular and high sensitivity antigen tests that detect influenza, and, at a minimum, differentiate influenza A and B viruses. Preference will be made for diagnostics that are low cost (target selling price under $20) and able to detect early infection and demonstrate performance comparable to existing molecular FDA-cleared diagnostics and must be TRL 4 or greater. Preference will be made for integrated patient management solutions that incorporate:

- Use case, acceptance by clinicians and patients; and
- Electronic information transfer (wireless is preferred) to healthcare provider for rapid treatment/patient management decisions and de-identified data transmission to public health for disease surveillance.

7.6.2 Pan-Influenza Diagnostics: Point-of-Care or Laboratory

Advanced development, clinical evaluation, and FDA clearance/approval of diagnostic assays 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. Diagnostic assays that can be readily used in clinical Point-of-Care or Laboratory settings may be proposed. TRL 4 or greater required.

7.7 [Suspended] Emerging Diseases Diagnostics

7.7.1 [Suspended] Diagnostic Assay for Human Coronaviruses

Submissions for Pan-coronavirus assays will not be considered during the open period of this BAA, unless specifically announced through amendments or special instructions.

7.7.2 [Suspended] Diagnostic Assay for Detection of SARS-CoV-2 Virus:

Submissions for SARS-CoV-2 Assays will not be considered during the open period of this BAA, unless specifically announced through amendments or special instructions.

7.7.3 [Suspended] Diagnostic Assay for Detection of COVID-19 Neutralizing Antibodies:

Submissions for Assays for Detection of COVID-19 Neutralizing Antibodies will not be

considered during the open period of this BAA, unless specifically announced through amendments or special instructions.

7.7.4 [Suspended] Diagnostic Assay Panel for SARS-CoV-2, Influenza A/B, and other Respiratory Viruses:

Submissions for Diagnostic Assay Panels for SARS-CoV-2, Influenza A/B, and other Respiratory Viruses will not be considered through this AOI during the open period of this BAA, unless specifically announced through amendments or special instructions.

7.7.5 [Suspended]Screening Tests at Point of Care (2-minute Time to Result):

Submissions for Screening Tests for SARS-CoV-2 at Point of Care will not be considered during the open period of this BAA, unless specifically announced through amendments or special instructions.

7.8 [Suspended] Sequencing System Development

7.8.1 Submissions for Sequencing System Development will not be considered through this AOI during the open period of this BAA, unless specifically announced through amendments or special instructions.

7.9 Threat Agnostic Diagnostics

7.9.1 Next Generation Sequencing (NGS)-based Agnostic Diagnostic for Viral Pathogens

Next-generation sequencing (NGS) technology has demonstrated the ability to detect and analyze pathogen genomes but the translation of this technology to an FDA-cleared/approved diagnostic for the agnostic detection of any novel or unknown pathogen has met multiple challenges, including sample/library preparation, sequencing/base calling, and bioinformatics analysis. NGS-based agnostic diagnostics refer to any assay/platform that doesn't target any specific organism or pathogen but analyzes all nucleic acids in a given sample and returns positive results when any possible human pathogen is found or negative results when no possible human pathogen is present. BARDA is interested in initially filling this gap by supporting advanced development, clinical evaluation, and FDA clearance/approval of NGS-based agnostic diagnostic assays targeting new, novel/emerging, and known viral pathogens. Both laboratory and Point of Care tests are sought for use on existing NGS-based sequencing platforms or on platforms already in development. Minimum Technology Readiness level (TRL) is TRL4.
Submissions should also address the following:

- A sample to answer solution to demonstrate with feasibility data, an NGS-based assay that uses existing sequencing platforms and reagents or platforms in development that can agnostically detect RNA and/or DNA from new, novel/emerging, and known viral pathogens. Standardized assays that require no or minimal research and development efforts are preferred.
- Must provide a regulatory strategy to achieve FDA 510(k) clearance/de novo approval for an agnostic diagnostic indication for viral pathogens based on feedback from the FDA, with the final milestone of achieving 510(k) clearance/de

novo approval. Consideration of any current versions of existing FDA guidance documents may be helpful for framing initial discussions.

- Offer a complete sample to answer solution including sample/library preparation, enrichment/depletion (if needed), sequencing, and data analysis against a validated database of known pathogens that is accepted by the FDA. Access to reference target sequences obtained using a method acceptable to the FDA for the viral pathogens is required. Respondents must submit a clear plan for creating contrived specimens with varying viral loads and for obtaining clinical specimens. The inclusion of publicly accessible database development in a submission is acceptable. Medium- to high-throughput assays with automated sample preparation, library preparation, sequencing, and analysis, and minimum hands-on time are preferred.
- Include proof that new variants or recently mutated viruses that are known human pathogens and viruses that have jumped from animals to humans can be detected and identified.
- Able to use multiple clinical sample types and submissions must include feasibility data which demonstrates that viral pathogen nucleic acids can be adequately extracted and analyzed from at least one (1) sample type.
- Detection and identification of viral traits such as resistance mutations to inform proper use of therapeutics (e.g., antivirals, monoclonal antibodies) is preferred.
- Provide clear, clinically actionable data reports, with total time from sample-to-answer in no more than 12 hours; a sample-to-answer time of less than 8 hours is preferred.

Out-of-Scope Topics for AOI 7.9.1:

- Submissions for targeted NGS-based diagnostic platforms that are pursuing pathogen-specific indications.
- Research and development activities for Laboratory Developed Test (LDT) or Research Use Only (RUO) NGS-assay development that do not support a regulatory path or FDA clearance/approval.
- Development of new sequencing platforms. BARDA is primarily interested in products which leverage existing clinical health infrastructure and would require minimal capital investment for laboratories to implement or sequencing platforms already in development.

7.10 [Suspended] Diagnostics for Effective Therapy Utilization

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

Learn more about Diagnostics

Technical Point of Contact: DDDI_Tech_Contact@HHS.gov

Contracting Point of Contact: BARDA-BAA@hhs.gov with the subject line “Contracting questions: AOI 7 (Diagnostics): <brief description>”

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

Offerors for Area of Interest #8.1 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 and approaches that will improve preparedness and response against pandemic influenza and emerging infectious diseases with pandemic potential. Successful Offerors will discuss and provide evidence that the proposed effort substantially enhances pandemic influenza preparedness and response, and describe plans and requirements for long-term sustainability.

8.1 [ACTIVE] Advanced development of more effective vaccines. Candidates and approaches that have achieved TRL 6 or greater and that will improve preparedness and response against pandemic influenza are requested. 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. Vaccine candidates and approaches that provide one or more of the following are of particular interest: a) licensure of domestically manufactured vaccines amenable to both rapid production from time of strain identification to release of bulk product, and rapid scale up and manufacturing technology transfer to new facilities; b) clinical trials to expand the age range on the label of currently licensed vaccines; c) decrease response time, such as adjuvants or other technologies that allow a priming and protective response with a single vaccine dose; or d) improve the stability, sustainability and/or utility of stockpiled vaccines. All Offerors should provide commercialization and life cycle planning approaches and any sustainability costs that would be requested to maintain the capability. Proposed clinical activities should support development toward FDA licensure or additional label claims. Offerors proposing to develop vaccines not yet licensed by FDA should provide data supporting proposed vaccine potency and release assays that are specific for the influenza vaccine candidate, and clinical data supporting dose, schedule, mechanism of action, and safety of the vaccine candidate, as well as immunogenicity against pandemic strains of influenza. The Offeror should provide a regulatory strategy for FDA approval of the vaccine candidate and data demonstrating the proposed improvements to pandemic influenza response/preparedness. Proposed efforts might include qualification and validation of correlates of protection and other assays used to evaluate the immune response to the vaccine.

8.2 [ACTIVE] Innovative vaccine production enhancements. Support for improvements in vaccine production and administration that accelerate the availability of pandemic influenza vaccines and for which feasibility data is available. Vaccine production enhancements are not expected to adhere to TRLs.

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.

    c. development or implementation of assays (e.g. sterility, adventitious agent, etc.) that accelerate vaccine lot release.

4. Administration:

    a. development of alternative routes of vaccine administration that would significantly reduce dependence on needles and syringes, enable rapid and/or layperson administration, obviate the need for cold-chain storage and/or facilitate improved (e.g. single dose, enhanced immunogenicity, mucosal delivery, etc.) vaccine effectiveness.

8.3 [SUSPENDED] COVID-19 Vaccine.

Note: White Paper and Full Proposal submissions under AOI #8.3 are suspended until further notice. All white papers or full proposals submitted to this area of interest will be considered automatically non-responsive. However, evaluation of vaccine development under Operation Warp Speed[23] (OWS) program continues outside of BAA-18-100-SOL-00003. If promising candidates are identified, there is an opportunity for this area of interest to be reopened or for potential partnership with our colleagues at the Joint Program Executive Office[24] (JPEO-CBRND).

A challenge to the national and global health security is the newly emerged SARS-CoV-2 virus. BARDA is seeking proposals for the development of vaccine countermeasures to this newly emerged disease. The countermeasure produced may consist of the vaccine itself, viral or genetic (DNA or RNA) vectors, or other technologies that can quickly generate a safe and protective immune response. The manufacturing technology for the proposed vaccine should be suitable for commercial scale production and for product delivery. The description of the manufacturing process should address domestic bulk and fill finish manufacturing timelines, the ramp-up time for additional doses based

[23] https://www.hhs.gov/about/news/2020/06/16/fact-sheet-explaining-operation-warp-speed.html
[24] https://www.jpeocbrnd.osd.mil/coronavirus

on the approximate dosage versus existing capacity, and take into account any need for process scale-up or finding new capacity. Manufacturing of products in a 21 CFR 210, 211 current Good Manufacturing Practices compliant facility must occur in the United States. The pre-clinical and clinical testing plan, as well as the regulatory pathway, for obtaining approval for use of the vaccine developed should be outlined. Regulatory challenges should be identified and addressed. The technology readiness level (TRL) of the vaccine should be described. While there is no TRL minimum requirement, more advanced submissions are preferred. Preference will be given to technologies that leverage late stage or licensed platforms and those that have non-clinical data from SARS or MERS-CoV and human exposure data to include safety and potential immunogenicity.

8.4 [SUSPENDED] COVID-19 Immune Assay(s) Development and Implementation

As part of BARDA's continuing support for COVID-19 vaccine development, assessing impact of variants on vaccine immunogenicity, and analyzing correlates of protection, BARDA is seeking proposals for advanced research and development activities for novel immunogenicity assays (herein immune assays) and sample collection technologies.

