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

BAA-23-100-SOL-00004

Amendment 2

December 22, 2023

Biomedical Advanced Research Development Authority (BARDA)

Division of Contract Management & Acquisition (CMA)

400 7th Street, SW, Washington, DC 20024

MedicalCountermeasures.gov

Table of Contents

INTRODUCTION 5

Disclaimers 5

OVERVIEW INFORMATION 7

Agency Name 7

Issuing Office 7

Development Opportunity Title 7

Announcement Availability 7

Eligible Offerors 7

Research and Development Opportunity Description 8

Research and Development Areas of Interest 8

Technological Maturity 8

Number of Awards 8

Type of Award 8

General Market Research (TechWatch Program) 9

Application Process 9

Submission Deadlines and Government Response Time 10

Contact and Submission Information 10

Electronic Portal Submission Instructions 10

Limitation on Communication After Submission 11

Special Instructions 11

Proposal Handling and Submission Information 11

BACKGROUND 12

Part I: Development and Technical Objectives 14

Program Management Approach 14

Regulatory Approach 14

Development and Manufacturing Approach 15

Part II: Reporting Requirements and Deliverables 19

Part III: Special Considerations 19

Contractor Responsibility Regarding Sensitive Information 19

Security Plan 20
Identification and Disposition of Data 20
Confidentiality of Information 20
Publications 20
Press Releases 20
Export Control Notification 20
Manufacturing Standards 20
Prohibition on Contractor Involvement with Terrorist Activities 21
Part IV: Pre-Submission Call and Quad Chart/Market Research Abstract Instructions (Stages 1 & 2) 24
Stage 1: Pre-submission Call with Technical POC 25
Stage 2: Quad Chart and Market Research Abstract Preparation 25
Stage 2: Quad Chart and Market Research Abstract Submission 26
Part V: Quad Chart/Market Research Abstract Assessment 26
Part VI: Proposal Instructions (Stage 3) 27
Stage 3: Proposal Preparation 27
Stage 3: Proposal Submission 38
Part VII: Proposal Evaluation 38
1. Program Relevance 38
2. Overall Scientific and Technical Merits of the Proposal 39
3. Offeror's Capabilities and Related Experience, Including the Qualifications, Capabilities, and Experience of the Proposed Key Personnel 39
Other Evaluation Factors and Considerations 39
Evaluation Rating 40
Additional Information 40
Part VIII: Research and Development Areas of Interest 41
Area of Interest #1: CBRN Vaccines 41
Area of Interest #2: CBRN Antivirals and Antitoxins 42
Area of Interest #3: Antimicrobials 45
Area of Interest #4: Radiological/Nuclear Threat Medical Countermeasures 46
Area of Interest #5: Chemical Medical Countermeasures 49
Area of Interest #6: Burn and Blast Medical Countermeasures 51

Area of Interest #7: Diagnostics 53
Area of Interest #8: IEID Vaccines..... 58
Area of Interest #9: IEID Therapeutics 61
Area of Interest #10: ImmuneChip+..... 66
Area of Interest #11: [SUSPENDED] COVID-19 Immune Assay(s) Development and Implementation 70
Area of Interest #12: Flexible and Strategic Therapeutics (FASTx)..... 71
Part IX: Appendix 73
Appendix 1: Government Notice for Handling and Submitting Proposals 73
Appendix 2: Cost Certification..... 74

INTRODUCTION

Within the Administration for Strategic Preparedness and Response (ASPR), the Office of Biomedical Advanced Research and Development Authority (BARDA) was established and mandated by Congress as the organization within the U.S. Government to catalyze innovation in advanced research and development (R&D), manufacturing, and procurement of Medical Countermeasures (MCMs). These lifesaving MCMs are needed to protect people during public health emergencies from threats such as chemical, biological, radiological, and nuclear (CBRN) incidents (whether accidental or intentional), pandemic influenza, COVID-19, and other emerging infectious diseases. BARDA works closely with interagency partners through the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) to ensure a coordinated, whole-of-Government approach to MCM preparedness and response.

The BARDA model has proven successful in leveraging public-private partnerships to accelerate development of MCMs that are vital to national security. BARDA helps its partners promote innovation and develop countermeasures from early research through U.S. Food and Drug Administration (FDA) approval and clinical application. Over the last 15 years, BARDA has supported over 85 FDA approvals, licensures, and clearances of MCMs.

The COVID-19 pandemic serves as a stark reminder of the need to protect individuals from public health emergencies. BARDA was critical in the development, manufacturing, and procurement of MCMs that saved countless lives during the pandemic. The COVID-19 pandemic revealed gaps and challenges at BARDA as noted in the BARDA Strategic Plan 2022-2026. Increasing the speed of partnering was identified as an area of improvement in the strategic plan.

To achieve objectives outlined in the BARDA strategic Plan, BARDA is modernizing the Broad Agency Announcement (BAA). The new BAA, BARDA BAA-23-100-SOL-00004, is designed to enable BARDA to accelerate partnering, improve responsiveness and meet expanding demand to develop MCMs. By releasing this BAA, BARDA seeks to improve efficiency, improve responsiveness, and decrease time to award, by modernizing our 15+-year BAA[1] to meet the demands of an expanding mission and portfolio of industry partners. Change to this BAA reflects experience and growth of the acquisition vehicle and the need for BARDA to more quickly pivot and respond during a pandemic or public health emergency.

Disclaimers

This BAA, which sets forth R&D areas of interest (AOIs) for 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 including FAR-based contracts and Other Transactions, as well as grants and cooperative agreements.

Significant change compared to the prior BAA: Under this BAA, Stage 1 and Stage 2 submissions are considered market research, outside the scope of FAR Part 35, and used by BARDA to collect and analyze information about capabilities within the market to satisfy agency needs. Should the Stage 2 submission

[1] BARDA's BAA has been open continually under various forms and solicitation number since originally released in 2008.

be assessed favorably, then the Respondent will be invited to submit a Stage 3 Proposal. Stage 3 proposals will be evaluated consistent with FAR Part 35. Further information regarding the three stages of this BAA process is discussed in Part IV through Part VII of this announcement.

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 Street, 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)/ Division of Contract Management & Acquisition (CMA), 400 7th Street, SW, Washington, DC 20024

Development Opportunity Title

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

Announcement Availability

This BAA is available on the following websites:

- SAM.gov
- MedicalCountermeasures.gov
- Grants.gov

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 and must be registered in the System for Award Management (SAM) at SAM.gov prior to receiving an award.

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 Offeror.

Historically Black Colleges and Universities (HBCUs), Minority Institutions, 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 HUBZone Small Business concerns are encouraged to submit proposals and to join other entities as team members in submitting proposals.

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

Research and Development Opportunity Description

The Division of Contract Management & Acquisition (CMA) on behalf of BARDA will engage in market research and solicit proposals for the advanced R&D of MCMs for 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 MCMs toward approval, licensure, or clearance by the FDA. This BAA will also serve to advance the knowledge and scientific understanding, including but not limited to candidates' platform technologies, modeling and forecasting, and visual analytics.

The purpose of this BAA is to solicit proposals that focus on R&D in the solicited AOIs as described in Part VIII 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 I. Efforts proposed by Offerors may cover all aspects of MCM Advanced R&D, including but not limited to Nonclinical R&D, Process Development, Platform Development, Formulation, Manufacturing, and Clinical Evaluation.

Technological Maturity

Interested parties should identify in their Quad Chart and Market Research Abstract the current Technology Readiness Level (TRL) of their product, and the TRL identified should meet or exceed the requirements of the given Development AOI. Each Market Research Abstract and Proposal must 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 the BARDA BAA Toolkit. Note that all activities within a TRL (or sublevel) must be completed to have achieved that TRL status. 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 AOI, 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) type contracts.

Offerors submitting Proposals should submit CS contract (or C contract) proposals. When CS 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 CS contract (see FAR 16.303) (or C contract [see FAR 16.302]) is appropriate, then the Offeror should provide (see B. Basic Cost/Price Information in Volume II – Cost Proposal Overview) an explanation (i) as to why there is no probability that the Offeror would receive any present or future benefits from an award, (ii) if the R&D is expected to be of only minor value to the Offeror, or (iii) if a statute 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 Transaction 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.

General Market Research (TechWatch Program)

Offerors are encouraged to participate in the TechWatch program prior to starting the application process, including any Market Research Abstract or Proposal submission under this BAA. Participation in the TechWatch program affords Offerors an opportunity to present their capabilities to BARDA scientific subject matter experts, program managers, and CMA acquisition professionals, as well as interagency partners in the PHEMCE, regardless of whether there is a relevant open AOI. 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. Entities with a Market Research Abstract or Proposal currently under review under any ASPR solicitation are not eligible to schedule a TechWatch meeting related to that submission.

Application Process

Stage 1: The Government realizes that the preparation of a development proposal often represents a substantial investment of time and effort by the Offeror. To minimize this burden, BARDA encourages organizations and individuals interested in submitting proposals to make targeted inquiries with the technical point of contact (POC) of the AOI as to the general need for the type of R&D effort contemplated before expending extensive effort in preparing a detailed abstract and proposal or submitting proprietary information. Refer to Part IV for instructions on requesting a pre-submission call. For more general inquiries about potential partnerships with the U.S. Government and to speak with a larger BARDA audience as well as PHEMCE partners, consider requesting a TechWatch meeting as noted above in the General Market Research (TechWatch Program) section.

Stage 2: Prepare a cover sheet, Quad Chart, and Market Research Abstract in accordance with the preparation guidance. Interested Parties must submit their Stage 2 submission documents in accordance with the instructions provided in Part IV. Stage 2 submission documents should describe the effort in sufficient detail to allow subject matter experts and program staff to assess the concept's technical merit and its potential contribution to the BARDA mission. BARDA will assess Market Research Abstracts based on the criteria provided in Part V.

Respondents whose Stage 2 submission receives a favorable assessment in the Market Research Phase will be invited via email to submit a Proposal in Stage 3. Respondents whose Stage 2 submission does not receive a favorable assessment will be notified via email 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 2 Respondents.

Stage 3: Offerors must submit their Proposals in accordance with the instructions provided in Part VI. 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 (Figure 1) in Part IV.

Submission Deadlines and Government Response Time

TABLE 1: SUBMISSION DEADLINES AND GOVERNMENT RESPONSE TIME

Proposal Stage	Deadline for Submission*	Government Response
Stage 1: Pre-submission Call	A pre-submission call can be initiated at any time during the open period of the BAA.	Requests for pre-submission calls will be acknowledged via email within 1 week.
Stage 2: Quad Chart and Market Research Abstract	A Quad Chart and Market Research Abstract may be submitted at any time prior to the submission deadline, which is September 25, 2028, at 4:30pm Eastern Time, unless otherwise indicated in an AOI.	An automated receipt confirmation will be sent upon submission to the BARDA Digital Resources (BDR) Portal. A response will be provided within 120 days of the receipt of the submission.
Stage 3: Proposal	As specified in the Invitation Letter. A Proposal may be submitted on any day during the open period of the BAA. Proposal submission deadline is September 25, 2028, at 4:30pm Eastern Time, unless otherwise indicated in an AOI.	An automated receipt confirmation will be sent upon submission to the BDR Portal. A response will be provided within 120 days of the receipt of the submission.

Contact and Submission Information

Contractual: After a Market Research Abstract or Proposal has been submitted, all Contractual inquiries regarding this BAA must be sent to: BARDA-BAA@hhs.gov. Note: Offerors should not submit any proprietary information via this email, as all information received via this email is assumed non-proprietary. Offerors should submit any proprietary information via the BDR Portal only.

Technical: Technical questions only should be directed to the Technical POC listed under each AOI in Part VIII. Contracting Officers will not be present during Stage 1 Pre-Submission Calls.

Submissions: All submissions, including the Market Research Abstract and Proposal, will only be reviewed after they are submitted in the BDR Portal.

Electronic Portal Submission Instructions

All submissions must be submitted to the BDR Portal via the process described below.

Offerors will be required to register for a BDR Portal account before a Market Research Abstract or Proposal can be submitted. A BDR account can be requested by visiting the BDR Portal 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, email 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.

If you experience any issues, please reach out to BDR_Admin_Inbox@hhs.gov. Failure to propose your submission on time for any reason (e.g., due to late registration in BDR Portal) will result in the submission not being considered for award. Respondents will be provided an automated confirmation of successful submission of either a Stage 2 Market Research Abstract or a Stage 3 Proposal.

All Stage 2 and Stage 3 submissions must be proposed electronically via the process described on the BDR Portal and in the following format:

- Single searchable 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.

Limitation on Communication After Submission

Be advised that after a Market Research Abstract (or Proposal) has been submitted to the BDR Portal, all communications related to that submission must be through the Contracting Office at BARDA-BAA@hhs.gov. Communications following the Government response to a Market Research Abstract or Proposal submission must be through the Contracting Officer identified in the response letter. Please include the BDR Portal submission ID in your email for tracking purposes.

Special Instructions

Special instructions will be advertised via the BAA as they become apparent. These additional instructions would be tailored to specific AOIs 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 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 (18 U.S.C. § 207). 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 the prospective Offeror.

Unsuccessful Proposal Disposition: 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 Appendix 1: Government Notice for Handling and Submitting Proposals for inclusion requirement of the Government notice.

BACKGROUND

This BAA sets forth advanced development AOIs for BARDA, a component of ASPR within the U.S. Department of Health and Human Services (HHS). This BAA is issued under paragraph 6.102(d)(2) of the 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 soliciting proposals for the advanced R&D of MCM for CBRN agents; the ever-present and ever -evolving threat of pandemic influenza; and the re-emergence and emergence of infectious diseases that threaten the U.S. civilian population.

- BARDA's Division of CBRN Countermeasures is dedicated to development and licensure of MCMs to help the Nation prepare for, respond to, and recover from public health emergencies arising from naturally occurring and intentionally engineered threats. To achieve its mission of making available at least one MCM against every material threat, CBRN is pursuing a three-pronged strategy, which includes (1) investing in MCMs to treat the injury, not the threat, (2) developing innovative MCMs for unknown threats, and (3) delivering novel MCMs against bacterial and viral threats. For past investments, see CBRN's MCM portfolio.
- BARDA's Influenza and Emerging Infectious Diseases (IEID) Division uses a comprehensive portfolio approach to develop and acquire a broad array of MCMs for pandemic influenza and emerging infectious diseases. This includes efforts to accelerate and improve the development of vaccines, therapeutics, diagnostics, and non-pharmaceutical countermeasures for influenza preparedness and to establish a sustainable end-to-end solution for vaccine domestic manufacturing infrastructure.
    - The Pandemic Influenza Program is dedicated to supporting continued innovation and advancement in pandemic influenza preparedness. Strategic priorities include: modernization of influenza vaccines; recombinant pandemic influenza vaccine development, including funding of ongoing clinical trials; development of faster platforms and more sustainable approaches for seasonal, pandemic, and emerging infectious diseases; development of alternative delivery models; development of adjuvants, which can be used to increase the supply of pandemic influenza vaccine and may have the potential to enhance the efficacy of vaccines; and strengthening U.S.-based vaccine manufacturing.
    - The Emerging Infectious Diseases (EID) Program invests in MCMs to address known and a wide range of emerging infectious diseases, including COVID-19, Ebola, Zika, pandemic influenza, and more. BARDA is investing in flexible agreements, platform technologies that result in faster development, programs that expand access to MCMs, sustainable approaches, improved delivery, and increased production capacity. For past investments in support of the Federal COVID-19 response, see BARDA's COVID-19 MCM portfolio.
- BARDA's Detection, Diagnostics, and Devices Infrastructure (DDDI) Division funds the development of testing and medical device countermeasures, along with select cases for domestic manufacturing capacity, to produce them to address all threats in BARDA's mission space: CBRN, influenza, and emerging diseases. Investment areas include home-use and point-of-care diagnostics, domestic test manufacturing expansion, rapid test availability in emerging disease outbreaks, rapid screening tests, threat-agnostic tests, and laboratory diagnostics.
- BARDA's Division of Research, Innovation & Ventures (DRIVe) seeks to accelerate the development and availability of transformative technologies and approaches to protect Americans from health security threats. DRIVe pushes innovation boundaries to tackle the biggest health security challenges while seeking new ideas and new approaches to prevent and protect against health security threats.

BARDA offers multiple core services to assist in the development and production of MCMs in a matter that is timely, reliable, and cost effective. Awards resulting from this BAA may benefit from these services,

which include an animal study network, flexible manufacturing facilities, and technical expertise in development, manufacturing, regulatory affairs, quality systems, and clinical studies.

BARDA's advanced R&D priorities and the requirements herein are driven by and closely aligned with other federal reports and strategic plans (Table 2). Refer to AOIs in Part VIII for specific investment areas.

TABLE 2. DIVISION OR ORGANIZATIONAL-WIDE STRATEGIC DOCUMENTS

Document*	Date of Publication	Relevant Program Areas
National Health Security Strategy 2023-2026	March 2023	All
National Biodefense Strategy	October 2022	All
2022 PHEMCE Strategy and Implementation Plan	October 2022	All
BARDA Strategic Plan 2022-2026	May 2022	All
White House's American Pandemic Preparedness: Transforming Our Capabilities	September 2021	All
National Action Plan for Combating Antibiotic-Resistant Bacteria (CARB), 2020-2025	October 2020	CBRN
National Influenza Vaccine Modernization Strategy (NIVMS) 2020-2030	June 2020	PI
HHS Pandemic Influenza Plan	June 2017	PI

*Specific documents driving program requirements can be found in the respective AOIs in Part VIII

For additional requirements information, visit:

- The Pandemic and All Hazard Preparedness Act Pub. L. No. 109-417 and 42 U.S.C. § 241 et seq. (PAHPA).
- The Pandemic and All Hazard Preparedness Reauthorization Act Pub. L. No. 113-5 (PAHPRA).
- The Pandemic and All-Hazards Preparedness and Advanced Innovation Act of 2019 Pub. L. No. 116-22 and 42 U.S.C. § 247d-7e (PAHPAIA).

Learn more about legal authorities, policies, and committees and strategies and reports for BARDA-supported MCMs.

Part I: Development and Technical Objectives

The information in this section is provided to assist and guide Offerors in preparing their Market Research Abstracts and 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 nonclinical studies, manufacturing, and regulatory strategy. Offerors should address these in the Market Research Abstract and Proposal in sufficient detail (within space limitation) to demonstrate that Offeror understands the scope of work needed. Offerors shall submit a SOW in their 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 discrete segments that are non-severable in their activity. 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 TRL indicated for each Development AOI in Part VIII. Development programs at a maturity level less than that indicated for each Development AOI 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. Proposal preparation and submission instructions are contained in Part VI.

Program Management Approach

Market Research Abstracts and Proposals for all AOIs must address Program Management Activities, which may include but are not limited to:

- Identification and management of 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;
- Establishment 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;
- 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;
- Maintaining and managing staff (in-house and contracted) to assure the necessary expertise and dedicated effort to perform the work;
- Conducting performance measurement that shall include:
    - establishing an initial plan;
    - defining measurable parameters;
    - defining how these parameters relate to cost and schedule impacts;
    - 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;
- Directing and overseeing subcontractors and consultants to assure successful performance of planned activities within the cost and schedule constraints of the contract; and
- Development of a risk evaluation and mitigation strategy for the overall project.

Regulatory Approach

Market Research Abstracts and Proposals for all AOIs must address regulatory activities, as appropriate for the MCM, which may include but are not limited to:

- A clear and comprehensive regulatory master plan that focuses on the crucial pathway integrating all products, risk evaluation and mitigation at all development stages, nonclinical 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;
- Establishment and filing of regulatory submissions to the correct office at the FDA;
- Maintenance of a plan for additional studies to support future filing for FDA approval/clearance;
- Development of a potential Plan for consideration of an Emergency Use Authorization (EUA) of a medical product when appropriate;
- 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; and
- Conducting site initiation, monitoring, and closeout visits to contract research organizations subcontracted to perform studies.

Development and Manufacturing Approach

Product development, including clinical/nonclinical studies and manufacturing activities, is 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:

- Nonclinical Toxicology, PK, and Efficacy
- Clinical Evaluation
- Chemistry, Manufacturing, and Controls (CMC)

Nonclinical Toxicology, PK and Efficacy R&D Activities include but are not limited to:

- Evaluating the safety, toxicology, pharmacokinetics / pharmacodynamics, bioavailability, solubility, formulation, of the MCM using both in vitro and animal models following Good Laboratory Practice (GLP) guidelines (as described in 21 CFR § 58), as and when appropriate;
- Screening of small molecule libraries for antitoxin / antimicrobial / antiviral activities (for already approved or licensed product);
- Expand assessment of antiviral potential for therapeutics previously approved for other indications; and
- Evaluating the immunogenicity, safety, efficacy, pharmacokinetics / pharmacodynamics, bioavailability, solubility, formulation, dose, route and schedule of the MCM using both in vitro and animal models following GLP guidelines (as described in 21 CFR § 58), as appropriate.

Clinical Evaluation Activities include but are not limited to:

- 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 (GCP) guidelines for Investigational New Drug (IND) applications (as described in 21 CFR § 312 and International Council for Harmonization [ICH] Guidelines document E6);
- Design and conduct of a Phase 2 and/or Phase 3 clinical studies in accordance with all Federal regulations and GCP guidelines;
- 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); and
- Design and conduct clinical trials to evaluate optimal use of influenza antivirals or immunomodulators for informing clinical and public health management decisions.

CMC Activities include but are not limited to:

- Development of master and working cell banks under current Good Manufacturing Practice (cGMP) guidelines (as described in 21 CFR § 211);
- 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;
- Formulation development to evaluate combinations of excipients and their influence on the Target Product Profile (TPP) and on product stability;
- Manufacture of Good Manufacturing Practice (GMP) and of non-GMP pilot lots of candidate product in amounts sufficient to carry out required/proposed nonclinical and Phase 1 and/or Phase 2 clinical trials;
- Identification of critical quality attributes and critical process parameters;
- Manufacturing scale-up plan to lead to consistency lot manufacturing of the candidate product;
- Process flow for personnel, material and waste disposal;
- Proposed packaging design and execution of fill-finish process of final drug product;
- Design of stability testing plan and conduct of stability studies on bulk and final product;
- Manufacturing/Testing facility plan to support Phase 1 through commercial scale product supply;
- 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;
- Development of Validation Protocol for stability-indicating analytical and assay methods to define product manufacturing control, performance, potency, and stability;
- Development of processes that would benefit from alternative manufacturing or analytical techniques using continuous manufacturing (e.g., continuous perfusion, continuous synthesis, non-column based chromatography), if applicable;
- Integration of continuous mode(s) into manufacturing process and the development of in-line process analytical technologies, if applicable;
- Continuous processing for homogeneous production of final dosage forms (e.g., tableting, strip film manufacturing system, injection molding, and printing) if applicable;
- Development of Risk Evaluation and Mitigation Strategies (REMS) or similar risk mitigation strategy proposals; and
- Manufacturing/Testing facility plan to support clinical trial lots through commercial scale product supply, including consideration of a surge in manufacturing capacity in the event of a pandemic (e.g., influenza).

Vaccines

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

- Nonclinical
- Analytical Assays
- Clinical Evaluation
- CMC

Nonclinical Activities include but are not limited to:

- Limited evaluation in ancillary nonclinical studies as required to support proposed activities with a maturity of TRL 6 or greater.

Analytical Assays Activities include but are not limited to:

- 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; and

- Development of Validation Protocol for stability-indicating analytical and assay methods to define product manufacturing control, performance, potency, and stability.

Clinical Evaluation Activities include but are not limited to:

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

CMC Activities include but are not limited to:

- Development of master and working cell banks under cGMP guidelines (as described in 21 CFR § 211, 21 CFR § 600, and 21 CFR § 610);
- 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;
- Formulation development to evaluate combinations of excipients and their influence on the TPP and on product stability;
- Continuous processing for homogeneous production of final dosage forms (e.g., tableting, strip film manufacturing system, injection molding, and printing), if applicable;
- 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;
- Identification of critical quality attributes and critical process parameters;
- Manufacturing scale-up plan to lead to consistency lot manufacturing of the candidate product;
- Process flow for personnel, material and waste disposal;
- Proposed packaging design and execution of fill-finish of final drug product;
- Design of stability testing plan and conduct of stability studies on bulk and final product;
- Development of REMS or similar risk mitigation strategy proposals; and
- 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 a pandemic (e.g., influenza).

Diagnostics

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

- Product Development
- Manufacturing Development
- Clinical Evaluation

Product Development Activities include but are not limited to:

- Perform natural/case history studies of threat agent(s), if needed;
- Review the pathology of human disease related to threat agent(s);
- Identification of diagnostic markers of disease for threats of interest, if needed;
- Performance of human or non-GLP animal studies to demonstrate the clinical relevance, performance, and/or diagnostic utility of biomarkers;
- Performance of appropriate studies to demonstrate acceptable clinical performance of the assay with specimens and specimen volumes relevant to diagnostic intended use;

- 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;
- Development of verification and validation protocols and execution of these protocols to prove performance of products developed;
- Identification of reference standard for use in validation and/or verification;
- Development of requirements that incorporates all potential users and environments of use for the product;
- Development of design control documents using an FDA-compliant Quality Management System (QMS);
- Development of a product risk evaluation and mitigation strategy; and
- Production of non-GMP-compliant prototypes and reagent lots at laboratory scale.

Manufacturing Development Activities include but are not limited to:

- Identifying/developing pilot scale manufacturing facilities capable of producing diagnostic systems, assays, reagents, and consumables in compliance with GMP guidelines (as described in 21 CFR § 820);
- Development of full-scale manufacturing processes and procedures;
- Development of tooling to manufacture products appropriate for pilot scale manufacturing;
- 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;
- 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;
- Manufacturing scale-up plan to lead to consistent lot manufacturing of the candidate product;
- Process flow for personnel, material and waste disposal;
- Design of stability testing plan and conduct of stability studies assays and reagents;
- Development of a manufacturing REMS or similar risk mitigation strategy proposal;
- Development of procedures and equipment/components for quality acceptance or quality assurance of manufactured products under QMS; and
- Performance of Installation Qualifications (IQ) or Process qualifications (PQ).

Clinical Evaluation Activities include but are not limited to:

- Design and execution of clinical studies/trials to evaluate the effectiveness, safety, sensitivity, and specificity of Diagnostic Systems in humans in accordance with FDA requirements and, where applicable, with GCP guidelines (as described in 21 CFR § 812, 21 CFR § 50, and 21 CFR § 56).

Respiratory Protective Devices (Masks & Respirators) and Ventilators

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

- Product Development
- Manufacturing Development
- Clinical Evaluation

Product Development Activities include but are not limited to:

- Perform natural/case history studies of threat agent(s), if needed;
- Performance of animal studies to demonstrate the clinical performance of ventilator, as needed;
- Performance of appropriate studies to demonstrate acceptable clinical performance of the assay with specimens and specimen volumes relevant to diagnostic intended use;
- Development of devices, respiratory protective 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;
- Development of verification and validation protocols and execution of these protocols to prove performance of products developed;

- Identification of reference standard for use in validation and/or verification;
- Development of requirements that incorporates all potential users and environments of use for the product;
- Development of design control documents using an FDA-compliant QMS;
- Development of a product REMS;
- Production of non-GMP-compliant prototypes; and
- Performance of usability studies.

Manufacturing Development Activities include but are not limited to:

- Identifying/developing pilot scale manufacturing facilities capable of producing RPDs or ventilators and consumables in compliance with GMP guidelines (as described in 21 CFR § 820);
- Development of full-scale manufacturing processes and procedures;
- Development of tooling to manufacture products appropriate for pilot scale manufacturing;
- Process development activities to increase efficiency, yield, quality, and reduce the variability and risk factors in the manufacture of RPDs or ventilators and consumables;
- 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;
- Manufacturing scale-up plan to lead to consistent lot manufacturing of the candidate product;
- Process flow for personnel, material and waste disposal;
- Design of stability/durability testing plan and conduct of stability/durability studies assays and reagents;
- Development of a manufacturing REMS or similar risk mitigation strategy proposal;
- Development of procedures and equipment/components for quality acceptance or quality assurance of manufactured products under QMS; and
- Performance of IQ or PQ.

Clinical Evaluation Activities include but are not limited to:

- 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 GCP guidelines (as described in 21 CFR § 812, 21 CFR § 50, and 21 CFR § 56).

Part II: 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 reports (as negotiated) throughout the period of performance. Each document must be submitted electronically in Microsoft Word, Microsoft Excel, Microsoft Project, and/or Adobe Acrobat PDF file.

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

Part III: Special Considerations

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 Contracting Officer's Representative (COR) will determine the severity of the violation. Any contractual actions resulting from the violation will be determined by the Contracting Officer.

Security Plan

In the event a security plan is needed for this requirement, the Contracting Officer will 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.

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.

Confidentiality of Information

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

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.

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 five business days prior to the issuance of the press release.

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 CFR § 120-130) and /or the Department of Commerce regarding the Export Administration Regulations (15 CFR § 730-774).

Manufacturing Standards

The GMP Regulations (21 CFR § 210 and § 211) pertaining to drugs, regulations pertaining to biological products (21 CFR § 600 and § 610), and regulations pertaining to diagnostic products (21 CFR § 820) 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.

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.

Invoices - Electronic Submission of Payment Requests

(a) *Definitions.* As used in this clause –
Payment request means a bill, voucher, invoice, or request for contract financing payment with associated supporting documentation. The payment request must comply with the requirements identified in FAR 32.905(b), "Content of Invoices" and the applicable Payment clause included in this contract.