1. Offerors shall develop assay(s) to analyze clinical study samples to evaluate immune responses to COVID-19 vaccines, licensed or under development. Assays shall quantify responses relevant to ancestral SARS-CoV-2 and circulating variant(s) of concern. Core immunological assays to support regulatory submissions shall be validated as required by FDA guidelines while exploratory assays shall be fit-for-purpose or qualified, as needed. As required, Offerors shall document quality systems along with assay validation reports in the Drug Master File (DMF) submitted to FDA. Immune assays of interest include:

    i. Establish SARS-CoV-2 variant specific lentivirus-based S-pseudotyped virus neutralization assays for sera and mucosal samples. Offerors shall address the following requirements in the development of assay:
        - Offerors shall include plans to update the assay target virus as needed based on SARS-CoV-2 variant emergence and evolution, within 2 months of USG request (and availability of appropriate reagents).
        - Qualification and Validation studies shall include precision, sensitivity, specificity and dilutional linearity.
        - Mucosal assays will need to consider limited sample volume. The assays should have the appropriate reference standards, with the understanding that they may not be commercially available and will have to be produced.
        - Under USG directive, the Offerors shall coordinate the validation of devices for self-collection of clinical samples (i.e., nasal secretions and saliva, serum etc.) by testing self-collected samples from various sources in their assay. Offerors shall modify the assays as appropriate to be able to support testing on various matrices (serum, nasal secretions, and saliva) and taking into account the reagents present in various collection devices.

- Offerors proposing to perform laboratory assay testing shall describe quality systems and statistical analyses capabilities.

ii. Establish multiplexed SARS-CoV-2 antigen panels for human antibody (e.g. IgA, IgG, etc.) quantification by electrochemiluminescence. Data from antigen panels that quantitate antibodies to SARS-CoV-2 and SARS-CoV-2 variants have been used by regulatory agencies as one of the standard binding assays for immunogenicity assessments to support Emergency Use Authorization (EUA) and licensure of the current COVID-19 vaccines. Offerors shall address the following requirements in the development of assay:
   - On USG request, Offerors shall rebuild antigen panels to include newly emerging SARS-CoV-2 variants
   - The antigen panels shall be capable of measuring antibodies that block binding of angiotensin-converting enzyme 2 (ACE2) to the Spike and RBD, bind to the whole Spike, receptor binding domain and nucleocapsid antigens of the SARS-CoV-2 ancestor and variants
   - Antigen panels shall include appropriate standards and controls to support development and validation of assays described below in iii.
   - Offerors should include plans to update the antigen panels as needed based on SARS-CoV-2 variant emergence and evolution, within 2 months of USG recommendation

iii. Establish IgG and IgA multiplex MSD antibody binding assays to SARS-CoV-2 proteins (including multiple variant spike, receptor binding domain and nucleocapsid proteins) for sera and mucosal samples. Offerors shall address the following requirements in the development of assays:
   - For the antibody binding assays, the assays shall be capable of measuring antibodies that bind to the whole Spike, receptor binding domain and nucleocapsid antigens of the SARS-CoV-2 ancestor and variants.
   - Offerors should include plans to update the assay target virus as needed based on SARS-CoV-2 variant emergence and evolution, within 2 months of USG request (and availability of appropriate antigen panels).
   - Qualification and Validation studies shall include precision, sensitivity, specificity and dilutional linearity
   - Under USG directive, the Offerors shall coordinate the validation of devices for self-collection of clinical samples (i.e., nasal secretions and saliva, serum etc.) by testing self-collected samples from various sources in their assay. Offerors shall modify the assays as appropriate to be able to support testing on various matrices (serum, nasal secretions, and saliva) and taking into account the reagents present in various collection devices.
   - Offerors proposing to perform laboratory assay testing should describe quality systems and statistical analyses capabilities.

iv. Establish MSD-based multiplexed angiotensin-converting enzyme 2 (ACE2) receptor blocking assays to the SARS-CoV-2 Spike and RBD antigens, including variants of the SARS-CoV-2 virus for sera and mucosal samples. Offerors shall address the following requirements in the development of assays:
    - Offerors shall include plans to update the assay target virus as needed based on SARS-CoV-2 variant emergence and evolution, within 2 months of USG request (and availability of appropriate antigen panels).
    - Qualification and Validation studies shall include precision, sensitivity, specificity and dilutional linearity.
    - Under USG directive, the Offerors shall coordinate the validation of devices for self-collection of clinical samples (i.e., sera, nasal secretions and saliva etc.) by testing self-collected samples from various sources in their assay. Offerors shall modify the assays as appropriate to be able to support testing on various matrices (e.g., sera, nasal secretions, and saliva) and taking into account the reagents present in various collection devices.
    - Offerors proposing to perform laboratory assay testing shall describe quality systems and statistical analyses capabilities.

v. Establish multiparameter intracellular staining (ICS) assay to identify and quantify SARS-CoV-2 spike-specific T cells for PBMC samples. Offerors shall also address the following requirements in the development of assay:
    - Focus on T cell lineage, Th1, Th2 and Th 17 response, memory, regulatory, cytotoxicity markers, homing markers understood to direct the cells to the airway mucosa.
    - Offerors shall include plans to update the assay target virus as needed based on SARS-CoV-2 variant emergence and evolution within 3 months of USG request (and availability of appropriate reagents).
    - Validation studies shall be performed for analysis of Th1/Th2 CD4+ T cells and CD8+ T cells
    - Qualification and Validation studies shall include precision, sensitivity, specificity and dilutional linearity
    - Offerors proposing to perform laboratory assay testing should describe quality systems and statistical analyses capabilities.

vi. Qualification of methods and devices for collection of clinical samples for use in the immune assays described above. Offerors shall focus on solutions based on a model of decentralized clinical trials, with the goal of moving sample collection closer to the home.
Offerors shall address the following requirements:
    - Offerors must provide preliminary feasibility data for the methods and devices demonstrating that adequate sensitivity and specificity are achievable in relevant clinical matrices (i.e., sera, blood, nasal secretions and saliva etc.).

- Feasibility data may include testing with surrogate assays (e.g., metabolic testing or other relevant disease analytes).
- Offerors shall provide a qualification strategy that includes sample size calculations and study populations details in the proposed clinical study design.

2. Offerors shall establish laboratory testing capability using the assays developed under 8.4.1 (including rapid establishment of testing using updated assays for variants) at the organization developing the assay or a subcontractor. Data from these assays should meet regulatory requirements. Data may be used to support a U.S. FDA EUA or Biological License application (BLA).

    i. Establish laboratory testing capability for SARS-CoV-2 variant specific S-pseudotyped virus neutralization assays for sera and mucosal samples. Offerors shall address the following requirements in the establishment of testing capacity:
        - Perform vaccine-product specific partial validation, if required by the FDA.
        - Testing of clinical trial specimens with a 2, 3, and 4-variant per assay options.
        - Sample throughput of 4,000 samples/week.
        - Offerors proposing to perform laboratory assay testing should describe quality systems, data management and statistical analyses capabilities.
    ii. Establish laboratory testing capability for IgG and IgA multiplex MSD antibody binding assays to SARS-CoV-2 proteins (including multiple variant spike, receptor binding domain and nucleocapsid proteins) for sera and mucosal samples. Offerors shall address the following requirements in the establishment of testing capacity:
        - Perform vaccine-product specific partial validation, if required by the FDA.
        - Sample throughput of 4,000 samples/week
        - Offerors proposing to perform laboratory assay testing should describe quality systems, data management and statistical analyses capabilities.
    iii. Establish laboratory testing capability for ACE-2 receptor blocking assays to SARS-CoV-2 proteins for sera and mucosal samples. Offerors shall address the following requirements in the establishment of testing capacity:
        - Perform vaccine-product specific partial validation, if required by the FDA.
        - Sample throughput of 2,000 samples/week
        - Offerors proposing to perform laboratory assay testing should describe quality systems, data management and statistical analyses capabilities.

iv. Establish laboratory testing capability for multiparameter ICS assay to identify and quantify SARS-CoV-2 spike-specific T cells for PBMC samples. Offerors shall address the following requirements in the establishment of testing capacity:
    - Perform vaccine-product specific partial validation, if required by the FDA.
    - Sample throughput of 500 samples/week
    - Offerors proposing to perform laboratory assay testing should describe quality systems, data management and statistical analyses capabilities.

Proposals that are not focused on lentivirus based pseudovirus assays, intracellular cytokine staining assays and MSD-ECL platforms, as described in AOI# 8.4.1., will be considered non-responsive. In addition, submissions that focus on the following information will be considered non-responsive:

Point-of-care assays
Laboratory space establishment and expansion
Respiratory pathogens other than SARS-CoV-2

Interested parties seeking to share their technology and approach on AOI #8.4 have an additional opportunity to receive feedback from the technical staff by requesting a TechWatch at the TechWatch website no later than 4:30 PM Eastern Time on April 28, 2023. Approved TechWatch requests will be scheduled for May 1 and 2, 2023.

Area of interest #8.4 will be open until May 17, 2023, at 4:30 PM Eastern Time. Note that an initial Quad Chart/White Paper will not be sought for this area of interest. Offerors must submit Full Proposals in accordance with the instructions provided in Part VI Full Proposal Instructions of the BAA.

Learn more about NIH/NIAID's Resources for Researchers: Influenza[25] and NIAID's Research: Vaccines[26].

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

DMIDResources@niaid.nih.gov

Technical Point of Contact: Chuong Huynh; Chuong.Huynh@hhs.gov

Contracting Point of Contact: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI8 (IEID Vaccines): <brief description>"

[25] https://www.niaid.nih.gov/diseases-conditions/influenza
[26] https://www.niaid.nih.gov/research/vaccines

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

Offerors for AOI #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), for all topic areas except for AOI 9.7. 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. Proposals for AOI 9.7 will not be assessed for TRL. On AOI 9.8 BARDA will prioritize candidates that have reached TRL6 or later. However, earlier stage candidates may be considered.

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 [ACTIVE] Influenza Antiviral Therapeutics

BARDA seeks to develop new direct-acting or host-directed antiviral therapeutics to treat influenza in outpatient ambulatory settings. The proposed product candidate must have a novel mechanism of action (new neuraminidase inhibitors will be considered non-responsive) and demonstrate superiority to oseltamivir in preclinical influenza animal models. Candidate therapeutics must have a safe toxicology profile making it suitable for use in all populations.

The proposed therapeutic should prevent the rapid emergence of drug resistance and have proven broad influenza strain neutralization activity (minimum for influenza A: H1N1, H3N2, H5N1, and H7N9). Demonstrated efficacy of the proposed product candidate at least 48 hours after symptom onset in influenza patients or appropriate preclinical influenza animal models is required. The strongest proposals should have data demonstrating a broad-spectrum antiviral activity against both influenza A and B and other viral pathogens such as SARS-CoV-2.

Candidate therapeutics must have reached a TRL 6 level or higher to apply. Candidate therapeutics must have an active Investigational New Drug Application filed with the FDA to treat influenza and have demonstrated safety in a Phase 1 study as evidenced by a clinical study report available for review in the submission. Candidate therapeutics that benefit special populations, such as pediatrics, will be viewed more favorably.