(b) Except as provided in paragraph (c) of this clause, the Contractor shall submit payment requests electronically using the Department of Treasury Invoice Processing Platform (IPP) or successor system. Information regarding IPP, including IPP Customer Support contact information, is available at *www.ipp.gov* or any successor site.

(c) The Contractor may submit payment requests using other than IPP only when the Contracting Officer authorizes alternate procedures in writing in accordance with HHS procedures.

(d) If alternate payment procedures are authorized, the Contractor shall include a copy of the Contracting Officer's written authorization with each payment request.

Electronic Invoicing and Payment Requirements – Invoice Processing Platform (IPP)

- All invoice submissions for goods and or services delivered to facilitate payments must be made electronically through the U.S. Department of Treasury's IPP System.

- Invoice Submission for Payment means any request for contract financing payment or invoice payment by the Contractor. To constitute a proper invoice, the payment request must comply with the requirements identified in the applicable Prompt Payment clause included in the contract, or the clause 52.212-4 Contract Terms and Conditions – Commercial Items included in commercial items contracts. The IPP website address is: https://www.ipp.gov.

- The Agency will enroll the Contractors new to IPP. The Contractor must follow the IPP registration email instructions for enrollment to register the Collector Account for submitting invoice requests for payment. The Contractor Government Business POC (as listed in SAM) will receive Registration email from the Federal Reserve Bank of St. Louis (FRBSTL) within 3-5 business days of the contract award for new contracts or date of modification for existing contracts.

    - Registration emails are sent via email from ipp.noreply@mail.eroc.twai.gov. Contractor assistance with enrollment can be obtained by contacting the IPP Production Helpdesk via email to IPPCustomerSupport@fiscal.treasury.gov or phone (866) 973-3131.

- The Contractor POC will receive two emails from IPP Customer Support, the first email contains the initial administrative IPP User ID. The second email, sent within 24 hours of receipt of the first email, contains a temporary password. You must log in with the temporary password within 30 days.

- If your organization is already registered to use IPP, you will not be required to re-register.

- If the Contractor is unable to comply with the requirement to use IPP for submitting invoices for payment as authorized by HHSAR 332.7002, a written request must be submitted to the Contracting Officer to explain the circumstances that require the authorization of alternate payment procedures.

Additional Administration for Strategic Preparedness and Response (ASPR) requirements:

(i) The contractor shall submit monthly invoices under this contract unless otherwise agreed upon by all parties. For indefinite delivery and blanket purchase agreement vehicles, separate invoices must be submitted for each order.

(ii) Invoices must break-out price/cost by contract line item number (CLIN) as specified in the pricing section of the contract.

(iii) Invoices must include the Unique Entity Identifier (UEI) of the Contractor.

(iv) Invoices that include time and materials or labor hours CLINS must include supporting documentation to (1) substantiate the number of labor hours invoiced for each labor category, and (2) substantiate material costs incurred (when applicable).

(v) Invoices that include cost-reimbursement CLINs must be submitted in a format showing expenditures for that month, as well as contract cumulative amounts. At a minimum the following cost information shall be included, in addition to supporting documentation to substantiate costs incurred.

a. Direct Labor – include all persons, listing the person's name, title, number of hours worked, hourly rate, the total cost per person and a total amount for this category;
b. Indirect Costs (i.e., Fringe Benefits, Overhead, General and Administrative, Other Indirects) – show rate, base and total amount;

c. Consultants (if applicable) – include the name, number of days or hours worked, daily or hourly rate, and a total amount per consultant;

d. Travel – include for each airplane or train trip taken the name of the traveler, date of travel, destination, the transportation costs including ground transportation shown separately and the per diem costs. Other travel costs shall also be listed;

e. Subcontractors (if applicable) – include, for each subcontractor, the same data as required for the prime Contractor;

f. Other Direct Costs – include a listing of all other direct charges to the contract, i.e., office supplies, telephone, duplication, postage; and

g. Fee – amount as allowable in accordance with the Schedule and FAR 52.216-8, if applicable.

(vi) 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.

IPP Waiver Request Instructions

Offerors may request a waiver from using the Department of Treasury IPP for payment requests, which may be approved by the Contracting Officer for a specific situation, as follows:

- As specified in Office of Management and Budget (OMB) Memorandum M-15-19, electronic invoicing is not appropriate for the Federal procurement: of relocation services, utilities, or for vendors using Personal Identifiable Information (PII) for identification

- Contractor is in the process of transitioning to electronic submission of payment requests but needs time to complete such transition. Contractor must indicate timeline for transition.

- Contractor demonstrates that electronic submission is unduly burdensome. Contractor must provide full explanation to include substantiating documents when necessary.

IPP waiver requests and supporting documentation shall be included in the business proposal.

Part IV: Pre-Submission Call and Quad Chart/Market Research Abstract Instructions (Stages 1 & 2)

The application process is in three stages as follows:

- Stage 1: Pre-submission call with Technical POC;
- Stage 2: Quad Chart/Market Research Abstract; and
- Stage 3: Proposal, which consists of:
    - Volume I – Technical Proposal;
    - Volume I – Technical Proposal Attachments;
    - Volume II – Cost Proposal; and
    - Volume II – Cost Proposal Attachments.

and is described in the BARDA BAA Process Flow (Figure 1).

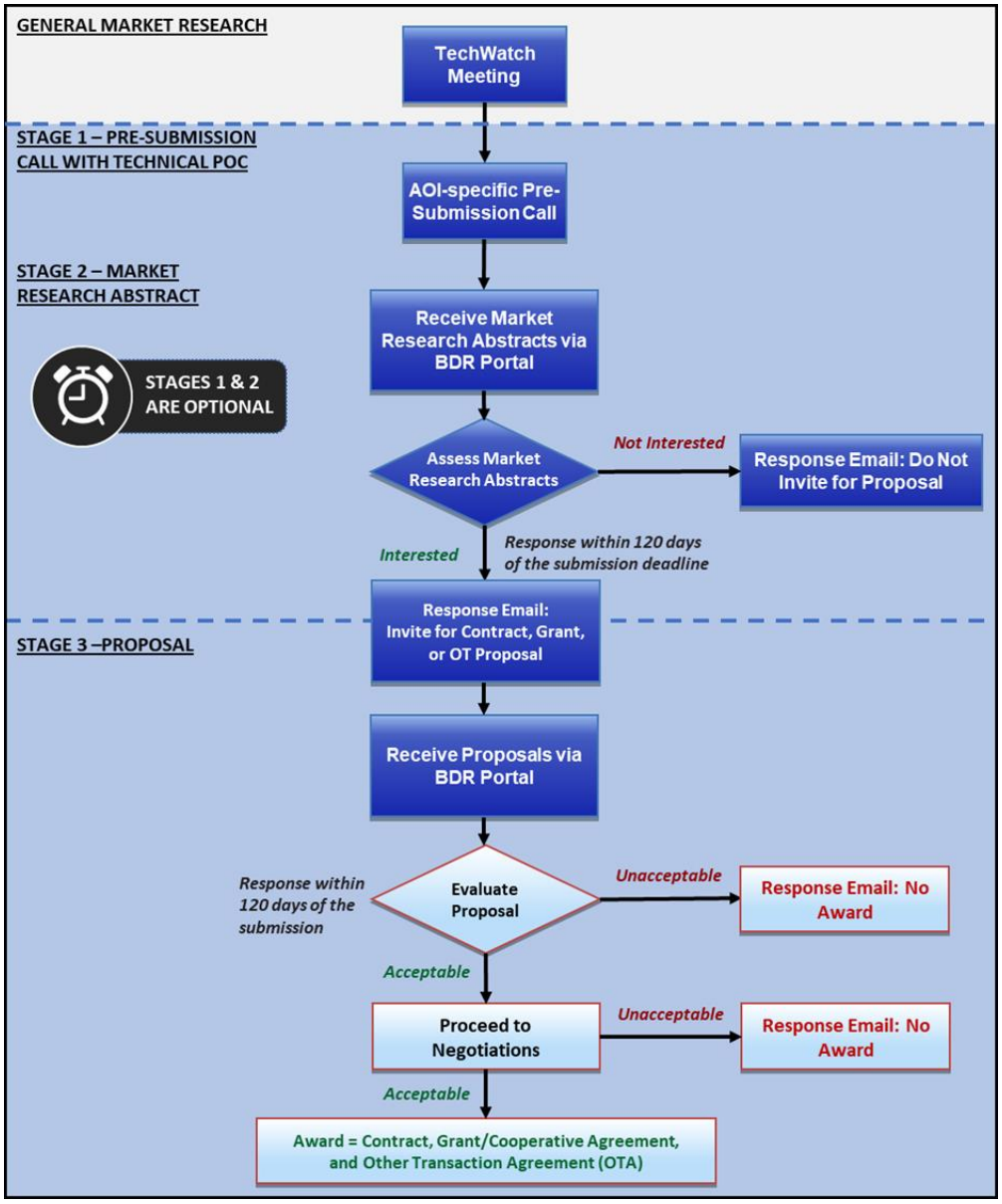

FIGURE 1. BARDA BAA PROCESS FLOW CHART

Stage 1: Pre-submission Call with Technical POC

BARDA acknowledges that the preparation of submissions often represents a substantial investment of time and effort by the Offerors. In attempt to minimize this burden, BARDA highly encourages Offerors that are interested in proposing a submission to schedule a pre-submission call with an AOI representative to discuss their general technology and alignment with programmatic priorities. This should allow Offerors to better understand if their project aligns with the intent of the specific AOI before expending effort in preparing a submission or sending proprietary information via the BDR Portal. For more general inquiries about potential partnerships with the U.S. Government and to speak with a larger BARDA audience as well as PHEMCE partners, consider requesting a TechWatch meeting as noted in the General Market Research (TechWatch Program) section.

How to schedule a call: Participating in a pre-submission call before proposing a submission to the applicable AOI is highly encouraged, and requests may be sent directly to the Technical POC listed under the respective AOI in Part VIII. We recommend you note subject line of your email "Stage #1 - Pre-Submission Call: AOI X.X" so it is clear you are requesting a call under this BAA.

Stage 2: Quad Chart and Market Research Abstract Preparation

Interested Parties shall submit a Quad Chart and Market Research Abstract. The initial submission is limited to a cover page, a one-page Quad Chart, a Market Research Abstract (including a Rough Order of Magnitude [ROM]) 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 (see Electronic Portal Submission Instructions for additional formatting requirements).

Quad Chart and Market Research Abstract, including a ROM estimate of costs, must be submitted in accordance with the preparation guidance below. Stage 2 submission documents should describe the effort in sufficient detail to allow assessment of the concept's technical merit and its potential contribution to the BARDA mission. Respondents whose Stage 2 submission receives a favorable assessment will be invited by email to submit a Proposal (Stage 3). Respondents whose Stage 2 submission does not receive a favorable assessment will be notified as well by email. Note that a respondent who receives an unfavorable assessment is not precluded from submitting a Proposal; however, it is strongly recommended the Interested Party resubmit a revised Market Research Abstract.

Note: As a Market Research Abstract is not considered a "proposal," no debriefing per the procedures in FAR Subpart 15.5 will be provided.

***IMPORTANT**: Project titles in the Quad Charts, Market Research Abstracts, and Proposals should be descriptive of the work proposed and not be merely a copy of the title of this solicitation or AOI.*

Quad Chart Format: Please visit the BARDA BAA Toolkit for the required information and sample template. All Quad Charts should be laid out in landscape format. Any Quad Chart submitted that exceeds the one-page limit will not be read or assessed.

Market Research Abstract Format: The Market Research Abstract 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 Market Research Abstract should include, at a minimum, the following core elements:

- A brief discussion on how the proposed countermeasure aligns with the objectives of the PHEMCE Implementation Plan and the BAA Development AOI to which the submission is responding;
- Sufficient data to justify the proposed 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;
- A clear and concise plan for meeting product development objectives that includes all key activities (e.g., nonclinical, clinical, manufacturing, and regulatory activities);
- A high-level Gantt chart showing an overview of the proposed activities and timelines;

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

The cost portion of the Market Research Abstract shall contain a brief cost estimate outlining all the component parts of the proposal, as described below.

ROM Preparation: A ROM cost estimate is required with the Quad Chart and Market Research Abstract submission. The ROM cost estimate is based on the top-level task(s) or objective(s) set forth in the Market Research Abstract. It uses a top-down estimating approach based on expert knowledge and/or previous experience. For the Market Research Abstract, 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.

Addendum: As an addendum to the Market Research Abstract, 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.

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

Restrictive markings: Submissions will be protected from unauthorized disclosure in accordance with 41 U.S.C. § 2102 and applicable regulations. **Note that any Market Research Abstract submitted under this solicitation may be shared with other Government agencies for non-BARDA funding considerations and assessment.**

Classification: All Stage 2 submission documents must be UNCLASSIFIED.

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

Furthermore, Market Research Abstracts that are outside the scope of the BAA may be rejected. In addition, if the Market Research Abstract does not meet the required TRLs or does not contain one or more of the required items listed above, it may be deemed non-responsive and will not be reviewed.

Stage 2: Quad Chart and Market Research Abstract Submission

Interested Parties must submit their Quad Chart and Market Research Abstract via the BDR Portal as outlined in Electronic Portal Submission Instructions. Refer to Table 1 for submission deadlines.

Part V: Quad Chart/Market Research Abstract Assessment

The decision to invite a Potential Offeror to submit a Proposal will be based on an assessment of each Potential Offeror's Market Research Abstract and Quad Chart. The Stage 2 Market Research Abstract and Quad Chart submissions will be assessed by a program manager with primary focus on the submission's technical merit and relevance to BARDA programmatic priorities based on target timelines (Table 1) and generally in line with the criteria outlined in Part VII. The program manager may leverage a market research review team to include Federal staff, consultants, subject matter experts, and other members supporting BARDA. Written technical feedback on *Stage 2 Quad Chart and Market Research Abstract* submissions will be provided in the response letter from BARDA.

This Stage 2 review will result in the Respondent receiving a notice of "Interested" or "Not Interested." Based on the AOI, the relevant program manager will make a recommendation to the Contracting Officer. The Contracting Officer will issue the notice to the Respondent. The Source Selection Authority (SSA) will not typically be involved in Stage 2 of the process as this is considered market research and award recommendations are not being made. Respondents receiving an "Interested" notification will be invited to submit a Stage 3 proposal.

Part VI: Proposal Instructions (Stage 3)

With a successful review of the Potential Offeror's Market Research Abstract, the Potential Offeror will be invited to submit a proposal. Offerors may also submit a proposal in the absence of a Stage 1 call or Stage 2 submission. Offerors must ensure that the proposal is valid for at least 120 days from the date of proposal submission. Potential Offerors invited to submit a 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 Proposal.

Stage 3: Proposal Preparation

The 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. Templates and additional resources to prepare proposals are found in the BARDA BAA Toolkit.