The white paper or full proposal submission should address manufacturing capacity to provide an adequate supply of the product candidate to complete the proposed clinical studies. Manufacturing of products in a 21 CFR 210, 211 current Good Manufacturing Practices (cGMP) compliant facility within the United States is preferred.

White papers and full proposals that do not have in vitro and in vivo efficacy data against influenza virus, a clinical study report (interim or final) with the human safety data including the dose proposed for influenza treatment, a detailed cGMP manufacturing plan, or a regulatory strategy that leads to FDA approval/licensure will be considered non-responsive.

9.3 [ACTIVE] Immunomodulators or therapeutics targeting lung repair.

BARDA seeks to develop immune modulators or other host-directed therapeutics promoting tissue repair that can prevent, treat, and/or improve clinical outcomes of acute lung injury (ALI)/acute respiratory distress syndrome (ARDS) caused by the pandemic or seasonal influenza and other respiratory viral infections. Only projects proposing clinical trials to evaluate the safety and efficacy of the proposed candidate therapeutic to prevent disease progression and/or reduce disease severity and mortality in hospitalized patients of ALI/ARDS due to influenza or other respiratory viral infections will be considered.

Candidate therapeutics for the treatment of influenza and other respiratory viral infections must have reached a TRL 6 level or higher. Repurposed products that are already FDA approved/licensed or in the late stages of development with clinical exposure data will be considered as well. A combination therapy that includes a new investigational therapeutic candidate and an approved/licensed therapeutic would also be applicable. The combination rule should be addressed in the submission if the combination therapy is proposed.

The proposed product candidate must have an active Investigational New Drug application filed with the FDA (or open IND) for treatment of ALI/ARDS and have demonstrated a favorable safety profile in a Phase 1 study as evidenced by a clinical study report (interim or final) available for review in the submission. The white paper or full proposal submission must provide clear evidence demonstrating the specific mechanism(s) of the proposed candidate therapeutic in modulating host immune responses in the lungs of influenza patients or relevant animal models of influenza and other viral respiratory diseases. The product candidate with a sound therapeutic rationale for the mechanism of action (e.g., relevant longitudinal immune-related biomarker data and its association with clinical outcomes) in specific patient populations (for example, but not limited to, ALI/ARDS patients associated with a distinct immunological profile or patients with ALI/ARDS-related pulmonary fibrosis) will be prioritized.

The white papers or full proposal submission should include information about any ongoing and completed clinical trials of their product candidate and justify how the proposed project differs from those clinical studies. The white paper and full proposal submission should address manufacturing capacity to provide an adequate supply of the product candidate to complete the proposed clinical studies. Manufacturing of products in a 21 CFR 210, 211 current Good Manufacturing Practices (cGMP) compliant facility within the United States is preferred.

White papers and full proposals that do not have in vivo efficacy data of the proposed candidate therapeutic to treat ALI/ARDS associated with influenza, a Phase 1 clinical study report (interim or final) with human safety data including the dose regimens proposed for ALI/ARDS treatment, a detailed manufacturing plan, and a regulatory strategy that leads to FDA approval/licensure will be considered non-responsive.

9.5 [SUSPENDED] Pre-exposure and Post-exposure Prophylaxis

There is a need to develop antivirals that may be used for pre-exposure prophylaxis for those at high risk of SARS-CoV-2 (2019-nCoV) exposure such as healthcare workers. In addition, there is a need for post-exposure prophylaxis in those that are at high risk for serious disease caused by SARS-CoV-2 (2019-nCoV). Single dose antivirals that can potentially protect against infection for at least 30 days will be prioritized for

consideration. BARDA will prioritize platform candidates with demonstrated safety in a phase 1 study; however, earlier stage candidates may be considered. White papers and proposals should address any ongoing clinical trials of their candidate therapeutic, and how a proposed study is different than the ongoing studies. White paper and proposal submissions should address clinical supply of candidate therapeutics. Submissions that have enough drug to complete the proposed clinical study and at least 10,000 treatment courses available within 6 months will be prioritized.

Immune modulating mechanisms of action or candidates that require daily dosing will be considered non-responsive.

9.6 [ACTIVE] Pre-exposure Prophylaxis – Influenza

Development of antivirals to provide pre-exposure prophylaxis treatment options for people in whom influenza vaccines have inadequate efficacy and are at a high risk of severe influenza. Presumptive target population for pre-exposure prophylaxis includes those who do not have an adequate response to current vaccines which would include the elderly and immune compromised populations among others. Phase 1 clinical studies may include healthy volunteers.

A single dose of the antiviral would ideally provide 6 months of protection but must be able to provide at least one month of protection with a goal of demonstrating a 70% reduction in the relative risk of symptomatic influenza infection. The antiviral coverage must include both seasonal (H1N1 and H3N2) and pandemic influenza strains (H5N1 and H7N9), coverage of both influenza A and B is preferred. Phase 2, phase 3 and other clinical studies required for BLA submission can be considered for funding; however, human challenge studies will not be funded by this program.

Candidate antivirals must have completed phase 1 clinical studies including the dose and route of administration proposed for phase 2 clinical studies. Intravenous administration is the least preferred route of administration. Candidate drugs must have an open-IND with the US FDA for the pre-exposure prophylaxis of influenza infection.

Host targeted mechanisms of action or candidates that require daily or weekly dosing will be considered non-responsive. In addition, submissions that do not include the following information will be considered non-responsive:

- phase 1 data that support no more than once a month dosing,
- activity against both seasonal and pandemic influenza strains,
- an open IND with the US FDA,
- a full development plan including FDA licensure or
- a plan for US-based manufacturing.

Manufacturing of products in a 21 CFR 210, 211 current Good Manufacturing Practices compliant facility within the United States will be a requirement. **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 Researchers:Influenza[27] and NIAID's Microbiology and Infectious Diseases Resources[28].

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

DMIDResources@niaid.nih.gov

9.7 [SUSPENDED] Implementation of phase 2 clinical trial to investigate novel host-directed therapeutics candidates to treat acute respiratory distress syndrome (ARDS)

ARDS is a life-threatening lung injury primarily caused by severe pneumonia and sepsis due to bacterial and viral infections (e.g., influenza), leading to high morbidity and mortality in hospitalized patients. To date, there are no approved or licensed pharmacological therapies available for the treatment of ARDS. Identifying new treatments for patients with ARDS remains challenging since ARDS is a highly heterogeneous syndrome. Many drugs have been tested in previous clinical trials with no success, although post-hoc analyses often provide positive signals in subsets of patients with ARDS. Therefore, there is an urgent need to understand the clinical and biological features to better classify patients into sub-phenotypes that might be more responsive to a given therapy.

BARDA is interested in full proposals to implement a randomized, double-blind, placebo-controlled, multicenter phase 2 trial in the US to evaluate the safety and efficacy of novel host-directed therapeutic candidates in hospitalized adults with ARDS. It is expected that full service clinical research organizations (CROs) will be a part of the proposed team. This platform trial is designed to collect relevant clinical and biological markers that can define subsets of patients with ARDS who may benefit from specific host-targeted therapeutics. During the study, extensive biomarker data will be collected from baseline to end of hospitalization to demonstrate the specific mechanism(s) of the proposed candidate therapeutic in modulating the host immune response, the natural history of ARDS, and the potential treatment triggers for the therapeutic candidates. The results from this phase 2 trial are not intended to be pivotal, but the trends seen within the data may help identify distinct subgroups of patients with ARDS most likely to benefit from the candidate intervention and triggers for treatment to inform the design of future clinical trials in ARDS.

1. CLINICAL TRIAL PLANNING AND EXECUTION OBJECTIVES INCLUDE BUT ARE NOT LIMITED TO:

Offerors must clearly describe their ability to perform the following clinical trial planning and execution assumptions related to the proposed phase 2 platform trial (see the protocol synopsis and transfer of obligations table in Attachment), including but not limited to:

- Serve as the IND holder with the US FDA for the clinical trial, management of safety reporting, submission of safety reports, annual reports, and all information

[27] https://www.niaid.nih.gov/research/resources
[28] https://www.niaid.nih.gov/research/microbiology-and-infectious-diseases-resources

requests received from the US FDA. Please note, the IND will be for the clinical trial only, and drug sponsors are expected to be the sponsor of the INDs for their individual drugs with the US FDA.

- Design and conduct the proposed clinical trial to evaluate host-directed therapeutic candidates in ARDS patients at the US sites in accordance with Good Clinical Practice guidelines (GCP: as defined by 21 CFR § 312 and ICH Guidelines document E6).
- Create a clinical trial development plan that outlines activities and associated key milestones for the proposed trial. Work with drug sponsors to develop three protocol appendices to the main study for three products in their cohorts.
    - **Period of Performance:** Recruit and enroll 600 hospitalized adult patients with selected ARDS severities (200 patients per cohort with a 2:1 randomization ratio for treatment vs. placebo, 3 cohorts) at up to 50 sites within the US in 3 years. Offeror may propose changes to the proposed number of US clinical sites and/or recruitment duration as long as technical justification and the associated overall project timeline are included for consideration.
        - ❖ Offeror shall furnish all the necessary services independently (at the prime or subcontractor level), qualified personnel, material, equipment, and facilities, not otherwise provided by the Government, as needed to perform the study, analyze resulting data, and provide reports as directed. Include an Integrated Quality Assurance Plan relevant to tasks to be done within the agreed-upon timeline.
    - **Option(s):** In addition to the services outlined above to be provided for the base requirement, please include optional periods of performance for additional therapeutic agents (more than 3 as outlined above) to assess in the trial.
    - **Performance Optimization Plans:** Offeror may provide two performance optimization plans, one for the Offeror and one for the Study Sites, that allow for incentivizing shortened timelines for key deliverables. Consider the incentives and barriers present in current research when conducting ARDS clinical trials and how they may be addressed. The Offeror Performance Optimization Plan and the Study Site Performance Optimization Plan should be developed in accordance with all federal, state, and local regulations and/or guidelines.
        - ❖ **Offeror Performance Optimization Plan**: Due to the inherent difficulty with completing ARDS clinical studies in a timely manner, performance incentives should be considered to improve overall implementation of the clinical study. Offeror will define the Key Performance Indicators (KPIs) relevant to the program (i.e., clinical site readiness, adherence to proposed timelines, query aging, etc.), how they will be measured, and how often they will be assessed/reported. The Offeror performance optimization plan should include incentives that align with the Key Milestones incorporated into the contract and that meet IRB approval and ethical considerations. For example, Offeror may receive a one-time monetary bonus for exceeding study start-up metrics, enrollment milestones and/or database lock. Offeror may also include in the

performance optimization plan enrollment competitions or campaigns across the sites managed centrally by the CRO and foster cooperation across sites. Offeror should monitor participant enrollment and quality metrics as well as establish and maintain centralized monitoring reporting systems to track enrollment status of individual site activities, such as numbers of subjects screened, enrolled, withdrawn, and completed.