Volume I – Technical Proposal Overview

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 (excluding FDA communication data) *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. Refer to Electronic Portal Submission Instructions for additional formatting requirements. The technical proposal should include the following items:

A. Cover Page

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

- The words "Volume I: Technical Proposal;"
- BAA number;
- R&D AOI;
- Proposal Title (descriptive of the work proposed and not a copy of the title of the solicitation);
- Proposal Description: brief 1-2 sentence of the purpose or goal of submission;
- Date of submission;
- Offeror and complete list of subcontractors, if applicable;
- Offeror Unique Entity ID (UEI) number and Commercial And Government Entity (CAGE) code;
- Technical contact (name, address, phone, electronic mail address);
- Administrative/business contact (name, address, phone, electronic mail address); and
- Proposed period of performance.

B. Official Transmittal Letter

This is an official transmittal letter including:

- The name, title, mailing address, and telephone number of the company or organization;
- The name, title, mailing address, telephone number, and email address of the division POC regarding decisions made with respect to the Offeror and who can obligate the proposal contractually;
- The name, title, mailing address, telephone number, and email address and those individual(s) authorized to negotiate with the Government; and
- A statement indicating you are submitting a final 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 OFFERORS: 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 for SOW 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 submitted as part of the technical submission. The break points of different phases proposed in the contract should be indicated.

Visit the BARDA BAA Toolkit for templates.

I. Deliverables

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

Visit the BARDA BAA Toolkit for sample deliverables table.

J. Key Personnel

A listing of key personnel (including proposed consultants) who possess the necessary education, training, and experience to successfully perform the work identified in the technical proposal (resumes to be included in the Appended material). A summary of related activities must also be provided for key personnel; see Vol. II, Attachment 6: Summary of Related Activities.

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:

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

- Major equipment and layout (e.g., preliminary piping and instrumentation drawing);
- Manufacturing capacity expansion plans to match the proposed manufacturing scale-up;
- Overview of the management of Quality Systems at the facility;
- List of capabilities for clinical activities conducted in house and at contract research organizations. List of clinical sites engaged for product evaluations;
- Qualified animal facilities where GLP studies would be conducted and appropriate certifications for humane care and use of vertebrate animals;
- 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;
- Validation master plan for key equipment, analytical methods, and manufacturing process;
- Commercial capabilities of the Offeror, including current products, and marketing, distribution, and customer support capabilities (as applicable); and
- List of key vendors or service providers, locations, and brief description of their expertise/experience.

M. Past Performance Information

The Offeror shall provide a list of the last three Government contracts as a prime contractor during the past three years and all contracts currently being performed that are similar in nature to the proposed project. Contracts listed must include those entered into by the Federal Government, agencies of state and local governments and commercial concerns. Offerors must 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 $250,000.

For small business prime offerors, in addition to including past performance as prime contractors, a small business may: (1) use the past performance of a joint venture of which it is a member, provided that the small business worked on the joint venture's contract or contracts; and (2) use past performance it obtained as a first-tier subcontractor on a prime contract with a subcontracting plan. For this latter method of obtaining qualifying past performance, the small business may seek a past performance rating from the prime contractor and submit the rating with the small business' offer on a new prime contract, as authorized by Section 868 of the National Defense Authorization Act (NDAA) for Fiscal Year 2021, Public Law 116–283.

Include the following information for each contract or subcontract listed:

- Name of Contracting Organization;
- Contract Number (for subcontracts, provide the prime contract number and the subcontract number);
- Contract Type;
- Total Contract Value;
- Description of Requirement;
- Contracting Officer's Name and Telephone Number;
- Program Manager's Name and Telephone Number; and
- North American Industry Classification System (NAICS) Code.

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

N. Additional Requirements

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

- Research involving Human Subjects/Anatomical Substances (if proposed);
- Research involving Animals (if proposed);
- Evidence of GLP Compliance (if appropriate);
- Evidence of GMP Compliance (if appropriate);
- Evidence of GCP Compliance (if appropriate);
- Evidence of Laboratory Licensure Requirements (if appropriate);

- Compliant Use of Select Agents (if appropriate); and
- All required Representations and Certifications are completed and on file.

Volume I – Technical Proposal Attachments

Attachments should contain supplemental data that accompanies the technical proposal. The combined page total of Attachments 1-9 in Volume I will be 70 pages[2] unless otherwise specified in the Proposal invitation letter. Additional specific information to be included is referenced below. If a particular item is not relevant to the proposed effort, state that it is not applicable along with any supporting justification. Visit the BARDA BAA Toolkit for additional templates and resources.

Vol. I, Attachment 1: Quad Chart

Required: Yes

Instructions: Offerors must include a revised Quad Chart showing differences from the original Quad Chart submitted during Stage 2.

Refer to the BARDA BAA Toolkit for template.

Vol. I, Attachment 2: Protection of Human Subjects

Required: If applicable

Instructions: 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 involve human subjects.

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) 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 Contractor 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 Contractor fails to take such an action within the 30 calendar-day period, then the contract may be terminated.

For any resultant award involving human subjects engaged in biomedical, behavioral, clinical, or other research, in which identifiable, sensitive information is collected or used, the Contractor shall protect the privacy of individuals who are subjects of such research in accordance with subsection 301(d) of the Public Health Service (PHS) Act (42 U.S.C. § 241).

Vol. I, Attachment 3: Animal Welfare

Required: If applicable

Instructions: 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. 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

[2] Attachment 10 (FDA communication data) does not count against the 70-page limit for Volume 1 attachments

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:

- 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.
- Justify the use of animals, the choice of species, and the numbers used. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and their numbers.
- Provide information on the veterinary care of the animals involved.
- 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.
- Describe any euthanasia method to be used and the reasons for its selection.
- 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.

Vol. I, Attachment 4: Intellectual Property

Required: Yes

Instructions: 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.

Vol. I, Attachment 5: Biographical Sketches

Required: Yes

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

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

Vol. I, Attachment 6: Use of Select Agents

Required: If applicable

Instructions: 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 § 73, 7 CFR § 331, and/or 9 CFR § 121.

For more information, refer to the Federal Select Agent Program.

Vol. I, Attachment 7: Laboratory License Requirements

Required: If applicable

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

Vol. I, Attachment 8: Target Product Profile (TPP)

Required: Yes, except for Diagnostics, Ventilators, RPDs, Platforms, Modeling, and Visual Analytics

Instructions: Offerors should use the template provided in the BARDA BAA Toolkit to develop the TPP for the proposed candidate MCM. The discussion should include:

- The intended use or indication of the proposed MCM;
- The intended product profile (strength, quality, purity and identity) noting the performance specifications and features of the MCM that provide benefit;
- A description of the MCM as it is currently configured;
- A description of the manufacturing process including expected formulation (configuration) of the final product;
- 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; and
- Discussions with appropriate FDA reviewers that are relevant to development activities for the proposed MCM, including:
    - plans for generating data to support an 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; and
    - summary of audits and inspections relative to the current development or proposed manufacturing (Including at key subcontractors) of the intended product.

Vol. I, Attachment 9: Supporting Data

Required: No

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

Vol. I, Attachment 10: FDA Communication Data

Required: Yes

Instructions: Provide all relevant official communication with FDA regarding product with BAA submission (e.g., Complete pre-IND minutes, Type C minutes). 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 Overview

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. SOW Options should be priced separately.

A. Cover Page

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

- The words “Volume II: Cost Proposal”;

- BAA Number;
- Title of proposal (descriptive of the work proposed and not a copy of the title of the solicitation);
- Development AOI;
- Offeror (name, address, telephone number, and email address);
- Technical contact (name, telephone number, email address);
- Administrative contact (name, address, telephone number, and email address) (if available);
- Audit Office (name, address, telephone number, and email address) (if available);
- Proposed cost and/or price; profit or fee (as applicable); and total;
- 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."*

- Date of submission;
- Authorized representative (name, title, and signature); and
- UEI 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:

- Direct Labor – Individual labor category or person, with associated labor hours and unburdened direct labor rates;
- 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;
- 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.;
- 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:
    - Complete company name and mailing address, technical and administrative/business POCs, email address, and telephone number;
    - Include the UEI number and CAGE code;
    - A commitment letter from the proposed subcontractor's business official that includes:
        - Willingness to perform as a subcontractor for specific duties (list duties) or a SOW;
        - Proposed period of performance;
        - Supporting documentation for proposed costs (personnel documents to verify salaries, vendor quotes for equipment, negotiated indirect cost rate agreement); and
        - 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), a cost proposal conforming to all requirements of this section shall be provided, and shall reference the WBS of the prime contractor's proposal; and

- 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), 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.

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

- 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). Include supporting documentation, e.g., vendor quotes, catalog price lists, and past invoices of similar purchases;
- 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; and
- 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 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 Proposal is requested and is subject to the appropriations used to fund the effort.

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.

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.

The salary rate limitation also applies to individuals under subcontracts.

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.

E. Cost Certification

Include a cost certification statement (Appendix 2: Cost Certification) in the Cost Proposal, if required under FAR 15.403-4, based on the total contract price threshold defined in the FAR clause.

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 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.

Vol. II, Attachment 1: UEI, TIN, CAGE, and NAICS

Required: Yes

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

Vol. II, Attachment 2: Representations and Certifications

Required: Yes

Instructions: In accordance with FAR 4.1201, prospective contractors shall complete and update the annual representations and certifications at SAM.gov.

Vol. II, Attachment 3: Breakdown of Proposed Estimated Cost (Plus Fee) and Labor Hours

Required: Yes

Instructions: It is requested that you use the spreadsheet that is provided in the BARDA BAA Toolkit (or to be provided with the Proposal invitation letter or prior to entering into negotiation) to prepare your cost proposal. This template is provided as a guideline and 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.

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:

> 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 format should be revised to accommodate direct labor proposed as a percentage of effort.

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

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

For all travel, list the specifics for each trip.

For any subcontract proposed, submit a separate breakdown format.

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

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

Vol. II, Attachment 4: SF-424

Required: If applicable (SF-424, SF-424A, SF-424B, SF-LLL Required for Grants)

Instructions: 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 proposal for additional details and form requirements.

SF-424 family forms are available on grants.gov website.

Vol. II, Attachment 5: HHS Small Business Subcontracting Plan

Required: If applicable

Instructions: Successful contract proposals that exceed $750,000, submitted by all but small business concerns, will be required to submit a Small Business Subcontracting Plan in accordance with FAR 19.704.

Template available on the BARDA BAA Toolkit.

Vol. II, Attachment 6: Summary of Related Activities

Required: Yes

Instructions: 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.

Template available on the BARDA BAA Toolkit.

Vol. II, Attachment 7: Lobbying Activities

Required: Yes

Instructions: In accordance with Prohibition on the Use of Appropriated Funds for Lobbying Activities [HHSAR 352.203-70], 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."

For Grants, refer to SF-LLL: Disclosure of Lobbying Activities. For Contracts, refer to: HHSAR 352.203-70.

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

Required: If applicable

Instructions: Complete the spreadsheet available at the BARDA BAA Toolkit, 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.

Vol. II, Attachment 9: Financial Capacity & Annual Financial Report

Required: Yes

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

Vol. II, Attachment 10: Past Performance

Required: Yes

Instructions: The Offeror shall provide a list of the last three Government contracts as a prime contractor during the past 3 years and all contracts currently being performed that are similar in nature to the BAA scope. Contracts listed must include those entered into by the Federal Government, agencies of state and local governments and commercial concerns. Offerors must 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.

For small business prime offerors, in addition to including past performance as prime contractors, a small business may: (1) use the past performance of a joint venture of which it is a member, provided that the small business worked on the joint venture's contract or contracts; and (2) use past performance it obtained as a first-tier subcontractor on a prime contract with a subcontracting plan. For this latter method of obtaining qualifying past performance, the small business may seek a past performance rating from the prime contractor and submit the rating with the small business' offer on a new prime contract, as authorized by Section 868 of the NDAA for Fiscal Year 2021, Public Law 116–283.

Include the following information for each contract or subcontract listed:

- Name of Contracting Organization;
- Contract Number (for subcontracts, provide the prime contract number and the subcontract number);
- Contract Type;
- Total Contract Value;
- Description of Requirement;
- Contracting Officer's Name and Telephone Number;
- Program Manager's Name and Telephone Number; and
- NAICS Code.

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

Vol. II, Attachment 11: Reason for the Proposed Award Type

Required: If applicable (see Type of Award).

Instructions: If applicable, provide a rationale for the proposed award type (see Type of Award).

Stage 3: Proposal Submission

Offerors must submit Proposals via the BDR Portal as outlined in Electronic Portal Submission Instructions. Do not mail paper copies of proposals as they will not be reviewed.

Offerors shall include in the proposal cover sheet:

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

Notification to Offerors: All Offerors will receive an automated email acknowledging receipt of their Proposal.

Information to be requested from Offerors: Offerors whose proposals are selected for negotiation or 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 negotiation or 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: Proposal Evaluation

The selection of one or more sources for award will be based on an evaluation of each Proposal. 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 merits, importance to agency programs, and funds availability. Therefore, when together non-cost/price-related evaluation criteria significantly outweigh cost-related evaluation criteria.

1. Program Relevance

- MCMs that address the priorities outlined in the Development AOIs;
- MCMs, devices, diagnostics, and supporting analytics that align with the objectives outlined in BARDA's Strategic Plan, the HHS Pandemic Influenza Plan, PHEMCE Strategy and Implementation Plan, or other Federal Government strategy documents;
- MCMs that are readily administered/used during a public health emergency;
- The maturity level of the proposed product as determined by applicable TRL criteria. Technological maturity should be justified by the inclusion of relevant data;
- MCMs that are suitable for use with pediatric and other special populations;
- The extent to which the proposed effort fills an unmet programmatic need;
- MCMs as specified in the AOIs 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; and
- The Offeror has proposed a product with a sustainable commercial value to ensure long-term access to the MCM.

2. Overall Scientific and Technical Merits of the Proposal

- The degree of innovation and potential to offer a revolutionary increase in capability and/or a significant reduction in cost commensurate with the potential risks of the innovative approach;
- The soundness, feasibility, and validity of the proposed plans, methods, techniques, and procedures of the technical proposal;
- The Offeror's understanding of the scope of the proposed work and the technical effort needed to complete it;
- The reasonableness of the proposed schedule;
- The Offeror's understanding of the statutory and regulatory requirements for FDA licensure or approval status of the proposed work;
- The Offeror's freedom to operate given the intellectual property status of the proposed technology;
- The degree of development of the technology and its readiness for the marketplace; and
- 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 Experience of the Proposed Key Personnel

- The level of expertise of technical personnel proposed;
- The Offeror's demonstrated experience in relevant efforts with similar resources;
- The soundness and reasonableness of the proposed project management approach and demonstrated expertise of the project management personnel proposed;
- The necessary facilities and infrastructure to carry out the proposed effort (The Offeror may identify specific subcontractors and other partners); and
- An organizational chart of the Offeror's personnel that demonstrates the Offeror has relevant infrastructure to support the project.