- ❖ **Study Site Performance Optimization Plan:** The study site performance optimization plan should be outlined separately and should avoid any payment for "finder's fees." The performance optimization plan may include compensation for patient referral sources for the time and effort spent on the referral process. Providing extra temporary staffing support (Clinical Research Coordinators) to a study site would also be considered appropriate in the study site performance optimization plan as an incentive for large academic sites where staffing may affect enrollment rates.

- Provide protocol development and writing support services, including the development of protocol-related documents, such as written or electronic informed consent. Protocol development and subsequent trial enrollment should consider the diversity of the clinical trial populations, as applicable, by taking into account principles outlined in "Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry."
- Translate all essential study documents to Spanish to allow for patient enrollment of Spanish language-only subjects.
- Conduct clinical site management and site monitoring (onsite or remote risk-based monitoring) visits to ensure the conduct of the trial follows the approved protocol, federal and local regulations, and GCP.
- Manage all drug depot activities, including labeling (as investigational, according to IND requirements), kitting, storage, and distribution of the investigational product and placebo.
- Develop and implement a plan for purchasing all necessary clinical/laboratory supplies for biospecimen collection, storage, and analysis, as applicable. Budget for specific services (e.g., central laboratory, biospecimen repository, and analytics), as needed, including a validated research specimen tracking and reporting system and establish necessary sub-contracted services.
- Provide full-scope statistical programming support for generating SDTM and ADaM datasets (including supporting documents such as annotated CRF, define.xml, Pinnacle 21 validation, and reviewer's study guide) and validated tables, listings and figures (TLFs) for the study.
- Provide full-scope data management support, ensure processes are in place for data integrity, and use validated systems in compliance with 21 CFR part 11 (e.g., clinical database development and support, safety database development and support, IWRS development and support, data cleaning review, data listings, data status metrics, preparation of study-related materials and instructions, medical and drug coding, Serious Adverse Event reporting, database training and the assessment of clinical site capabilities for data collection and management, etc.)

- Work with BARDA to establish and manage a Scientific Steering Committee to consult on study design and potential drug candidates for the trial and establish the standard of care definitions. Develop the Scientific Steering Committee Charter. The Scientific Steering Committee is independent of the Data Safety Monitoring Committee. Offeror should identify 3-4 ARDS and critical care experts as members of the Scientific Steering Committee that are independent of the CRO, drug sponsor, and BARDA and provide qualifications to BARDA for approval.
- Work with BARDA and drug sponsors to organize and manage a Data Monitoring Committee (DMC), also known as Data and Safety Monitoring Board (DSMB) or Data and Safety Monitoring Committee (DSMC), to carry out independent assessments of the blinded and unblinded clinical data to assess patient safety. Identify independent DSMB members and provide qualifications for BARDA approval. Develop and implement plans for safety assessment and safety monitoring/pharmacovigilance activities, including identification, reporting, and tracking systems for AEs/SAEs, study pausing/stopping rules, etc. Offeror will include an unblinding plan consistent with International Conference on Harmonization E6(R2) to accommodate safety regulatory requirements. Offeror will provide an unblinded statistician to support the work of the DMC.
- Work with BARDA to organize and manage an Adjudication Committee. The Adjudication Committee is independent of the Data Safety Monitoring Committee and some overlap with the Scientific Steering Committee is acceptable. Offeror should identify members of the Adjudication Committee that are independent of the CRO, drug sponsor, and BARDA and provide qualifications for BARDA approval. Develop and implement plans for all Adjudication Committee activities that will be included in an Adjudication Committee Charter.
- Develop and implement plans for providing 24-hour medical monitoring support with qualified medical monitors training in appropriate therapeutic areas.
- Select home health care services for patient follow-up visits (estimated up to 20% of the recruited population in the trial) after discharge from the primary facility.
- Work with BARDA to develop a statistical analysis plan (SAP) for each product (the treatment vs. placebo) in individual cohorts and as a separate core SAP for pooled data across all treatment and placebo groups to assess biomarkers of disease and therapeutic response. Request information for structure and checklist (e.g., master SAP with addendums) as needed.
- Collect and analyze the data and write the final clinical study reports for each product and a separate final clinical study report for all products. E.g., work with BARDA to ensure that data collection procedures are harmonized and data formats are standardized. Develop and assess data quality metrics. Archive raw and processed datasets generated by the study sites.
- Provide Secure (21 CFR Part 11 compliant validated), study-specific internet-based portal that is password protected with managed user access roles.
- Administer and maintain a web-based document/content management system and study portals for secure electronic communications of study data, safety and laboratory data, and reports.

Offerors that do not provide the following information in their proposals will be considered non-responsive:

- Offerors must include overall program/project management, protocol development, medical writing, report publishing, site identification, site monitoring/management, statistical/data management, safety oversight including the establishment of the safety monitoring committee, budget management, and quality functions.
- Offerors must be included in the management team to ensure robust clinical monitoring as well as data quality and integrity.
- Offerors must provide the generated data from this trial to BARDA in FDA's standard Electronic Common Technical Document (eCTD) format for pooled biomarker analysis and subsequently published in peer-reviewed literature.

2.1 Application Guidance

This area of interest will be open until March 14, 2023. Note that an initial Quad Chart/White Paper will not be sought for this area of interest. Offerors must submit Full Proposals in accordance with the instructions provided in Part VI Full Proposal Instructions of the BAA. Changes to the protocol and transfer of obligations table will not be considered a part of the technical proposal page limit. Therapeutics for inclusion in the clinical trial will be solicited through a different mechanism, and proposals including candidate therapeutics will not be considered non-responsive. This area of interest has no TRL requirements.

Proposals that do not conform to the requirements outlined in the BAA will be considered non-responsive.

Please include "BARDA BAA AOI 9.7 Questions and Comments" in the subject line of all correspondence.

All administrative and general correspondence regarding this amendment shall also be submitted to the above e-mail addresses.

2. ATTACHMENT

Please read the Draft Protocol Synopsis and an example of a transfer of obligations table in the attachment. Full proposals will need to consider the protocol and expected transfer of obligations carefully. Full proposals should include proposed changes to the protocol and transfer of obligations table with a rationale for the change.

9.8 [SUSPENDED] COVID-19 Monoclonal Antibody Therapeutics for Pre-Exposure Prophylaxis (PrEP)

Monoclonal Antibodies (mAbs) can provide rapid pre-exposure protection against SARS-CoV-2 infection, particularly in special populations, such as adults and pediatrics who may be moderately to severely immune compromised and may not be able to mount an adequate immune response to COVID-19 vaccination or for whom vaccination with any available COVID-19 vaccine is not recommended.

BARDA seeks to advance the development of candidate antibody therapeutics (single or combination products) through FDA licensure; however, no US government procurements are anticipated for products developed under this topic. Candidate therapeutics should have data demonstrating:

- *In vitro* potency against human coronaviruses, to include:
  - *In vitro* activity against currently known variants of SARS-CoV-2, as designated by the World Health Organization (WHO) or the U.S. Centers for Disease Control (CDC) as a Variant of Concern (VOC) or Variant Being Monitored (VBM) due to shared attributes and characteristics that may necessitate a public health response. Variants should include but not be limited to those listed in *AOI 9.8 Table 1* below.
    - For SARS-CoV-2 potency is expected to be in the nanomolar range.
    - It is expected that data provided in this proposal is generated from qualified and/or validated live virus and/or pseudovirus neutralization assays.
    - The best proposals will demonstrate *in vitro* potency against MERS-CoV, SARS-CoV, and SARS-CoV-2.

AOI 9.8 Table 1		
WHO Label	**Pango Lineage**	**CDC Status at time of AOI posting:**
Alpha	B.1.1.7 and Q lineages	VBM
Beta	B.1.351 and descendent lineages	VBM
Gamma	P.1 and descendent lineages	VBM
Delta	B.1.617.2 and descendant lineages	VBM
Epsilon	B.1.427 and B.1.429	VBM
Eta	B.1.525	VBM
Iota	B.1.526	VBM
Kappa	B.1.617.1	VBM
N/A	B.1.617.3	VBM
Omicron	B.1.1.529 and descendant lineages	VOC
Zeta	P.2	VBM
Mu	B.1.621, B.1.621.1	VBM

- Epitope mapping demonstrating that all antibody contact residues within the SARS-CoV-2 epitope are greater than 95% conserved compared to the GISAID database or its equivalent of SARS-CoV-2 sequences.
  - Proposals with candidate products that are not targeting conserved regions will be considered non-responsive.
- Approach for achieving half-life extension greater than 35 days.
  - Proposal should include the expected half-life for candidate mAb(s) with supporting data demonstrating the typical half-life for mAbs with the planned modification.

- Potency to support intramuscular and/or subcutaneous administration with no more than two injections once every six months.

Proposals should address:

- Nonclinical Development Plan
  - IND enabling studies (safety and toxicology) and associated timelines, as well as an outline of risks and proposed approaches to risk mitigation.
  - It is expected that products that have not completed in vivo efficacy studies or tissue cross-reactivity studies will complete these activities within the first 3 months after contract award.
- Regulatory strategy and clinical development plan for obtaining FDA licensure, using aggressive risk management, and taking advantage of any regulatory flexibilities.
  - Regulatory strategies may include application for an Emergency Use Authorization (EUA), if an EUA is being pursued, proposals should anticipate moving into Phase 3 clinical trials by Q1 2024. Preference will be given to those able to begin Phase 3 enrollment in 2023.
  - Offerors may propose treatment Phase 3 trials as *optional* work if the clinical development plan includes multiple indications.
- Manufacturing strategy
  - Plan to perform at-scale manufacturing and fill-finish using cGMP validated manufacturing processes for bulk Drug Substance and fill and finished Drug Product to support evaluation through licensure.
  - The proposal should include a validation plan and associated timelines, as well as an outline of risks and proposed approaches to risk mitigation.
  - Preference will be given to candidate products with a demonstrated manufacturing process to support use in clinical trials at the time of proposal submission.
  - Manufacturing of products in the United States will be a requirement.

In addition to the *in vitro* and *in vivo* efficacy prioritization, products with reduced dosing, administration, and monitoring requirements will be preferred. BARDA will prioritize candidates that have reached TRL6 or later. However, earlier stage candidates may be considered.

Proposals shall include a cost-share, as well as address additional considerations to be received by the Government throughout the development effort. Consideration may include, but is not limited to, in-kind contributions of goods or services and should be long-term reflecting US taxpayer support for the development program.

White Papers submitted to AOI 9.8 will be accepted through May 17, 2023. Offerors may submit a Full Proposal in the absence of a White Paper submission. The submission deadline for Full Proposals is May 17, 2023, or as specified in the invitation for Full Proposal letter in response to a White Paper submission.

9.9 [SUSPENDED] COVID-19 Monoclonal Antibody Therapeutics for Treatment

BARDA is interested in supporting the manufacturing, FDA Emergency Use Authorization (EUA) and regulatory licensure of new monoclonal antibodies (mAbs)

effective at treating SARS-CoV-2 infection, particularly in special populations, such as adults and pediatrics who may be moderately to severely immune compromised. No US Government procurements of products developed under this topic are anticipated.

BARDA seeks candidate antibody therapeutics (single or combination products) that have:

- An active Investigational New Drug (IND) with the FDA, safety and toxicology data, and a demonstrated manufacturing process to support use in clinical trials at the time of proposal submission.
- A regulatory strategy to accelerate clinical evaluation of the candidate product.
  - Regulatory strategy is expected to target an EUA in Q3 2023.
    - Proposals that cannot achieve an EUA in 2023 or that cannot reference a previously completed phase 3 efficacy study will be considered non-responsive.
  - Proposals should include supporting documentation demonstrating FDA buy-in for any regulatory flexibilities the Offeror intends to leverage to accelerate the clinical development of the candidate therapeutic, such as immunobridging.
  - Preliminary data should be included demonstrating feasibility of the proposed approach.
- *In vitro* potency data against human coronaviruses shall include:
  - *In vitro* activity against currently known variants of SARS-CoV-2, as designated by the World Health Organization (WHO) or the U.S. Centers for Disease Control (CDC) as a Variant of Concern (VOC) or Variant Being Monitored (VBM) due to shared attributes and characteristics that may necessitate a public health response. Variants should include but not be limited to those listed in *AOI 9.8 Table 1* below.
    - For SARS-CoV-2 potency is expected to be in the nanomolar range.
    - It is expected that data provided in this proposal is generated from qualified and/or validated live virus and/or pseudovirus neutralization assays.
    - The best proposals will demonstrate *in vitro* potency against MERS-CoV, SARS-CoV, and SARS-CoV-2.

AOI 9.8 Table 1

WHO Label	Pango Lineage	CDC Status at time of AOI posting:
Alpha	B.1.1.7 and Q lineages	VBM
Beta	B.1.351 and descendent lineages	VBM
Gamma	P.1 and descendent lineages	VBM
Delta	B.1.617.2 and descendant lineages	VBM
Epsilon	B.1.427 and B.1.429	VBM
Eta	B.1.525	VBM
Iota	B.1.526	VBM
Kappa	B.1.617.1	VBM
N/A	B.1.617.3	VBM

Omicron	B.1.1.529 and descendant lineages	VOC
Zeta	P.2	VBM
Mu	B.1.621, B.1.621.1	VBM

- Manufacturing strategy to perform at-scale manufacturing and fill-finish using cGMP validated manufacturing processes for bulk Drug Substance and fill and finished Drug Product to support commercial availability by the end of 2023.
    - A description of the manufacturing facility, quality assurance, and regulatory acceptance, including quality systems and regulatory milestones towards facility approval, is required. BARDA will prioritize manufacturing in the United States.
- The proposal should include an outline of risks and proposed approaches to risk mitigation.

Proposals shall include a cost-share, as well as address additional considerations to be received by the Government throughout the development effort. Consideration may include, but is not limited to, in-kind contributions of goods or services and should be long-term reflecting US taxpayer support for the development program.

Note that an initial Quad Chart/White Paper will not be sought for this area of interest. Offerors must submit Full Proposals in accordance with the instructions provided in Part VI Full Proposal Instructions of the BAA.

Technical Point of Contact (AOI 9.1, 9.3, and 9.6): Peter Adams; Peter.Adams@hhs.gov

Technical Point of Contact (AOI 9.8, 9.9) Sabrina Stronsky; Sabrina.Stronsky@hhs.gov

Contracting Point of Contact: BARDA-BAA@hhs.gov with the subject line “Contracting questions: AOI9 (IEID Therapeutics): <brief description>”

Area of Interest #10: [SUSPENDED] MCM Production Platform Systems

Note: White Paper and Full Proposal submissions under AOI #10 are suspended until further notice.

10.1 [SUSPENDED] 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.

10.2 [SUSPENDED] Vaccine Production Platform

In alignment with the Executive Order on Modernizing Influenza Vaccines, BARDA is seeking to support the establishment of proven rapid vaccine production technologies (platforms) that are sustainable and "ready to use" for the production of vaccines against pandemic influenza and potentially other threats. Sustainment could be achieved through multiple commercial approaches, including a vaccine against other diseases (infectious diseases or other), using the same platform to limit reliance on annual USG support. This is a targeted request to support messenger ribonucleic acid (mRNA) technologies that have the potential to decrease the time required to go from sequence of a novel strain of influenza with pandemic potential to initiating clinical trials. This is not a request for development of vaccines against SARS-CoV-2. Minimal requirements for consideration of funding include the following: 1) capabilities substantiated by at least Phase 1 clinical safety and immunogenicity data (TRL6) of a vaccine manufactured with the proposed platform while data from a Phase 2 trial is preferred; 2) evidence of a vaccine candidate manufactured with said platform that is immunogenic following two or less doses in naïve individuals; 3) US based manufacturing capability and capacity to address a potential pandemic or plans to move manufacturing to the US and timing; 4)

delivery and administration configurations amenable to a mass vaccination scenario including considerations for cold-chain requirements; 5) evidence demonstrating rapid entry into clinical trials from R&D (e.g., determination of gene sequence) into a Phase 1 clinical trial within 60 days; 6) evidence, or substantiated plans, of the ability to rapidly scale-up or scale-out manufacturing capacities and; 7) plan for commercial sustainability of the proven technology by addressing other diseases.

Additional attributes of great interest include: 1) completion of the platform technology from candidate generation to full manufacturing; 2) evidence of an active IND(s) and other current regulatory status; 3) applicability of the technology to a range of pathogens and disease targets that address the commercial applications of the technology; 4) use without variation for each new application; 5) costs to develop, manufacture, deliver and administer product compared to current technologies; 6) clinical or pre-clinical data on a pandemic and/or seasonal influenza vaccine and; 7) evidence of stability at 2-8oC and/or 15-28oC for at least 6 months.

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, demonstration of its feasibility to meet a rapid response need, and sustainability in the vaccine market. While BARDA's interest is primarily Pandemic Influenza, a multi-product approach could be proposed with the second product being a vaccine other than influenza, to support long-term sustainability. In those situations, BARDA support will not include direct development funding (e.g. clinical trials) for candidates outside of the BARDA mission space. Support will instead be directed to activities such as labor, materials, equipment and studies needed to create and/or establish the vaccine production platform capability. Facility construction or retrofit cannot be supported under the Broad Agency Announcement. The proposed work should support verification of the successful production and clinical testing up to and including Phase 2 safety and immunogenicity trials of a pandemic influenza vaccine.

White Papers and Proposals submitted to AOI 10.2 will be accepted through February 28, 2021.

Technical Point of Contact: Dr. Ruben Donis; Ruben.Donis@hhs.gov

Contracting Point of Contact: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI10 (MCM Production Platforms): <brief description>"

Area of Interest #11 for DRIVe: [SUSPENDED] Solving Sepsis

This is a placeholder.

Area of Interest #12 for DRIVe: [SUSPENDED] Early Notification to Act, Control and Treat (ENACT)

This is a placeholder.

Area of Interest #13: [SUSPENDED] Advanced Manufacturing Technologies

Note: White Paper and Full Proposal submissions under AOI #13 are suspended until further notice.

The development and demonstration of innovations and enhancements to pharmaceutical manufacturing platforms to support the development of necessary medical countermeasures specifically vaccines and therapeutics in prevention, preparation, and response to COVID-19. The purpose of the innovations and enhancement to advanced manufacturing technologies may include but is not limited to improving pharmaceutical quality, rapidly scale manufacturing capabilities, shorten supply chains, increase manufacturing resilience to disruption, accelerate availability of emerging therapies/vaccines, and reduce the risk of pharmaceutical shortages. Specifically excluded from this AOI are manufacturing technologies related to personal protective equipment (PPE) and medical devices (ventilators, respirators, etc.). Advanced manufacturing technologies may include but is not limited to continuous manufacturing and additive manufacturing (including 3D printing). Priority will be given to products manufactured in a 21 CFR 210, 211 current Good Manufacturing Practices compliant facility within the United States.

Technical Point of Contact: Timothy Belski; Timothy.Belski@hhs.gov

Contracting Point of Contact: BARDA-BAA@hhs.gov with the subject line “Contracting questions: AOI13 (Adv Manufacturing Tech): <brief description>”

Area of Interest #14: Flexible and Strategic Therapeutics (FASTx)

To support BARDA’s mission to prepare for outbreaks and respond rapidly to emerging viral threats, BARDA seeks proposals to advance cost-effective, quickly adaptable therapeutic platforms to treat viral infections. These platforms may include, but are not limited to, monoclonal antibodies (mAbs), multispecific mAbs, nucleic acid expressed mAbs, nanobodies/single-domain antibodies (sdAbs), double-stranded RNA-mediated interference (RNAi), clustered regular interspaced short palindromic repeat-associated proteins (CRISPR-Cas), and locked nucleic acids (LNAs). Ideal proposals will demonstrate adaptability to multiple viral families by proposing investigative products for more than one viral target and a development path aimed at advancing a platform that

has the potential to yield cost effective therapeutics in a competitive timeline (<6 months from viral identification to Investigational New Drug (IND) submission).
Candidate Eligibility: Candidates for funding under this area should be at TRL-4 (candidate optimization) or higher, as indicated below. However, candidates earlier in development may be considered if it is anticipated they will significantly improve existing capabilities. A competitive antiviral platform candidate will encompass some or all of the following characteristics to build upon existing capabilities of the United States Government:

- Ability to leverage common aspects of the platform's manufacturing, safety, or mechanism of action to pivot rapidly for accelerated development of investigative products against new or re-emerging pathogens
- Ability to move from viral identification to IND submission in less than 6 months, with the potential to accelerate to 3 months with appropriate investment
- Demonstrated application of the technology (in vitro or in vivo) to multiple acute viral infections
    - Proposals focused on Pre-exposure prophylaxis (PrEP) will be considered but should see "Guidance for proposals pursuing a PrEP indication" below
- Data from a completed Phase 1 trial for any indication with a product produced using the proposed platform
- Demonstrated Pharmacokinetics/Pharmacodynamics necessary for treatment of acute viral infection; further priority for platforms achieving those endpoints without a requirement for intravenous administration
- Proposals directed at host targets are not responsive to this AOI

BARDA is seeking proposals that include the following:

A. Development activities necessary to support a candidate antiviral through Phase 1 studies for at least one viral indication and include options for technology demonstrations with additional viral targets. Ideal viral targets must have a well-defined animal model, disease kinetics amenable to therapeutic treatment during acute infection, and a clear path for regulatory approval. Suggested primary viral targets are SARS-CoV-2, filoviruses, and Influenza; however, a secondary target (preference for respiratory viruses and viruses causing hemorrhagic fever) of the developer's choosing may be proposed in addition to the primary target so as to validate the flexibility of the platform.