Other Evaluation Factors and Considerations

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

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.

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.

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, HUBZone Small Business concerns, HBCUs, and Minority Institutions.

Requested Proof-of-Concept Studies

Proposals, which were requested to provide proof-of-concept studies, will be evaluated in regard to the proof-of-concept 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 proof-of-concept design will result in a negotiation for a contract to perform the proof of concept (or a negotiated proof of concept) 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.

Evaluation Rating

The 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.

Additional Information

Offerors selected for negotiations may be subject to inspections of their facilities and quality assurance/quality control 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 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, technical contract support personnel and members supporting BARDA including non-federal personnel such as contractors and consultants.

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 non-federal members of the TEP to review their proposal shall have their proposal returned without evaluation.

Offerors whose 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 pre-award 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 pre-award or a post-award debriefing. Offerors are entitled to no more than one debriefing.

Part VIII: Research and Development Areas of Interest

This section presents an overview of the R&D projects that BARDA seeks to support through this BAA.

Interested Parties contemplating submitting Quad Charts and Market Research Abstracts are strongly encouraged to contact the BARDA technical POC for the respective AOI (see Stage 1: Pre-submission Call with Technical POC) before submitting. Refer to Table 1 for submission deadlines.

Area of Interest #1: CBRN Vaccines

Vaccines are critical to effectively respond to the emergence or spread of a pathogen that poses a significant threat to national security or public health. The mission of the CBRN Vaccines Program is to develop vaccines to protect individuals who are at risk of being, or who have recently been, exposed to a threat agent and to prevent the spread of disease. The Vaccines Program seeks to develop new vaccines and capabilities that can provide effective responses to emerging threats, improve operational logistics, and enhance sustainability. The current AOI will focus on priority biological threats such as filoviruses, smallpox, and anthrax as well as flexible technologies that could address multiple threats.

1.1. Needle-Free Technologies to Administer Licensed Vaccines. The Vaccines Program seeks to improve the operational aspects of licensed countermeasures by reducing or removing downstream vaccine administration bottlenecks associated with the use of traditional ancillary supplies for the following programs:

- Anthrax vaccines
- Smallpox vaccines
- Ebola (Zaire ebolavirus) vaccines

BARDA seeks to support partnerships between product sponsors of licensed or late-stage vaccines and technology developers pursuing needle-free approaches for vaccine delivery. For these programs, microneedle patches are of high interest, but any needle-free approaches will be considered. Please note that BARDA will not be supplying antigen to technology developers without confirmed interest from product sponsors in a joint development program. It is recommended that any partnerships between the needle-free technology developers and product sponsors be defined prior to any proposal submissions.

Submissions should include the following:

- All nonclinical and CMC activities necessary to progress to IND submission
- Phase 1 clinical trial execution to compare safety and immunogenicity of a needle-free delivery to needle and syringe delivery

1.2. Sudan Ebolavirus and Marburg Virus. BARDA is interested in advanced development projects for monovalent vaccines against Sudan ebolavirus and Marburg virus. The proposed vaccine candidate must have the following data:

- Demonstrated protection from lethal challenge in non-human primate (NHP) studies using well-characterized NHP models
- Phase 1 clinical safety data

The objective of this program is to achieve an intermediate level of preparedness including the completion of Phase 2 clinical study(ies) and manufacture of sufficient clinical trial material to support an outbreak response. Multivalent candidates will be considered only upon completion of a Phase 2 clinical study with clear guidance from the U.S. FDA on a regulatory pathway.

1.3. Flexible Vaccine Manufacturing Technologies. To improve vaccine sustainability and enhance our preparedness posture, the Vaccines Program is interested in flexible vaccine manufacturing technologies that could be applied to rapidly develop and manufacture a range of different vaccines against multiple threat agents. While mRNA-based vaccines are of interest, the Vaccines Program seeks proposals for any antigen production technology that meet the following key requirements:

- Ability to progress a vaccine candidate based on gene sequence to an IND submission in <6 month
- Successful application of the technology to multiple infectious disease targets
- Demonstration that technology is scalable to > 1 million doses

BARDA seeks proposals for the development of vaccines against known and unknown CBRN threats. Proposals should address at least two of the CBRN threats listed below may include optional work for vaccine development against "other threats of pandemic potential" and/or a threat "to be determined."

- Zaire ebolavirus
- Sudan ebolavirus
- Marburg virus
- Variola virus
- *Bacillus anthracis*
- Other threats of pandemic potential (optional CLINs only)

Submissions should include the following:

- Base period supporting nonclinical and CMC activities needed to progress one vaccine candidate against a CBRN threat to IND submission in less than six months (if needed)
- Option period(s) supporting nonclinical and CMC activities needed to progress a vaccine candidate against an additional CBRN threat to IND submission in less than six months
- Option period(s) to progress each of the candidates above into Phase 1 clinical trials and generate clinical trial material for further use
- Option period(s) to advance a vaccine candidate against an unknown threat (to be determined at a later time) from sequence identification through Phase 1 clinical trial

Qualities That Strengthen the Competitiveness of a Proposal:

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

Given that cold-chain requirements and availability of ancillary supplies are potential roadblocks to distribution and administration, CBRN Vaccines will prioritize approaches that emphasize the following product performance characteristics:

- Formulation of antigen to enable protection with a single dose
- Technologies that are amenable to on-site, on-demand manufacturing
- Reduced dependency on ultra-low temperature for distribution and storage

Candidates with Phase 1 clinical data for the vaccine candidate in question are preferred. However, earlier-stage candidates may be acceptable if the technology has been applied to other targets that have advanced into clinical development. Proposals that emphasize expedited paths to clinical development and manufacture of clinical trial material are preferred.

Learn more about the CBRN Vaccines Program.

Technical POC: CBRN-Vaccines@hhs.gov

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

Area of Interest #2: CBRN Antivirals and Antitoxins

The CBRN Antivirals and Antitoxins (AVAT) program supports the development of therapeutics that will improve preparedness and response against the following biological threats:

- Toxins produced by *Bacillus anthracis* and multidrug-resistant (MDR) *B. anthracis*
- Toxins produced by *Clostridium botulinum*

- Variola virus
- *Ebolavirus* and *Marburgvirus*

The U.S. Department of Homeland Security identified these agents as material threats to national health security due to their potential for substantial harm if used as biological weapons. The AVAT program supports therapeutic candidates that address these threats as well as those that have broad activity against multiple toxins, toxin classes, viruses, virus genera, or virus families.

2.1. Anthrax Antitoxins. CBRN is pursuing a comprehensive strategy to address anthrax, including procurement and stockpiling of antimicrobial drugs, vaccines, and antitoxins. Under this AOI, proposals for anthrax antitoxin therapeutics will be considered. Such proposals must improve current response capabilities to treat inhalational anthrax and must address the following requirements:

- Compatibility with, and mechanism of action that complements, antibiotic treatment and post-exposure prophylaxis (vaccination)
- Potential for efficacy against toxins produced by MDR and/or engineered *B. anthracis*
- Proposals should describe an appropriate path for regulatory review and eventual licensure in consideration of existing licensed countermeasures

2.2. Botulism Antitoxins. The AVAT program aims to support development of improved next-generation MCMs against botulinum neurotoxins. Candidates for funding must advance or enhance current response capabilities against intoxication. Products with efficacy against serotypes A-G will be prioritized; products with efficacy against less than seven serotypes will be considered if proposals include a strategy to address the remaining serotypes.

Candidate products may include, but are not limited to, antibody-based products, small molecules, or host-directed countermeasures.

- Candidates must have a clear mechanism of action that is appropriate for treatment of intoxication with botulinum neurotoxin serotypes A-G and proposals should describe an appropriate path for regulatory review and eventual licensure
- Products with the ability to reverse the symptoms of intoxication, including paralysis, will be most competitive

2.3. Smallpox Antivirals. The AVAT program seeks to develop next-generation antiviral therapeutics against smallpox given the potential for re-emergence of the virus via natural or intentional events. A highly competitive proposal for a therapeutic candidate will meet the following characteristics:

- Different product class and/or mechanism of action than existing FDA-approved smallpox therapeutics
- Potential to complement existing FDA-approved smallpox therapeutics for use as combination therapy
- Demonstrated preclinical efficacy against orthopoxviruses in appropriate animal models

2.4. Filovirus Antivirals. The AVAT program seeks to develop therapeutics to address the continuing threat of filoviruses, including species of *Ebolavirus* and *Marburgvirus*. Proposals should demonstrate preclinical efficacy against at least one filovirus species in a relevant animal model, with preference for candidates that exhibit efficacy when administered after symptom onset and against multiple filovirus species. In addition to antiviral products focused on treating acute infection, candidates that address the long-term sequelae associated with filovirus infection, host-directed candidates that treat symptoms associated with filovirus infection, and products appropriate for post-exposure prophylaxis are of interest. The following products will be considered competitive:

- Broad-spectrum antivirals with efficacy for multiple filovirus species. Products may be prioritized if they include one or more of the following attributes:
    - Provide added benefit when used in combination with monoclonal antibody products

    - Demonstrated efficacy against non-filovirus viral threats
    - Potential for multiple routes of administration, including oral and intravenous
    - Room temperature or 4°C storage conditions

- Monoclonal antibodies, single-domain antibodies, multi-specific antibodies, or related products that include one or more of the following characteristics:
    - Demonstrably high affinity/avidity, resulting in potentially lower required dose levels or non-intravenous routes of administration
    - Broad activity against multiple filovirus species
    - A manufacturing strategy aimed at achieving efficiencies that will result in a lower cost of goods
- Other antiviral approaches with broad filovirus or antiviral activity
- Host-directed therapeutics that treat the symptoms of filovirus infection or reduce long-term sequelae associated with infection
- Products being developed for post-exposure prophylaxis as the primary indication must have demonstrated or anticipated efficacy against multiple *Ebolavirus* species (preferable Ebola and Sudan viruses) or multiple *Marburgvirus* species, with preference for efficacy against all filoviruses; products with an oral route of administration and storage at room temperature of 4°C will be prioritized.

Ebola virus specific guidance:

Products being proposed for an Ebola virus therapeutic indication should complement existing FDA-licensed 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; and/or efficacy in severe acute infection as demonstrated by extending the treatment window in animal models when compared to the approved therapeutics, either alone or in combination with the approved therapeutics. Products must not have any known or anticipated drug-drug interactions/ counterindication with the licensed therapeutics.

Qualities That Strengthen the Competitiveness of a Proposal:

The AVAT program's strategy is to develop products that are sustainable, with a focus on improving operational logistics of interventions and reducing risk through diversification of countermeasures. Highly competitive proposals will include some or all of the following characteristics:

- Candidates that are TRL 5 or higher: advanced characterization of candidate is ongoing in non-GLP in vivo studies, assay development is initiated, an animal model is identified for efficacy and dose-ranging studies, and process development is initiated for GMP manufacturing. Candidates earlier in development will be considered if they significantly improve existing capabilities.
- Candidates that offer a significant improvement over existing licensed MCMs against a given threat, including but not limited to the following:
    - A distinct mechanism of action or product class, potentially complementary to approved MCMs
    - Operational improvements, such as non-intravenous (IV) route of administration, shelf-life >10 years, and/or elimination of cold-chain requirements
- Candidates and proposals that emphasize best manufacturing practices and innovation to decrease cost of goods will be prioritized. For example, mAb development efforts should focus on improved manufacturing yields, accelerated manufacturing timelines, scalability of manufacturing, and innovative manufacturing approaches that decrease cost of goods.

- Candidates that have the potential to have broad antiviral activity or host-directed products that have the potential to treat the symptoms of a range of viral infections or other indications will be prioritized. Products with a potential commercial market will be prioritized.

Learn more about Antiviral and Antitoxin MCMs.

Technical POC: CBRN-AVAT@hhs.gov

Contracting POC: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI 2 (AVAT MCM): <brief description>"

Area of Interest #3: Antimicrobials

Critical to national health security preparedness is the availability of safe and effective antimicrobial drugs for all patient populations. When responding to public health emergencies and mass casualty incidents, infections involving multidrug-resistant organisms (MDROs) can complicate patient care and recovery. Antimicrobial resistance (AMR) also poses a risk to our ability to respond to biothreat infections due to limited treatment options, particularly for special populations including pediatrics. The mission of BARDA's Antimicrobials Program is to minimize the morbidity and mortality caused by biothreat pathogens as well as secondary infections, including those caused by MDROs, that may be encountered during a CBRN, pandemic influenza, or emerging infectious disease incident. The Antimicrobials 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.

3.1. MDR Bacteria and Biothreat Pathogens. The Antimicrobials Program is interested in drug candidates that are active against biothreat pathogens and/or can be used to treat secondary infections during a CBRN, pandemic influenza, or emerging infectious disease incident. Infections of greatest interest are the following: hospital-associated/community-acquired bacterial pneumonia (HABP/CABP), bloodstream infections (BSI), complicated intra-abdominal infections (cIAI), acute bacterial skin and skin structure infections (ABSSSI), and complicated urinary tract infections (cUTI). Relevant biothreat pathogens include *Bacillus anthracis, Yersinia pestis, Francisella tularensis, Burkholderia mallei*, and *Burkholderia pseudomallei*. Preference will be given to candidates that combat infections caused by the MDROs identified by the Centers for Disease Control and Prevention (CDC) as serious and urgent threats.[3]

3.2. MDR Fungal Infections. The Antimicrobials Program seeks to support the development of first-in-class, broad-spectrum antifungal drug candidates with novel mechanisms of action that target *Candida* species, including *Candida auris*, and *Aspergillus* species. Drug candidates that also demonstrate activity against rare molds, such as Mucorales, are of interest.

Qualities That Strengthen the Competitiveness of a Proposal:

A well-conceived proposal should provide sufficient detail about the candidate's current state of development (nonclinical and clinical data, including data in support of dose selection), manufacturing scale, direction for future development, and regulatory status as well as the developer's plan to obtain product approval.

- **Substantial Improvements Over Existing Products**. Candidates that demonstrate 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. If a candidate belongs to an existing antimicrobial class (same/similar chemistry and molecular target),

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

it must demonstrate a significant improvement over other similarly marketed products or candidates in development (e.g., broader spectrum of activity, reduced toxicity, utility in special populations).

- **At-Risk Populations**. Drug candidates that offer therapeutic benefit to all segments of the population, including but not limited to pediatrics, older adults, and pregnant mothers, are a priority.
- **Biodefense**. If proposing development of a candidate to treat a biothreat infection, the drug candidate must demonstrate in vitro activity (MIC_{50} and MIC_{90}) against that biothreat pathogen(s). Proposals that include i*n vivo* efficacy data in relevant animal models of infection will be prioritized. Development of a pre-EUA package for the biothreat pathogen (e.g., animal efficacy studies and potentially a clinical trial for respiratory infections) within the proposed biothreat development path will be viewed favorably.
- **Development Stage of the Drug Candidate**. Drug candidates must be TRL 6 or higher. Candidates should minimally have an open IND with the FDA. 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. Candidates with FDA input into a path to approval would be prioritized.
- **Commercialization**. Offerors must provide a TPP as well as a commercial development strategy for the candidate and a corporate sustainability strategy. This information will help BARDA to understand the commercial landscape for the candidate 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 Antimicrobials.