B. Analysis of risks and gaps in the therapeutic platform technology, as well as mitigation approaches to mediate those risks. This analysis should be linked to the timelines from pathogen discovery to IND submission, with and without risk mitigation, below in C.

C. Timeline for current capabilities to advance candidates through IND submission and anticipated optimal timeline based on proposed process improvements.

D. Efforts to make strategic improvements to the platform to reduce regulatory risk and safety risks; reduce cost of goods; improve response timelines; and/or meet the criteria listed in "Candidate Eligibility" above should be proposed as options

or incorporated into base work.

E. Proposed manufacturing plan and scale.

Proposals shall address considerations to be received by the Government throughout the development effort. Consideration may include, but is not limited to, cost sharing and any short- and long-term efforts on the sponsor's part that would reflect cost-savings to the Government given US taxpayer support for the development program.

Guidance for proposals pursuing a mAb platform:
The proposed activities must encompass mAb development from discovery (utilizing only viral isolate and/or sequencing information as starting material, not to include clinical samples) through manufacturing in order to be considered a valid "platform" approach. Proposals offering CHO-based manufacturing for monoclonal antibodies should explicitly outline innovations in the manufacturing approach that improve yield, recovery, and/or downstream manufacturing processes resulting in a cost of goods <$250/g in order to be considered responsive. CHO-based manufacturing approaches for bi-or multi-specific antibodies will be considered, and proposals including innovations to reduce cost of goods will be prioritized. Work appropriate for funding under this AOI should substantially improve current mAb capabilities, such as (but not limited to) the following:

- Non-intravenous routes of administration for treatment of acute infection
- Delivery to immune privileged sites and/or ability to target mAbs to specific organs (for example the lungs or airways)
- Substantially and demonstrably reduced development timeline
- Innovative manufacturing approach to substantially and demonstrably reduce cost of goods and subsequent per dose cost
- Cost of goods at less than $250/gram
- US-based manufacturing is preferred

Guidance for proposals pursuing a PrEP indication:
PrEP indications will only be considered for influenza and SARS-CoV-2, and candidates should meet the following criteria:

- Requires only a single dose for at least six months of protection
- Oral, subcutaneous, transdermal, inhaled, or Intramuscular route of administration
- Influenza PrEP candidates must protect against Influenza A including seasonal (H1N1 and H3N2) and potential pandemic (H5N1 and H7N9) viruses
    - Preference will be given for PrEP candidates that protect against Influenza A and B
- SARS-CoV-2 PrEP candidates must target highly conserved regions of the virus and are expected to be resilient against new viral variants
    - Preference will be given to PrEP candidates that are efficacious against multiple coronaviruses (for example MERS-CoV and SARS-CoV)

Guidance for proposals for SARS-CoV-2:
BARDA has a specific interest in submissions proposing work focused on SARS-CoV-2. Proposals for **SARS-CoV-2** are due by June 15, 2023. Offerors may submit a Full Proposal in the absence of a White Paper submission; however, interested parties

should reach out via email to the technical point of contact below with a description of the proposed effort prior to submitting a full proposal.

There is currently no submission deadline for proposals focused on other (non-SARS-CoV-2) viral threats.

Technical Point of Contact: FASTxBAA@hhs.gov
Contracting Point of Contact: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI 14 (FASTx): <brief description>"

Area of Interest #15: Next-generation COVID-19 Vaccines

While licensed and authorized vaccines are available for COVID-19, next-generation candidates may offer performance advantages in terms of durability/breadth of protection. Given the numerous promising candidates being developed, and the lack of a clear correlate of protection for many of these candidates, BARDA is taking a targeted approach to de-risk key development efforts to have as broad an impact as possible across the vaccine development space, rather than focusing on funding entire development plans for just a small subset of vaccines. BARDA envisions several efforts to support this approach. However, the largest effort will focus on generation of proof-of-concept Phase IIb efficacy data. Demonstration that a particular vaccine is effective (or not) against disease will significantly de-risk the overall program and allow development partners to rapidly move forward. The Vaccines Program is soliciting proposals for clinical development (scope defined below) of next-generation COVID-19 vaccines that may meet the following minimum criteria in order to enable rapid acceleration into Phase IIb trials:

1. Program must have an active or complete Phase 1 clinical trial, with unblinded safety and immunogenicity data to support a Phase IIb trial available no later than 6 months after proposal submission
2. Program must have an active IND with the US FDA
3. Vaccine candidate must include one or more of the following aspects:
    1. Mucosal administration
    2. Inclusion of spike protein and at least one additional non-spike SARS-CoV-2 antigen
    3. Multi-RBD based approach (contains RBDs from more than two SARS-CoV-2 variant spike gene, presumed to provide broader protection against circulating variant strains than currently approved vaccines; RBDs can be expressed separately or as fusion proteins)
4. Program must have available sufficient clinical trial material to support the proposed Phase 2b study no later than 6 months after proposal submission
5. Offeror must be willing to allow immunogenicity analyses at a central laboratory determined by USG
6. Program must include plans for access to comparator (i.e., licensed product)

BARDA seeks proposals for the clinical development of vaccines against COVID-19. Specifically, BARDA is seeking proposals to conduct a Phase 2b clinical trial comparing sponsors' candidate to licensed products. **BARDA is seeking full proposals; potential**

offerors do not need to start the proposal submission process with a white paper. Proposals should align with the clinical trial synopsis in the AOI 15 Protocol Synopsis attachment. For any programs under this Area of Interest, it is expected that offerors are supporting CMC and regulatory activities at an appropriate level to enable the following clinical activities structured in this manner:

BASE PERIOD – Clinical trial planning activities for Phase 2b clinical trial comparing sponsor candidate to licensed/authorized product in the US (Base period activities would constitute a firm fixed price agreement of up to $10M total with milestones for each bullet to be negotiated). Go/No Go decision points to move into Option 1 will depend on timelines and availability of funding. Please note that parallel efforts are underway for USG-sponsored clinical trials. Based on expected timelines, availability of funding, and offeror's ability to manage the trial execution, offerors may also engage through the BARDA Division of Clinical Development who can provide any needed aspects of clinical trial infrastructure support and management. Efforts should include all preparation activities to execute the Phase 2b trial synopsis, including but not limited to:

- Protocol synopsis
- Submit IND updates as needed
- Provide Investigational Brochure
- Develop clinical trial protocol
- Develop study-specific documents (informed consent, pharmacy manual, lab manual, manual of procedures, etc.)
- Establish Product Agreement(s) and supporting documentation
- Select CRO and/or other vendors as needed
- Select Laboratory for per protocol research Assay(s) - consider as a standalone option
- Establish Safety Oversight Committee
- Develop Statistical Analysis Draft Plan
- Develop Data Management Plan
- Develop Risk Management Plan
- Develop Sample Management Plan (labeling, disposition, distribution)
- Develop Recruitment, Enrollment and Retention Plan including diversity
- Conduct Safety Oversight Committee meeting
- Confirm that Safety Oversight Committee recommendations have been reviewed, accepted, and implemented as indicated
- Establish publications agreement
- Conduct Site Readiness activities:
    - Site qualification visit completed, and all issues resolved
    - All regulatory documents are in and reviewed for appropriateness and determined to be complete
    - Monitoring plan has been accepted by BARDA

OPTION 1 – Clinical trial execution for Phase 2b clinical trial comparing sponsor candidate to licensed/authorized product in the US (please note, funding for Option 1 is expected to be a single execution with an assumption of no further funding being available in the event of cost overruns. The offeror should propose an approach to address the risk of overruns.)

- Confirm that IND is in effect (if applicable) and status has been confirmed by BARDA regulatory
- Conduct Site Readiness activities
  - IRB approval confirmed and if applicable sIRB
- Confirm site contract(s) in place
- Confirm that assay procedures that need to be completed for all study points are in place (safety, screening, and immunogenicity labs)
- Develop Statistical Analysis Final Plan
- Confirm data management system and/or data management process for all aspects for all study aspects of the study have been completed
- Conduct study initiation visit
- Confirm that NLM posting has occurred / clinical trial reporting
- Confirm that materials and supplies sourced and onsite
- Confirm study product available and onsite
- Execute Phase 2b clinical trial
- Conduct study Close-out at sites
- Conduct sample analysis for primary and secondary endpoints (note: offerors may provide their own immunogenicity analysis plans, but it is expected that aliquots of all samples will be made available for testing at central USG-supported labs)
- Perform database lock
- Perform data analysis
- Produce Clinical Study Report within 3 months of database lock
- Transfer clinical data and samples to BARDA
- Provide weekly (dashboard) reporting to BARDA
- Perform annual IRB/IND reporting
- Provide Investigational Brochure updates
- Provide Drug Safety Update Reports

OPTION 2 – Additional analyses for Phase 2b clinical trial

- Analyze exploratory endpoints
- Conduct unplanned additional analyses

Qualities That Strengthen the Competitiveness of a Proposal:

Competitive proposals will address (but are not limited to) the following factors:

- Proposals must involve vaccine candidates that meet the minimum criteria noted above
- Proposals must ONLY include the activities proposed above (i.e., planning and execution of a Phase 2b clinical trial)
- Proposals should include a clinical trial synopsis.
- Proposals should note a plan to access licensed/authorized product as a comparator
- Proposals should include detailed Gantt charts to reflect accurate timelines of activities noted above as well as any additional tasks the offeror feels will be necessary.
- Offerors should note that out-year funding may not be available. Offerors should provide details of any proposed cost-sharing, if applicable, and how potential cost overruns would be managed in the absence of additional USG funding.

- Proposals shall include a cost-share, as well as address additional considerations to be received by the Government throughout the development effort. Consideration may include, but is not limited to any short- and long-term efforts on the sponsor's part that would reflect cost-savings to the Government given US taxpayer support for the development program.
- Proposals should include a description of no more than 1 page of the overall development strategy, how this trial fits into that strategy, and the next steps that will be taken if the trial results are positive.
- Proposals should align with the following key tenets:

    1. The study protocols will be harmonized with respect to primary endpoints, a minimal common set of secondary endpoints, and statistical analysis plans. Specific secondary or experimental endpoints can be included for each program.
    2. Each Phase 2b clinical trial will obtain data and samples required for analysis of primary endpoints assays and key immune assays across studies which may be utilized to support assessment of immune responses to vaccination, assay development, or antigenic characterization of variant viruses as well as the collection of samples for secondary research (future use) that will be sent to the USG.

        a. Primary endpoint assays (PCR and serology) will be specified by the USG and run at a USG- authorized laboratory to allow comparability across trials. These assays will be funded by the USG.

        b. Key immune assays will be specified by the USG and run at a USG-authorized laboratory. Validated and/or qualified assays will be used where available. The key immune assays will be funded by the USG; however, offerors should proposal sample management plans that would enable other analyses as needed.

        c. Immunogenicity data from multiple trials are intended to be used in aggregate correlates or surrogates of protection studies and data will be shared with parties and published.