Technical POC: CBRN-Antimicrobials@hhs.gov

Contracting POC: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI 3 (Antimicrobials): <brief description>"

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

Nuclear detonation will result in casualties with radiation, blast trauma, and burn injuries alone or in combination. Radiation exposure results in a number of injuries including cell death, loss of progenitor cells, and vascular injuries (endotheliopathies) as well as other injuries that lead to acute radiation syndrome (ARS). Detonation forces cause a range of blast injuries, including blunt and penetrating trauma, where vascular damage can result in life-threatening hemorrhage. As the body responds to radiation injury or trauma, mechanisms that are intended to protect can transition to maladaptive pathophysiologies, including apoptosis, endotheliopathies, coagulopathies, inflammation, and disrupted immune responses like immunothrombosis. These occur as complex and interrelated conditions that lead to ischemia, infection/sepsis, multiorgan failure, and death.

The Radiological and Nuclear (Rad/Nuc) Countermeasures Branch supports advanced development of products to treat the medical consequences of radiological and nuclear threats. Nuclear detonation is the highest consequence threat in this space and is the focus of planning efforts and MCM requirements. Various medical consequences resulting from a nuclear detonation event are addressed here or under AOI#6. MCMs that address the systemic effects of radiation injury or blast trauma should be submitted under AOI#4 for Radiological/Nuclear Threat MCMs. MCMs that address burns or the detection, mitigation, or management of the consequences of blast injury 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.

4.1. Acute Radiation Syndrome (ARS). MCMs to treat radiation injury should be effective when administered 24 hours or later after exposure. The Rad/Nuc program is interested in proposals for the following types of MCM candidates:

- Novel or repurposed therapeutics to address thrombocytopenia caused by acute exposure to ionizing radiation.

- Novel or repurposed therapeutics to address pancytopenia caused by acute exposure to ionizing radiation.
- Cellular therapies that could be used to treat ARS and augment the current HHS Health Resources and Services Administration (HRSA) holdings of bone marrow and cord blood to ensure diverse and equitable representation.
- Novel or repurposed therapeutics to address endothelial and vascular injury caused by acute exposure to ionizing radiation.
- Novel or repurposed therapeutics to address other known sequalae from acute exposure to ionizing radiation with outcomes such as gastrointestinal (GI) or lung injury. Mechanism of action hypotheses should be well supported, and potency assay should be qualified.
- Technologies to produce hematopoietic stem and progenitor cells, including those that optimize directed differentiation and engraftment of functional and safe hematopoietic cells. Activities of interest are those that improve cell processing, optimize *ex vivo* expansion, and enable scaled up production and GMP manufacturing of human-derived or stem-cell derived blood products.
- Programs that can improve the diversity and equity of existing assets for bone marrow transplants.

4.2. Uncontrolled Hemorrhage. The current sustainability issues with the U.S. blood supply will be exacerbated during mass casualty incidents (MCIs). MCM candidates should be in development for a radiation exposure, trauma, or radiation/trauma combined injury indication. Candidates and technologies should minimize immunological barriers associated with transfusions and other transplantations (e.g., ABO and human leukocyte antigen [HLA] typing). The Rad/Nuc program is interested in proposals for the following technologies and MCM candidates:

- Strategies to improve the safety and availability of blood products during an MCI, including but not limited to:
    - Next-generation blood products derived from normal blood collections that show improved stability, shelf-life, usability, and/or effectiveness.
    - Next-generation blood products derived from stem and progenitor cells to generate non-alloimmunizing human blood components for use during transfusions.
    - Manufacturing strategies or platforms that could provide surge capacity to improve availability of existing/improved blood products during an MCI.
- Therapeutics that can replace blood products to treat hemorrhage or can extend the therapeutic window for resuscitation. Candidates should improve patient outcome, reduce transfusions, be fast acting, and be amenable for use in the field and prehospital space.
- Approaches to optimize transfusion medicine and hemostatic resuscitation, particularly in special or underserved populations.

4.3. Radiation Injury and Trauma Pathophysiology. The Rad/Nuc program is interested in understanding the fundamental basis and mechanisms of the pathophysiologies caused by radiation exposure and/or blast injuries, so the Program seeks to support tools and technologies to better define these pathophysiologies and identify treatments. Of particular interest are the following:

- Development of assays for key injury biomarkers to inform targeted and optimized treatments. 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 multiorgan failure.
- Development of therapeutic solutions that target key triggers of pathophysiologies along the continuum from radiation or traumatic injury to multiorgan failure. Interventions should ideally target upstream regulators to intervene as early as possible and prevent transition to maladaptive responses, but MCM candidates that treat downstream pathophysiologies or a failure state are also under consideration.
- Diagnostics that could elucidate the vascular and endothelial dysfunction from radiation injury and/or trauma. Technologies or platforms to elucidate endotypes of injury (radiation injury and/or trauma)

to help our understanding of the potential natural history outcomes for any casualty, to develop targets for treatment, and to potentially inform clinical guidelines.

- Natural history studies to elucidate the sex differences seen in radiation and trauma and identification of biomarkers to inform targeted and optimized treatments.

4.4. Enabling Technologies and Platforms. BARDA is interested in technologies that can elucidate the natural history of injuries resulting from radiological/nuclear incidents and that have applications for MCM development. Technologies could enable the following: 1) identification of novel therapeutic targets; 2)augmentation of existing natural history; 3) development of assays for diagnosis or prognosis; or 4) improvement of MCM testing and screening. BARDA is interested in the following technologies and areas:

- Tissue chip or 3-D microphysiological systems that define aspects of the natural history of radiation injury and aid in new therapeutic target identification.
- Platforms that promote ease of use in resource limited environments; for example, platforms that do not require specialized training to use or that enable self-administration.

4.5. Decorporation Agents. Decorporation agents can be either passive (limited generally to the blood pool) or active (preferred; seeks intracellular or distributed depots) chelators of radionuclides. BARDA is interested in decorporation agents with additional commercial utility (e.g., lead, gadolinium) and those that are 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.

Qualities That Strengthen the Competitiveness of a Proposal:

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

- **Regulatory Feasibility.** Offerors must have completed a pre-IND meeting with the FDA for a relevant indication prior to submitting a Market Research abstract and Quad Chart or Proposal to the BARDA BAA; FDA meeting minutes must be provided if requested. Candidates must have a well-defined mechanism of action that is relevant to ARS or trauma. Submissions must meet a TRL 5 maturity for ARS, trauma, or a related commercial indication to be considered.
- **Operational Relevancy for Radiological and Nuclear Incidents.** Emergency response to a radiological/nuclear incident will require a continuum of care framed by two general phases of treatment: field care and definitive care. The field or prehospital care phase generally includes the first 72 hours of the emergency response. The exceedingly scarce resources and trained personnel during this time will lead to delayed and limited access to advanced medical care and treatments. 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 an MCI, including favorable storage conditions (e.g., storage at room temperature) and ease of use (e.g., favorable deployment or administration that reduces the need for specialized training). MCMs must have sufficient efficacy that improves survival/mitigates morbidity within an operationally relevant timeframe.
- **Repurposing Commercially Available Products.** Regular use of an MCM in routine medical care will improve availability and practitioner familiarity during a radiological/nuclear MCI. The Rad/Nuc program will prioritize submissions for ARS or trauma MCMs that are already approved for a commercial indication (repurposed candidate) or have a high potential for future approval of a commercial indication (novel candidate). For the latter, Offerors may also propose additional MCM development activities for a commercial indication that has a shared injury or pathophysiological mechanism. Proposals should include a commercial strategy that describes potential end users and how a product would be sustained in the market.
- **Addressing Multiple Injuries and Threats.** The Rad/Nuc program is interested in MCMs that can treat similar injuries resulting from different threats. For example, vascular injuries like coagulopathy and endotheliopathy occur in in response to radiation injury, trauma, infectious agents, and some

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

Learn more about Rad/Nuc MCMs.

Technical POC: CBRN-RadNucMCM@hhs.gov

Contracting POC: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI 4 (Rad/Nuc MCM): <brief description>"

Area of Interest #5: Chemical Medical Countermeasures

The mission of BARDA's Chemical MCM Program is to develop MCMs that treat the acute and chronic health effects of chemical threats, are easy to administer in an MCI, 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 clinical (non-MCM) indication for their drug candidate as applicable. For subtopics 5.1-5.5, proposals that contemplate expansion of use 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 people, and the immunocompromised.

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 MCMs against chemical threats. The following thrust areas are prioritized:

5.1. Pulmonary Agents. Development of MCMs to prevent and treat lung damage (including acute respiratory distress syndrome [ARDS], pulmonary edema, pulmonary endothelial vascular injury, reactive airway syndrome, and pulmonary fibrosis) resulting from exposure to agents such as chlorine and phosgene.

5.2. Opioids and Other Respiratory Depressants. Development of MCMs to treat life-threatening respiratory depression caused by drug overdose (including multi-drug). These post-exposure treatments should be fast acting and effective against a variety of opioids, including novel 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, and threat-agnostic respiratory stimulants (e.g., those that may be effective against opioid and non-opioid respiratory depressants) are of particular interest. 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 ameliorate 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. Indications specific to the threat agent, which would require an 'animal-rule' regulatory pathway, are discouraged.

5.4. Nerve Agents and Organophosphorus (OP) Pesticides. Repurposing/label-expansion of already FDA-approved medications for new indications 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.

5.5. Knockdown Agents/Cellular Asphyxiants. Development of MCMs to treat acute symptoms from cellular poisons and asphyxiants (e.g., cyanides, hydrogen sulfide, and phosphine). Treatments should be easily administered by first responders in personal protective equipment. Preference is given to those treatments that are also safe and effective against smoke inhalation-related cyanide exposure.

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 MCIs.

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 human responses to toxic chemical exposure are of interest. 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.

Under AOI #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.

Qualities That Strengthen the Competitiveness of a Proposal:

Factors to be considered include (but are not limited to) the following:

- **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 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 that has similar symptomology to that arising from exposure to a chemical agent.
- **Regulatory Feasibility.** Offerors should have completed a pre-IND meeting with the FDA for approval for an MCM-relevant indication prior to the submission of a Market Research Abstract and Quad Chart or Proposal to the BARDA BAA. FDA meeting minutes must be provided.
- **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 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.
- **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.

The Chemical MCM Program requests that Offerors proposing product development 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 MCMs.

Technical POC: CBRN-ChemMCM@hhs.gov

Contracting POC: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI 5 (Chem MCM): <brief description>"

Area of Interest #6: Burn and Blast Medical Countermeasures

BARDA's Burn and Blast MCM program has a responsibility to build comprehensive national preparedness in management of burns and blast trauma injuries caused by disasters such as nuclear detonation or other man-made threats. The blast effects of nuclear detonation will result in a wide range of traumatic injuries and burns, either alone or in combination, and are covered under the areas listed below. Our strategic priority is to develop MCMs across the entire care continuum for burn and blast trauma, including early detection of injury and severity for triage, interventional support, and treatment. Our product development strategy focuses on enabling MCM adoption in routine care to promote product familiarity and commercial sustainability, so the products are readily available and easy to use in case of an MCI. In general, agnostic technologies with diverse clinical applications, ideally including routine care, are highly encouraged.

The Burn and Blast MCM program seeks technologies that address bottlenecks and improve efficiency in the delivery of care, especially in an MCI. Offerors should consider the treatment window for urgent or initial care intervention as well as for definitive care treatments. A clear assessment of how the MCM adds value instead of or in conjunction with the current standard of care should be outlined in the investigational plan.

Under this AOI, the proposed MCMs should have proof-of-concept data to support the intended use. Data from key parameters such as sensitivity, specificity, and effectiveness to mitigate injury in a reliable model or clinical evaluation should be presented. The MCMs should address one or more challenges or bottlenecks in the delivery of care and mitigation of morbidity associated with injuries from burn or blast trauma. The following areas are prioritized:

6.1. Enabling Technologies to Address General Burn & Blast Traumatic Injuries. Products must address specific unmet need(s) or limitations in the burn or trauma care continuum. Offerors should propose mitigation of at least one of the following types of injuries: extremity fractures, severe lacerations and/or penetrating trauma, crush injuries, or burn injuries. Products may include portable advanced imaging devices, non-invasive devices for detection of fractures or soft-tissue injuries, minimally invasive vital signs monitoring, continuous tracking of patient data, agnostic software, or telemedicine capabilities. Examples of enabling technologies could include, but are not limited to, platform technologies, detection/monitoring systems, smart drug delivery devices, as well as methodologies for pain management that can increase the efficiency and safety in delivery of care, especially in mass casualty environment. An essential goal should be to reduce morbidity/mortality and/or develop capabilities to treat, monitor, evaluate and manage patients.

6.2. Management of Head Injuries in Trauma. Products that utilize non-invasive or minimally invasive technologies to detect neurotrauma, moderate to severe acute traumatic brain injuries (TBI), including internal brain hemorrhage and elevated intracranial pressure (ICP), will be prioritized. Offerors must provide preliminary data evaluating the potential technology for early intervention to reduce morbidity and mortality. Products that enable diagnostic triage and initial care, including ability to detect early signs of deterioration, for management of TBI will be considered.

6.3. Detection and Management of Internal or External Hemorrhage from Non-Compressible Trauma Wounds and Penetrating Injuries. Products must detect and localize hemorrhage (including low volume hemorrhage) and/or provide rapid endovascular or other methods for control of hemorrhage in areas where application of compression is not feasible. Products, including gels and devices, that address management of hemorrhage, such as lacerations and junctional wounds in axilla, groin, neck, and torso are of special interest. Products for hemorrhage control intended for extremities that use tourniquet principles are out of scope. Drugs for hemorrhage control that act at a systemic level to re-establish hemostasis are directed to explore submissions under AOI #4.

6.4. Non-Autologous Topical Products to Prevent or Reduce Burn Wound Conversion (Defined as a Worsening of a Burn Wound From its Original Depth). Burn wound conversion is defined as deepening of a burn wound from its original depth, such as from partial-thickness (second degree) to deep-second- or third-degree requiring autografting. Products should specifically be focused on immediate prehospital use and ease of application to reduce the severity of burn wounds by using novel synthetic and/or non-autologous products. Products with nonclinical and/or clinical data demonstrating that they prevent exacerbation of burn injuries with reduced or no autografting will be prioritized.

Mechanical trauma sustained during a radiological/nuclear event may be due to blast forces, projectile debris, or thermal radiation, among others. MCMs that detect, mitigate, or manage 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. MCMs that address systemic dysregulation of vascular and immune homeostasis, which may include hemorrhage, coagulopathy, inflammation, and sepsis caused by 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 share submissions as they fit programmatic priorities.