    3. The Sponsors will be ultimately responsible to ensure medical case management. Importantly, the specific approach to ensuring optimal care for participants infected with COVID during the trial will belong to the Sponsor.
    4. The Phase 2b clinical trials will all be overseen by DSMBs fulfilling all standard duties of DSMBs, the composition of which will be set by the Sponsor and Funder.
    5. Awardees should provide a Diversity Plan to improve enrollment of participants based on 'Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials Guidance for Industry' (Draft April 2022) https://www.fda.gov/regulatory-information/search-fda-guidance-documents/diversity-plans-improve-enrollment-participants-underrepresented-racial-and-ethnic-populations. The Diversity Plan must include proposed targets to achieve deliverable. If necessary, the USG may pause enrollment to ensure diversity in the cohort.

Technical POC: Daniel Wolfe; Daniel.Wolfe2@hhs.gov
Contracting POC: BARDA-BAA@hhs.gov with the subject line "Contracting questions:

AOI 15 Next Gen COVID-19 Vaccine <brief description>”

Area of Interest #16 for DRIVe: ImmuneChip+

Accurately modeling human tissues under homeostatic and pathologic conditions *in vitro* is a key step to accelerating the pace of drug discovery and development: a necessary capability for effectively responding to pandemics and other CBRN emergencies. The use of advanced microphysiological systems (MPS; otherwise known as tissue- or organ-on-a-chip platforms) that structurally and functionally replicate components of human tissues could result in unprecedented opportunities for addressing mechanistic questions of health and disease, as well as assessing biomedical interventions.

Moving towards comprehensive histologically accurate approaches that include components of the human immune system, these MPS could serve as a predictive tool in the drug screening and the development process. The ultimate objective is to leverage development and application of these platforms for rapid testing of candidate countermeasures, identifying biomarkers or mechanisms that lead to a better understanding of injury and disease that supports emergency preparedness and rapid response capabilities against a broad set of known and unknown chemical, biological, radiological, and nuclear threats.

With this AOI, BARDA intends to advance toward the commercialization of a set of qualified multi-tissue MPS technologies.

Overview

BARDA requests submissions to support developing and characterizing of advanced *in vitro* platforms that replicate components of vital human tissues and the immune system and their interactions under homeostatic conditions. Submissions that qualify for this funding shall preferably focus on engineering 3-D *in vitro* human MPS representing various tissues (*e.g*., lung, liver, gut, heart tissue, brain-blood-barrier, or others) with immune component(s) (such as lymphoid follicle, spleen, thymus, or any other immune cells or tissues) integrated on a single platform. Specifically, respondents should add an immune component(s) to MPS previously established in their laboratories that could enable monitoring of toxicological, inflammatory, and immune (innate/adaptive) responses to chemical, biological, radiological, or nuclear threat agents. Submissions should ideally include two or more of the following five components:

1) a) infection with a relevant viral, bacterial, or fungal pathogen, or

   b) insult with toxins or toxicants, including but not limited to botulinum neurotoxin, or

   c) exposure to acute ionizing radiation, or

   d) exposure to chemical agents;

2) integration of at least two different tissues in addition to the immune component(s);

3) near-continuous monitoring of the MPS for at least two weeks;

4) (semi-)automated manufacturing of the platform; and,

5) biological characterization of the MPS and recapitulation of existing clinical data in response to injury / morbidity and various medical countermeasures.

Well-defined; specific; and, when possible, quantitative milestones, deliverables and benchmarks should be described in the Research Strategy.

Submission requirements and desired attributes:

Biological attributes:

1) Human tissue models are highly desired. Projects specifically focusing on platform optimization and comparing with known pre-clinical data from relevant animal models may use animal cells. Otherwise, the use of animal cells is discouraged but may support proof of concept studies in establishing methods where primary human cells are limited or unduly constrain the project.
2) The use of primary cells, organ explants, or pluripotent stem cells, *e.g.*, iPSC, is encouraged. The use of transformed or immortalized cell lines is discouraged. Multipotent or unipotent stem cells also may be utilized where appropriate.
3) All MPS should mimic the architecture, organization, multi-tissue interfaces, physiology, and replicate disease pathology of the native tissue.
4) Inclusion and monitoring of multiple immune elements enabling toxicological, inflammatory, innate, or adaptive responses (*e.g*., lymphocytes, macrophages, neutrophils, or mucosa-associated lymphoid tissue) is desired.
5) Projects should utilize MPS models previously developed and characterized by the Respondent, and functionally enhance them by integrating relevant components of the human immune system in a controlled manner. For example, the development and integration of multiple immune tissues such as lymphoid follicles, spleen, and thymus with each other is desirable, as is the integration of non-immune and immune tissues. Preliminary data should discuss all studies and analyses used to characterize the model.
6) Characterization of proposed disease or injury model(s) to understand how tissue interactions influence disease and treatment. The ideal submission will describe a plan to integrate at least two tissue models plus one or more relevant immune system components.

Functionality:

1) Key characteristics of the MPS include some or all of the following features: (a) multicellular architecture that represents key characteristics of the chosen tissue; (b) functional representation of normal and/or diseased human biology; (c) reproducible and viable operation under physiological conditions in culture for a minimum of two weeks (after any relevant cell and tissue differentiation); and (4) accurate representation of normal and/or disease phenotypes. Evidence of such achievement for MPS previously developed by the respondent should be included in all submissions.
2) The platform should demonstrate the capability to identify new or test existing candidate therapeutics, prophylactics, and vaccines (*e.g.,* in dose-response studies), where appropriate.

3) Proposed MPS should utilize platform material(s) that are tissue-compatible and appropriate for automated production.

4) Each platform should ideally include at least two different types of built-in biochemical / biophysical sensors that enable frequent monitoring of the developing tissues. Applicants should discuss the clinical value of the observed biomarkers.

Team and facility capability:

1) The ideal Respondent will have assembled a comprehensive team necessary to address all aspects of the proposal, including but not limited to tissue chip experts, microfluidics experts, immunologists, virologists, toxicologists, biochemists, biostatisticians, bioengineers, biosafety, chemical surety, radiation physics, and safety experts, as necessary.

2) Collaborative submissions from the private sector or private–academic partnerships are strongly encouraged.

3) Depending on the type of CBRN threat proposed, information on the following capabilities should also be provided by respondents:

    a. BSL-2, BSL-3, and/or BSL-4 capabilities (if necessary)

    b. Good Laboratory Practice (GLP) capabilities

    c. Laboratory Quality Management System(s)

    d. Chemical surety labs certified to work with compounds listed in "Desired Project Topics"

    e. NRC radiation safety programs support the use of controlled radioactive sources.

Commercialization:

BARDA's goal is to advance ImmuneChip+ developmental systems to the eventual commercialization of well-characterized research products, instruments, and associated technologies. Accordingly, Respondents should provide a commercialization plan and clearly outline the potential for commercialization of their MPS, or any MPS component, and how the current submission may facilitate that progress. The plan should also address manufacturing, quality control, and, if relevant, any need for regulatory validation.

Out-of-scope project attributes:

Proposed projects utilizing 2D tissue models, trans-well platforms, or spheroids / organoids are not responsive.

Offerors are encouraged to submit proposals that address one of the following topics:

Division of Research, Innovation, and Ventures (DRIVe) interest areas:

- Development of modular multi-tissue platforms. Submissions should outline how integration challenges (such as the need for a common tissue medium; fluidic connections; integration of tissue sensors) will be addressed.

- Characterization studies on known approved and unapproved therapeutic candidates to demonstrate agreement with established preclinical and clinical data.

Chemical Medical Countermeasures threat area:

- Natural history studies of chemical injury (*e.g,.* sulfur mustard, chlorine, phosgene, phosphine, xylazine) in target organ systems, including lung, dermal, ocular, and CNS.
- Natural history studies in animal chip models (*e.g,.* murine, ovine, or porcine) that can bridge *in vivo* findings and human chip studies.
- Respondents proposing studies of OPCW scheduled chemicals must have appropriate facilities and licensure to handle such chemicals.

Radiological/Nuclear threat area:

- Natural history studies of acute radiation syndrome in target organ systems (e.g., Hematopoietic, GI, Lung, Kidney, Cardiac) using human cells.
- Natural history studies in animal chip models (*e.g.,* NHP, porcine, or rabbit) that can bridge *in vivo* findings and human chip studies.
- Vascularized models with endothelial cells that can model vascular injury.
- Respondents proposing ARS studies should have appropriate facilities to expose models to energies and doses of ionizing radiation anticipated in a nuclear event.

Administrative considerations:

Participation in a market research call is highly encouraged ahead of submitting a proposal. Requests for calls should be submitted via email to immunechipbarda@hhs.gov.

All technical and administrative correspondence and questions regarding this AOI must be submitted via email to immunechipbarda@hhs.gov, with the Subject Line: "[Company Name] [ImmuneChip+]". Questions should not contain proprietary or classified information.

All awardees are expected to share project updates and results in a quarterly program meeting, with representatives from multiple federal agencies and other contractors present.

Technical Point of Contact: immunechipbarda@hhs.gov

Contracting Point of Contact: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI16 (ImmuneChip+): <brief description>"

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., older adults, 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., older adults, 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 the BARDA BAA Toolkit[29] and the ASPR Business Toolkit 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.

[29] https://www.medicalcountermeasures.gov/barda/barda-baa#toolkit

Part IV: Special Considerations

Special Instructions will be posted as amendments to the BAA on SAM.gov 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

and is described in the BARDA BAA Process Flow Chart (Part VIII: Attachment 10) and online on PHE's BARDA Broad Agency Announcement[30].

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

[30] https://www.phe.gov/about/amcg/BARDA-BAA/Pages/default.aspx

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 or do not contain one or more of the required items listed above may be deemed nonresponsive and 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.

Submission Data Integration Table

Complete Attachment 11: Submission Data Integration Table as an appendix to the submission to facilitate processing and tracking of the submission. This table will not count against the page count.

Quad Chart and White Paper Submission

Quad Charts and White Papers WILL NOT BE ACCEPTED after 4:30 PM (Eastern Time) on **September 25, 2023**.

Respondents must submit Quad Charts and White Papers in accordance with the Submission Instructions of this solicitation.

IMPORTANT: White Papers do not require any special forms, but must be submitted in the following format:

- Single PDF file
- 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 120 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 120 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

and is described in the BARDA BAA Process Flow Chart (Part VIII: Attachment 10) and online on PHE's BARDA Broad Agency Announcement[31].