Qualities That Strengthen the Competitiveness of a Proposal:

Proposals for candidate MCMs should provide a reasonable and realistic approach to do the following: (1) address one or more critical bottlenecks in delivery of routine care for burn/traumatic injuries such that the value is especially evident when used in a mass casualty; and (2) follow a regulatory and product development strategy that enables evaluation of the candidate's potential clinical value and impact.

Attributes. The following attributes are prioritized:

- Accelerates detection, evaluation of severity, and healing, and prevent injury exacerbation
- Demonstrates clinical benefits, improved recovery time, and reduced length of hospital stay
- Reduces resource requirements such as surgical and pain management needs and care facilities including physiotherapy
- Enables faster triage and decision assistance
- Stabilizes patients and expands the timeframe for effective use of definitive care
- Improves ease of administration and therapeutic index
- Exhibits robust stability and ease of storage and deployment

Data and FDA Input. All data supporting the development pathway for the candidate MCM must be provided, including all pertinent correspondences with regulatory agencies. Offerors should have held a pre-IND, pre-Investigational Device Exemption (IDE), or pre-submission meeting with the FDA to discuss licensure, clearance, or approval for a relevant indication prior to the submission of a Market Research Abstract to the BARDA BAA.

TRL Requirement. The technology should be TRL 5 or higher (i.e., completed all activities for TRL 5) for drugs and biologics or diagnostics and medical devices, as appropriate for the technology.

Health Economic Assessment and Market Sustainability. All submissions shall include a plan to assess the candidate's cost effectiveness value. Approaches to demonstrate anticipated benefits as well as objective analysis of limitations compared with current standard of care should be included.

Cost Sharing. Proposals that demonstrate a commitment of resources from the Offeror in the form of a cost share for the development costs are encouraged.

Learn more about Burn and Blast MCMs.

Technical POC: CBRN-BurnBlastMCM@hhs.gov

Contracting POC: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI 6 (Burn and Blast MCMs): <brief description>"

Area of Interest #7: Diagnostics

Diagnostic tests are important tools for accurately identifying conditions and diseases, determining an appropriate treatment, reducing community transmission, and improving healthcare outcomes for individuals and communities. There is a critical need for the development of new diagnostic tests for rapid detection and differentiation of individuals infected with or exposed to biothreat agents, antimicrobial-resistant pathogens, radiation, and influenza or other emerging infectious diseases.

BARDA AOI #7 seeks to accelerate innovation and product development through public-private partnerships that support advanced research, development, and FDA regulatory approval of clinical diagnostics in the following threat areas: (7.1) Biothreats; (7.2) Antibiotic resistance; (7.3) Influenza; and (7.4) Threat-agnostic diagnostics.

Definitions for the purpose of this AOI:

- *Diagnostic* is defined as an assay and, if required, a platform that together are submitted to the FDA for clearance or authorization.
- *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 Clinical Laboratory Improvement Amendments (CLIA)-waived or waivable and provide results in less than 30 minutes.
- *Home-use* is defined as a test that achieves regulatory authorization or clearance for use in a home setting either Over-the-Counter (OTC) or prescription at-home.
- *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.

TRL Requirement:

- 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 TRLs for MCM Products (Diagnostics and Devices).
- 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 for 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 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 Market Research Abstracts 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).

Home-use/Remote-use instruments should offer these essential elements:

- Small footprint, easily portable
- Lightweight – less than 5 lbs. preferred
- Rapid results - sample to answer in under 30 minutes (less than 15 minutes preferred)
- Broad assay menu with highly accurate assays
- Able to process multiple specimen types (e.g., blood, nasal swabs)
- Battery operation option
- Supports regulatory-compliant electronic data transmission; wireless is preferred
- Able to operate in non-temperature/humidity-controlled environments
- Low cost

Specimens and/or laboratory services, if required for proposed studies, may be provided as Government Furnished Material (GFM) or through other U.S. Government service agreements to assist Offerors that do not routinely work with or that do not have proper facilities to work with BSL-3/4 pathogens.

Design, manufacture, labeling, and packaging of all test components must be compliant with cGMP, as set forth in the Quality System Regulation (21 CFR § 820), and qualified for use in CLIA-regulated or OTC settings.

Products intended to be manufactured in the United States are also preferred.

7.1. Biothreat Agent Diagnostics

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

7.1.1. 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 specimen type and matrix, should be included in the proposal. TRL 4 or greater required.

7.1.2. 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 clinical diagnostic 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 specimen type and matrix, should be included in the proposal.
- Single threat and multiplex biothreat assays will be considered. TRL 4 or greater required.

7.1.3. 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 virus, Sudan virus, Bundibugyo virus, Marburg virus, and Ravn 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 (venous and/or fingerstick), plasma, and/or serum for living patients.

Tests should be low cost (target selling price under $20) 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 EUA submission as appropriate, and ultimately 510(k) submission and clearance.

The test should offer:

- Use in resource limited environments and/or remote locations:
    - Small footprint, easily portable
    - Lightweight – less than 5 pounds preferred
    - Able to operate in non-temperature/non-humidity-controlled environments
    - Ability to operate from batteries and/or solar power sources
    - Safely disposable and/or easily decontaminated
    - Ability to electronically transmit data when in range of Wi-Fi/cellular transceivers is preferred
    - Ability to interpret and clearly present the results to the end user
    - Target selling price <$100

7.2. Antibiotic Resistance Diagnostics for Priority Bacterial Pathogens

BARDA is providing support to advance innovative, rapid, and improved diagnostics to detect bacterial pathogens that cause hospital-associated and community-acquired drug-resistant infections (HAI/CAI), particularly those identified by the Centers for Disease Control and Prevention (CDC) as serious and urgent threats* 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."

7.2.1. Bacterial Antimicrobial Resistance (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. The workflow is preferred to be integrated from sample to answer with no intermediate hands-on time or transfer steps. Inclusion of external commercial specimen preparation and/or blood culture instruments in the workflow would factor into the 24-hour time frame. The assay must have clinically relevant sensitivity and specificity from whole blood and must be able to accept multiple specimen types (e.g., urine, 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 initiating testing. Priority will be given to antimicrobial susceptibility test (AST) solutions with reduced time to results, a small footprint, high throughput, and fully automated compared to current standard of care. TRL 4 or greater required.

7.2.2. 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 with multiple specimen types (e.g., respiratory, whole blood). Results should be available in less than 30 minutes. Priority will be given to solutions on platforms that are FDA-cleared for other diagnostic applications. TRL 4 or greater required.

7.2.3. AMR Sequencing Solutions

Advanced development, clinical evaluation, and FDA clearance/approval of clinically applicable sample-to-answer 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, nasal secretions). TRL 4 or greater required.

7.3. 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 (e.g., wet testing or in silico analysis as outlined in FDA guidance) to emerging, novel avian, and swine influenza viruses (e.g., H5N1, H7N9).

7.3.1. Influenza Home-Use Testing (for OTC or Prescription At-home)

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. Inclusion of other respiratory pathogens that would improve clinical utility may be considered. Diagnostics should be 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. The test solution should incorporate:

- Clearly defined intended use (e.g., patient population, specimen types, clinical indications), 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.

7.3.2. Pan-Influenza Diagnostics: Point-of-Care or Laboratory

Advanced development, clinical evaluation, and FDA clearance/approval of diagnostic assays to enable more rapid identification and differentiation of seasonal influenza viruses from novel influenza viruses (e.g., highly pathogenic avian influenza viruses, swine influenza viruses). Identification of novel influenza viruses may be based on exclusion from seasonal influenza viruses. TRL 4 or greater required.

7.3.3. Point-of-Care Multiplex Assay for Detection of Influenza Virus

Advanced development, clinical evaluation, and FDA clearance/approval of diagnostic assays to enable detection and differentiation of Influenza A and Influenza B in respiratory specimens at the point of care. Inclusion of other respiratory pathogens that would improve clinical utility may be considered. Instruments should have a small footprint, are CLIA waivable, produce results in less than 30 minutes (less than 15 minutes preferred) and have high sensitivity (comparable to a molecular test). Minimum TRL 4. The resultant product must at a minimum be able to perform a 4-plex assay in a single testing operation; greater ability to multiplex is preferred.

7.4. Threat-Agnostic Diagnostics

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 does not target any specific organism or pathogen but

analyzes all nucleic acids in a given specimen and returns positive results when any pathogen that can infect a human is present or negative results when no possible human pathogen is present.

Identification of a new/novel pathogen already occurs in the healthcare research community; however, there are currently no FDA-cleared diagnostic tests that use NGS for either known or unknown pathogen detection. BARDA is interested in first establishing a foundational FDA-cleared NGS testing capability for known pathogens. Once this foundation is established, modifying the product to detect a new, novel pathogen can be achieved quickly in an emergency.

7.4.1. Next-Generation Sequencing (NGS)-Based Diagnostic for Viral Pathogens

BARDA is interested in supporting the advanced development, clinical evaluation, and FDA clearance of NGS-based diagnostic assays focused on viral pathogens. The product sought is a highly flexible, rapidly adaptable, FDA-cleared/approved NGS detection system that identifies known viral pathogens (e.g., detection/identification of all known viral pathogens in a respiratory specimen) and can quickly be adapted in collaboration with the FDA to detect new 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. TRL 4 or greater required.

Submissions should also address the following:

- The proposed product should offer a complete solution including sample processing (e.g., extraction), library preparation, enrichment/depletion (if needed), sequencing, controls, and data analysis against a validated database of known pathogens that is accepted by the FDA. Medium- to high-throughput assays with automated sample preparation, library preparation, sequencing, and analysis, and minimum hands-on time are preferred.
- In order to identify pathogens in a specimen, collaboration with the FDA to determine the requirements of a comprehensive public sequence database that is acceptable for the proposed product is required. The database should include clinically relevant viral pathogens that provide a standardized and validated platform for detecting viral pathogens using metagenomic NGS thus ensuring the accuracy and reproducibility of results in a clinical setting.
- The NGS-based assay must utilize existing sequencing platforms and reagents or platforms in development. Standardized assays that require no or minimal R&D efforts are preferred.
- The offeror must provide a strategy for rapid modification of the assay to include the addition of a novel virus.
- The offeror must provide a regulatory strategy to achieve FDA 510(k) clearance/de novo approval for a 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 FDA guidance will be helpful for framing initial discussions.
- Respondents must submit a clear plan for creating contrived specimens with varying viral loads and for obtaining clinical specimens for validation.
- The proposal should include at a minimum in silico analysis of new variants or recently mutated viruses can be detected and correctly identified.
- The platform should be able to use multiple clinical specimen types and submissions must include feasibility data demonstrating that viral pathogen nucleic acids can be adequately extracted and analyzed from at least one (1) specimen type that is easily obtained (e.g., nasal swab, nasal pharyngeal swab, saliva, oral fluid, fingerstick or venous blood).
- Detection and identification of viral mutations such as those that cause antiviral resistance to inform proper use of therapeutics (e.g., antivirals, monoclonal antibodies) is preferred.
- Platforms should provide clear, clinically actionable data reports, with total time from specimen receipt to result no more than 12 hours (8 hours preferred).

Out-of-Scope Topics for AOI 7.4.1:

- R&D 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 that leverage existing clinical health infrastructure and that would require minimal capital investment for laboratories to implement or sequencing platforms already in development.

Qualities that Strengthen the Competitiveness of a Proposal to AOI #7 (Diagnostics):

- BARDA prefers highly adaptable platforms that are applicable to increased commercial sustainability with the ability to respond to new and emerging threats.
- BARDA prefers projects that utilize U.S. domestic manufacturing.
- BARDA is interested in complete solutions that clearly describe all steps of the testing process from specimen receipt to result. Providing clear descriptions/diagrams/photos of the instrument/test, workflow, specimen manipulations, chemistry, and result reports are encouraged.
- BARDA prefers that Offerors provide a regulatory strategy that includes FDA approval/clearance for their diagnostic products and any relevant communications with the FDA.
- BARDA prefers that Offerors provide a summary of their commercialization strategy for the proposed product such that BARDA can better understand how the company and product will be sustained.

Learn more about Diagnostics.

Technical POC: DDDI_Tech_Contact@HHS.gov

Contracting POC: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI 7 (Diagnostics): <brief description>"

Area of Interest #8: IEID Vaccines

Vaccines are the most effective MCMs to reduce overall public health impact of influenza pandemics and other emerging infectious disease outbreaks. Influenza viruses are constantly evolving in wild and domestic animal populations, causing frequent zoonotic infections in people and unpredictable pandemics that threaten national and global health security. Effective control of emerging infectious disease outbreaks and pandemics requires vaccines that can be developed, manufactured and administered at scale before the disease spreads widely in the U.S. population. The mission of the IEID Vaccines Program is to develop more effective influenza vaccines, vaccines for prioritized emerging diseases, support technologies that can make the vaccines more effective or available sooner with improved operational attributes, and approaches that can increase the sustainability of national pandemic preparedness capabilities.

Under this AOI, BARDA seeks proposals for products and technologies that will improve preparedness and response against pandemic Influenza and may be applicable to emerging infectious diseases with pandemic potential. Successful Offerors will discuss and provide evidence that the proposed effort will enable faster, more effective achievement of protection against disease in the U.S. population during a pandemic response and describe plans and requirements for long-term sustainability of this capability.

8.1. Advanced Development of Faster or More Effective Vaccines.

Proposals for product development that improve preparedness and response against pandemic influenza are requested. Vaccine products that provide one or more of the following are of particular interest:

8.1.1. Faster Vaccines

Development of licensed, domestically manufactured vaccines amenable to both rapid progression from time of new virus strain identification to release of first vaccine doses (goal: 100 days from sequence

availability), and rapid scale-up/technology transfer to new manufacturing facilities for production of doses sufficient to immunize the U.S. and global population (goal: 130 days from sequence availability).

8.1.2. More Effective Vaccines

Products or formulations, such as adjuvants or other technologies, that decrease pandemic response time by:

- Eliciting a priming and protective response in immunologically naïve recipients with a single vaccine dose; or
- Improving the stability, sustainability and/or utility of stockpiled vaccines.

8.1.3. Clinical trials to expand the age range on the label of currently licensed vaccines.

8.2. Innovative Vaccine Production Enhancements.

Support for improvements in vaccine production and administration that accelerate the availability or effectiveness of pandemic influenza vaccines and for which feasibility data is available. Enhancements include but are not restricted to:

8.2.1. Platforms

- Development or implementation of new technology platforms that promote high yield, facilitate rapid antigen change, or elicit broadly cross-reactive and durable immunity
- Methods and technologies that will allow the assessment of improved vaccine performance and potency assessment

8.2.2. Manufacturing

- Upstream and downstream methods to improve production yields
- Formulation improvements to enhance product performance and stability
- Device implementation if required for alternative administration technologies
- Process Analytic Technologies (PAT) to speed release and improve product quality along the manufacturing pathway

8.2.3. Assays for product release

- Methods to decrease the time required to produce essential potency reagents for vaccine release testing
- Development or implementation of new potency determination methods that so not relay on virus strain-specific standard reagents
- Development or implementation of assays (e.g., sterility, adventitious agents) that accelerate vaccine lot release

8.2.4. Administration

- Development of vaccines that are administered by alternative routes that do not require needles and syringes, enable rapid and/or layperson administration, obviate the need for cold-chain storage and/or facilitate improved vaccine effectiveness (e.g., protection of immunologically naïve recipients with a single dose of vaccine, enhanced immunogenicity and durability, mucosal delivery).