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 attached 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;"

[31] https://www.phe.gov/about/amcg/BARDA-BAA/Pages/default.aspx

2. BAA number;

3. Research and Development Area of Interest;

4. Proposal Title (descriptive of the work proposed and not a copy of the title of the solicitation);

5. Proposal Description: brief 1-2 sentence of the purpose or goal of submission

6. Date of submission;

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

8. Offeror DUNS number and CAGE code

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

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

11. 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 The BARDA BAA Toolkit[32] http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/Govt-Owned-Prop.pdf(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 BARDA BAA Toolkit[33] 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:

[32] https://www.medicalcountermeasures.gov/barda/barda-baa#toolkit
[33] https://www.medicalcountermeasures.gov/barda/barda-baa#toolkit

- 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 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[34].

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 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).

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

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.

R. Submission Data Integration Table

- Complete Attachment 11: Submission Data Integration Table as an appendix to the submission to facilitate processing and tracking of the submission. This table will not count against the page count.

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.

	Item	Required	Reference & Document Type
2	Protection of Human Subjects	If Applicable	Human Subject Research (45 CFR 46)[35]
3	Animal Welfare	If Applicable	Office of laboratory Animal Welfare (OLAW)[36]
4	Intellectual Property	Yes	
5	Biographical Sketches	Yes	Part VIII: Attachment 9 (NIH Biosketch[37])
6	Use of Select Agents	If Applicable	Federal Select Agent Program[38]http://www.cdc.gov/od/sap Agriculture Select Agent Service[39]
7	Laboratory License Requirements	If Applicable	
8	Target Product Profile (TPP)	Yes, except for Diagnostics, Ventilators, Respiratory Protective Devices, Platforms, Modeling, and Visual Analytics	Part VIII: Attachment 2 (for template)
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.
10	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

[35] http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html
[36] http://grants.nih.gov/grants/olaw/olaw.htm
[37] https://grants.nih.gov/grants/forms/biosketch.htm
[38] http://www.selectagents.gov/
[39] https://www.selectagents.gov/SelectAgentsandToxins.html

- 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 older adults (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[40].

- 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

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

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[41].

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

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

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.

10. FDA Communication Data

- 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]

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 DUNS[42] TIN[43] CAGE[44] NAICS[45]
2	Representations and Certifications	Yes	System for Award Management[46] (SAM)
3	Breakdown of Proposed Estimated Cost (Plus Fee) and Labor Hours	Yes	Part VIII: Attachment 7 BARDA BAA Toolkit[47] http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/Govt-Owned-Prop.pdf(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 BARDA BAA Toolkit[48] and Grants.Gov[49]
5	HHS Small Business Subcontracting Plan	If applicable	Small Business SubContracting Plan[50]
6	Summary of Related Activities	Yes	Part VIII: Attachment 4 (for template)
7	Lobbying Activities	Yes	For Grant: SF-LLL: Disclosure of Lobbying Activities[51] For Contract: HHSAR 352.203-70[52] https://www.whitehouse.gov/sites/default/files/omb/grant

[42] https://www.dnb.com/duns-number.html
[43] https://www.irs.gov/businesses/small-businesses-self-employed/apply-for-an-employer-identification-number-ein-online
[44] https://cage.dla.mil/Home/UsageAgree
[45] https://www.census.gov/eos/www/naics/
[46] https://www.sam.gov/
[47] https://www.medicalcountermeasures.gov/barda/barda-baa#toolkit
[48] https://www.medicalcountermeasures.gov/barda/barda-baa#toolkit
[49] http://www.grants.gov/web/grants/forms.html
[50] https://www.hhs.gov/grants/contracts/contract-policies-regulations/subcontractplan/index.html
[51] https://www.grants.gov/web/grants/forms/post-award-reporting-forms.html
[52] http://www.hhs.gov/grants/contracts/contract-policies-regulations/hhsar/subpart352/

	Item	Required	Reference & Document Type
8	Report of Government-Owned, Contractor-Held Property	If applicable	BARDA BAA Toolkit[53] http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/Govt-Owned-Prop.pdf(for template)http://oamp.od.nih.gov/sites/default/files/DGS/c
9	Financial Capacity and Annual Financial Report	Yes	
10	Past Performance Contact Information	Yes	Part VI, Section 10
11	Reason for the Proposed Award Type	If applicable	Overview Information, Type of Award

1. **DUNS[54], TIN, CAGE, and NAICS[55]:**

   - 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[56] (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.

[53] https://www.medicalcountermeasures.gov/barda/barda-baa#toolkit
[54] http://www.dnb.com/
[55] http://www.census.gov/eos/www/naics/index.html
[56] https://www.sam.gov/

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 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 BARDA BAA Toolkit[57], 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

[57] https://www.medicalcountermeasures.gov/barda/barda-baa#toolkit

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 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.

11. Reason for the Proposed Award Type

- If applicable, provide a rationale for the proposed award type.

Stage 2: Full Proposal Submission

Offerors must submit Full Proposals in accordance with the Submission Instructions listed on page 11 of this solicitation.

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.

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 regard 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

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

For use with:

- Area of Interest #2: CBRN Antitoxins and Therapeutic 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 #14: Flexible and Strategic Therapeutics (FASTx)

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

Table 4: Technology Readiness Level and Description for Area of Interest 7

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)[58,59] (For Use with Areas of Interest 2-6, 8-9, and 14)

For Areas of Interest 2-6 and 8-9, 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 2-6, 8-9, and 14

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 2-6, 8-9, and 14

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)).

[58] 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/

[59] 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)**[60] Scale-up and initiate validation of GMP manufacturing process. Conduct animal efficacy studies as appropriate.[61] Conduct Phase 2 clinical trial(s).[60] **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.[61] **7B** Complete expanded clinical safety trials as appropriate for the product (e.g., Phase 2).[60]

[60] 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

[61] 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

Level	Description
TRL 8	**Completion of GMP Validation and Consistency Lot Manufacturing, Pivotal Animal Efficacy Studies or Clinical Trials[60], 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.[60] **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.[62] **9B** Maintain manufacturing capability as appropriate.

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.

[62] 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 form in metric system and a description of identifying characteristics of dosage forms	*Summary information regarding completed or planned studies to support the 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 that will address adverse reactions associated with a particular drug class.*	*Summary information regarding completed or planned studies to support the target:* *Protocol #, Serial #, Submission date*
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[63]

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

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

- specification developers
- 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 BARDA BAA Toolkit[64] 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).

[64] https://www.medicalcountermeasures.gov/barda/barda-baa#toolkit

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.

Attachment 9: Biographical Sketch[65] (NIH, non-fellowship)

OMB No. 0925-0001 and 0925-0002 (Rev. 03/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME:

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE:

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY

A. Personal Statement

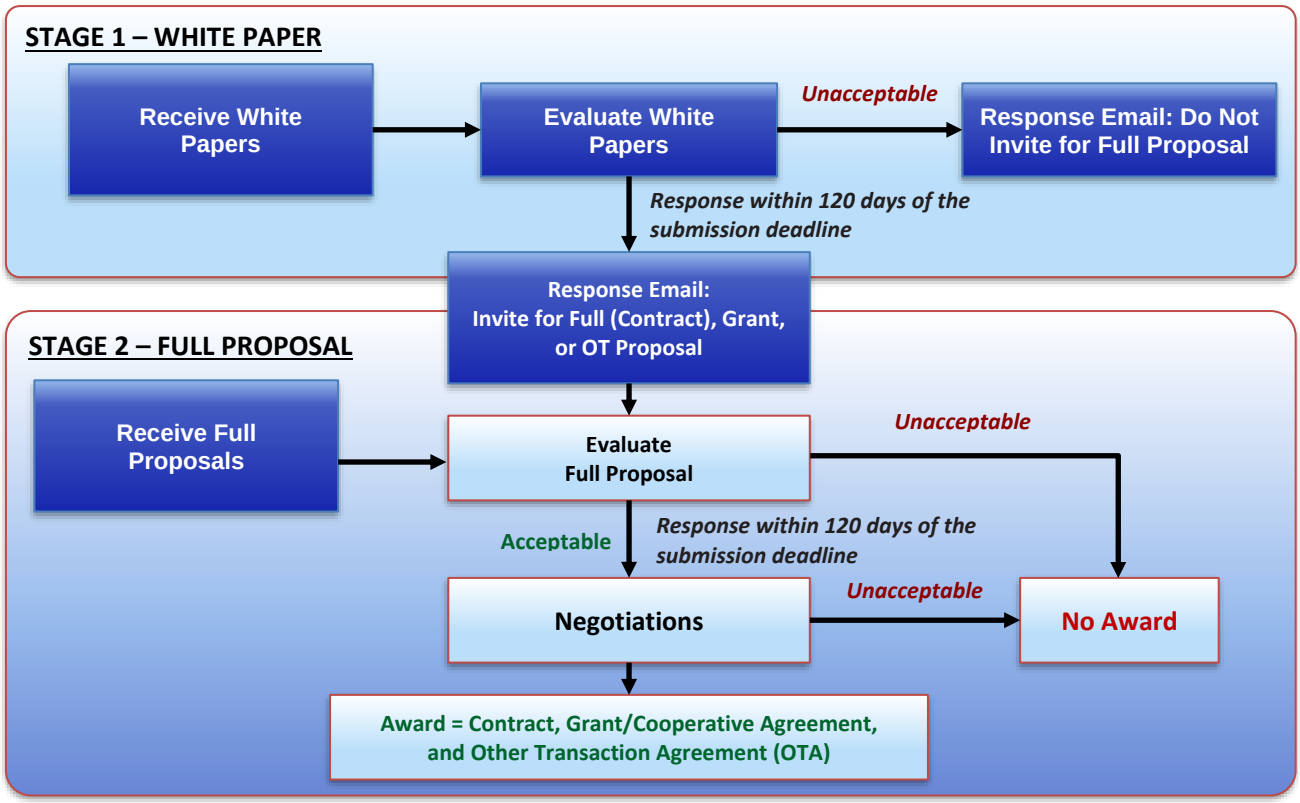
B. Positions and Honors

C. Contributions to Science

D. Additional Information: Research Support and/or Scholastic Performance

[65] https://grants.nih.gov/grants/forms/biosketch.htm

Attachment 10: BARDA BAA Process Flow Chart



Attachment 11: Submission Data Integration Table

On a separate page, complete the following table and include it in your submission as an appendix to facilitate processing and tracking of the submission. This table will not count against the white paper or full proposal page count.

Data Type:	**Explanation**
Area of Interest:	
Submission Title:	
Submission Description:	<brief description of purpose or goal of submission>
Organization Name:	
DUNS:	
CAGE:	
Street 1:	<street name, e.g. 123 Main Street>
Street 2:	<if applicable, e.g. Suite 123>
City:	
State or Province:	
Zip:	
Country:	
Point of Contact First Name:	
Point of Contact Last Name:	
Point of Contact Email:	
Product / Technology Type:	
Product Name:	
Technology Readiness Level:	