Qualities That Strengthen the Competitiveness of a Proposal:

Key Requirement: The vaccine candidate must offer a potential improvement in pandemic response. The improvement needs to be commensurate with the cost and risk associated with the proposed development plan. This may include, but is not limited to, the following areas:

- Candidate vaccines that provide broader protection or durable and more effective immunity than currently licensed products.

- Production platforms that will allow for a substantial increase in the vaccine supply or more rapid vaccine responsiveness.
- Operational improvements such as:
    - The ability to provide protection against a novel influenza virus with a single vaccine dose.
    - Improvements that could enable more effective and sustainable strategies such as less stringent vaccine storage conditions, a route of immunization that does not require needles or ancillary medical supplies or training, technologies that decrease the time from identification of a new virus strain to release of final product, or antigen-sparing technologies that might further extend the number of doses.

TRL Requirement: Typically, BARDA only funds programs that have achieved TRL 6 or above. The program should have completed all of the following activities:

- Manufacture GMP-compliant pilot lots.
- Prepare and submit IND package to FDA.
- Conduct Phase 1 clinical trial(s) to determine the safety and immunogenicity of the clinical test article.
- Vaccine production enhancements that do not involve the development of a new vaccine are not expected to adhere to TRLs and should be submitted under AOI 8.2. New vaccine development programs at a maturity level less than TRL 6 should consider funding opportunities offered by NIAID, other Federal agencies, or BARDA's DRIVe that fund earlier-stage R&D projects. that fund earlier-stage R&D projects.

A Strong Data Package Should Include the Following:

- Data supporting a plausible mechanism of action and correlate of protection.
- Preclinical and clinical data on the proposed mechanism of action and/or correlate of protection suggesting that that the candidate will be clinically efficacious.
    - The preclinical data package should include the following GLP studies.
        - Immunogenicity study demonstrating dose-dependent activation of the proposed mechanism of action and/or correlate of protection.
        - Efficacy study demonstrating superior prevention of infection and/or reduction of disease compared to an appropriately justified commercially available vaccine. Ferrets are the preferred animal model for demonstrating efficacy; however, other animal models will be considered if appropriately justified.
            - The efficacy study should follow the same regimen and route of administration that is used for clinical studies.
        - For vaccine candidates with claims of broad protection, BARDA would like to see data demonstrating protection compared against the homologous virus and at least one heterologous virus with pandemic potential.
        - Toxicology study demonstrating that the proposed product lacks dose-limiting toxicity or reactogenicity.
    - The clinical-IND package submitted to FDA to support clinical trials, Phase 1 clinical trial to establish safety, and immunogenicity is expected to include the following:
        - Safety data for at least 100 subjects at the same dose, regimen, and formulation that will be used for subsequent trials.
        - Immunogenicity data demonstrating vaccine-induced changes to the proposed mechanism of action/correlate of protection. Immunogenicity should be assessed using a qualified assay. Preference will be given to vaccines with immunogenicity data supporting protection against strains with pandemic potential.

        - Data from human challenge studies supporting efficacy will strengthen the package but is not required.
        - Comparison of the proposed candidate with commercially available inactivated, live, inactivated high-dose or adjuvanted vaccine will strengthen the package but is not required.
- Manufacturing aspects that should be addressed in the package are:
    - GMP-compliant pilot lots have been manufactured.
    - Qualification of manufacturing quality control and immunogenicity assays.
    - Discussion of the scalability of the process.
    - Clearly identified critical quality attributes and critical process parameters—which should be used for production of toxicology and clinical lots.
    - Potency and release assays are phase appropriate, qualified in-process, characterized, and stability indicating.
    - 12-month stability data has been generated.
    - Cost of Goods has been estimated and is reasonable for commercialization. A development plan that includes a detailed, data-driven discussion for scale-up, manufacturing, regulatory approval, and commercialization of vaccine. The developer should provide a TPP, including a planned indication, and documentation that they have had discussions with the FDA regarding the appropriate path to licensure of the vaccine.

Learn more about BARDA's IEID Vaccines Development Program.

Technical POC: Chuong Huynh; chuong.huynh@hhs.gov

Contracting POC: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI 8 (IEID Vaccines): <brief description>"

Note: *The data package described above is meant for planning purposes only. BARDA judges all products on a case-by-case basis in accordance with the BAA and completion of the criteria outlined above does not guarantee funding. Moreover, BARDA anticipates that some vaccines may not meet all clinical and manufacturing requirements prior to seeking funding. Companies are strongly encouraged to engage with BARDA early in the development process to ensure clear communication about BARDA's expectations.*

Learn more about NIH/NIAID's Influenza Resources for Researchers and NIH/NIAID's Vaccines Research.

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

DMIDResources@niaid.nih.gov

Area of Interest #9: IEID Therapeutics

The IEID Therapeutics Program focuses on the development of novel therapeutics for the treatment of influenza infections, as well as the treatment of emerging infectious diseases of pandemic potential. The IEID program has special interest in the development of new antivirals to treat influenza in outpatient settings: long-acting antivirals to provide pre-exposure prophylaxis options for people with a poor immune response to influenza vaccines, and immune modulators and other host-directed therapeutics to prevent, treat, and improve clinical outcomes of acute lung injury (ALI)/acute respiratory distress syndrome (ARDS) caused by pandemic and seasonal influenza. As such, the following areas are prioritized:

9.1. Influenza Antiviral Therapeutics: Development of new broad-spectrum direct-acting or host-directed antiviral therapeutics to treat influenza in outpatient ambulatory settings. The proposed candidate must have a novel mechanism of action compared to existing approved influenza antiviral drugs (neuraminidase inhibitors will be considered non-responsive). Candidate therapeutics should

demonstrate superiority to oseltamivir in preclinical influenza models and have a safe toxicology profile, making it suitable for use in all populations. The proposed therapeutic should mitigate the rapid emergence of drug resistance that could reduce the effectiveness of currently available therapeutics and have proven broad influenza strain activity (minimum for influenza A: H1N1, H3N2, H5N1, and H7N9). Demonstrated efficacy of the proposed candidate when administered at least 48 hours after symptom onset in influenza patients or appropriate preclinical influenza models is required.

9.2. Immune Modulators or Therapeutics Promoting Lung Repair: Development of immune modulators or other host-directed therapeutics promoting tissue repair that can prevent, treat, and/or improve clinical outcomes of ALI/ARDS caused by pandemic or seasonal influenza and other respiratory viral infections. Pathogen-specific drugs with antiviral or antimicrobial mechanisms of action will be considered non-responsive under this topic. 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 with ALI/ARDS will be considered. Repurposed products that are already FDA-approved/-licensed or in the late stages of development with clinical exposure data will be considered. A combination therapy that includes a new investigational therapeutic candidate and an approved/licensed therapeutic will also be considered.

9.3. Pre-exposure Prophylaxis – Influenza: Development of antivirals to provide pre-exposure prophylactic treatment options for pandemic preparedness (to bridge the gap between recognition of an influenza pandemic and vaccine availability) and for people in whom influenza vaccines have inadequate efficacy and are at a high risk of severe complications from seasonal influenza infections. Presumptive target population for pandemic pre-exposure prophylaxis includes frontline healthcare workers, first responders, and special populations such as the elderly and long-term care residents. Presumptive target populations for seasonal influenza include those who do not have an adequate response to current vaccines, which would include the elderly and immune compromised populations, among others. Candidate products must be able to provide at least one month of protection from a single dose with a goal of demonstrating a 70% reduction in the relative risk of symptomatic influenza infection; preference will be given to long-acting antiviral products that ideally provide 6 months of protection from a single dose. Candidates that require daily or weekly dosing will be considered non-responsive. 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 NDA/BLA submission can be considered for funding; however, human challenge studies will not be funded by this program.

9.4. COVID-19 Monoclonal Antibody Therapeutics for Treatment [SUSPENDED]: BARDA is interested in supporting the manufacturing and late-stage clinical development through FDA Emergency Use Authorization (EUA) of new monoclonal antibodies (mAbs) effective in treating SARS-CoV-2 infection, particularly in special populations, such as adult and pediatric subjects who may be moderately to severely immune compromised. No US Government procurements of products developed under this topic are anticipated. **Qualities That Strengthen the Competitiveness of a Proposal:**

A well-conceived proposal should demonstrate the product developer's knowledge and understanding of the market need and development pathway for the drug candidate. The proposal should meet the description provided in the area of interest and provide sufficient detail on the candidate's current state of development, manufacturing scale, the direction for future development, and the current regulatory status and regulatory approach. In addition to meeting the requirements stated under each of the AOI topics, additional factors to be considered include (but are not limited to) the following:

- Candidate therapeutics for the treatment of influenza and other respiratory viral infections must have reached TRL 6 or higher, evidenced by release of a final report for a phase 1 clinical study and a U.S. IND submission, unless otherwise indicated. A product can be described as achieving a TRL if it has completed all activities identified in that TRL.
- Demonstrated favorable safety profile in a phase 1 study as evidenced by a clinical study report available for review in the submission.

- 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 cGMP-compliant facility within the United States is preferred.

Additional Assessment Factors for the Specific Topic AOIs Include the Following:

AOI #9.1: Influenza Antiviral Therapeutics

- The strongest proposals should have data demonstrating broad-spectrum antiviral activity against both influenza A and B. Broad-spectrum drugs that are also active against other viral pathogens of pandemic potential, such as SARS-CoV-2, are preferred.
- Candidate therapeutics must have reached a TRL 6 level or higher to apply.
- Candidate therapeutics must have an active IND with the U.S. FDA for the treatment of influenza and have demonstrated safety in a Phase 1 study as evidence by a clinical study report (interim or final) available for review in the submission.
- Candidate therapeutics that benefit special populations, such as pediatrics and pregnant women, will be viewed more favorably.
- Market Research Abstract and Proposal submissions must 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 cGMP-compliant facility within the United States is preferred.
-
- Market Research Abstract and Proposal submissions that do not include the following information will be considered non-responsive:
    - In vitro and in vivo efficacy data against both seasonal and pandemic influenza viruses
    - Phase 1 clinical study report (interim or final) with human safety data including the dose proposed for influenza treatment
    - Detailed cGMP manufacturing plan
    - Regulatory strategy that leads to FDA approval/licensure

AOI #9.2: Immune Modulators or Therapeutics Promoting Lung Repair

- Candidate therapeutics must have reached a TRL 6 level or higher to apply.
- Candidate therapeutics must have an open IND with the U.S. FDA for the 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.
- Market Research Abstract and Proposal submissions must:
    - Address the U.S. FDA combination product rule (21 CFR 300.50) in the submission, if a combination therapy is proposed.
    - 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 preclinical models of ALI/ARDS due to influenza.
    - Product candidates 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 over drugs that propose to treat all patients with ALI/ARDS.
    - Include information about any ongoing and completed clinical trials of the product candidate and justification how the proposed project differs from ongoing or completed clinical studies.

    - 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 cGMP-compliant facility within the United States is preferred.

- Market Research Abstract and Proposal submissions that do not include the following information will be considered non-responsive:
    - In vivo efficacy data of the proposed candidate therapeutic to treat ALI/ARDS associated with influenza
    - Phase 1 clinical study report (interim or final) with human safety data including the dose regimen proposed for treatment of patients with ALI/ARDS
    - Detailed cGMP manufacturing plan
    - Regulatory strategy that leads to FDA approval/licensure

AOI #9.3: Pre-exposure Prophylaxis – Influenza

- Candidate therapeutics must have an open IND with the U.S. FDA for pre-exposure prophylaxis of influenza infection.
- Candidate antivirals must have completed phase 1 clinical studies including the dose and route of administration proposed for phase 2 clinical studies as evidenced by a clinical study report (interim or final) available for review in the submission. Phase 1 clinical studies may include healthy volunteers.
- Intravenous administration is the least preferred route of administration.
- Market Research Abstract and Proposal submissions should address manufacturing capacity to provide an adequate supply of the investigational product to complete the proposed clinical studies. Manufacturing of products in a 21 CFR 210, 211 cGMP-compliant facility within the United States is preferred.
- Market Research Abstract and Proposal 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
    - In vitro and in vivo efficacy data demonstrating activity against both seasonal and pandemic influenza strains
    - An open IND with the U.S. FDA
    - Detailed cGMP manufacturing plan
    - Regulatory strategy that leads to FDA approval/licensure

BARDA requests that Offerors proposing product development provide a summary of 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.

AOI #9.4: COVID-19 Monoclonal Antibody Therapeutics for Treatment [SUSPENDED]

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.
    - Proposals that do not include, at a minimum, key summaries of the pre-clinical package supporting the active IND will be considered non-responsive.
- A regulatory strategy to accelerate clinical evaluation of the candidate product.
    - Regulatory strategy is expected to target an EUA in Q2 calendar year 2024, or sooner.

        - Proposals that cannot achieve an EUA in 2024 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.
- A clinical development plan supporting EUA targeting Q2 calendar year 2024 leveraging existing clinical study data and/or proposed clinical studies/sub-studies to progress the candidate antibody therapeutic to EUA.
    - Proposals that do not include a Phase 1 clinical study report (interim or final) with human safety data or sufficient data to support the dosing strategy proposed for treatment, will be considered non-responsive.
- *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 9.4 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 9.4: Table 1

WHO Label	Pango Lineage	CDC Status at time of AOI posting:
N/A	Variants containing the F456L spike mutations*	VOI
Omicron	BA.2.86	VBM
Omicron	XBB.1.9.1	VBM
Omicron	XBB.1.9.2	VBM
Omicron	XBB.2.3	VBM
Omicron	XBB.1.16	VBM
Omicron	XBB.1.5	VBM
Omicron	CH.1.1	VBM
Omicron	BA.2.74	VBM
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 (parent lineages) **	B.1.1.529 and descendant lineages	VOC
Zeta	P.2	VBM
Mu	B.1.621, B.1.621.1	VBM

* Many lineages have acquired the F456L mutation and common examples include EG.5, FL.1.51, and XBB.1.16.6.

** Omicron parent lineages include BA.1 or similar.

- 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 Q2 calendar year 2024.
    - 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.
- AOI 9.4 proposals are expected to include a cost-share, proposed commercial pricing consideration, and to 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/Market Research Abstract will not be sought for this area of interest (AOI 9.4). Offerors must submit Proposals in accordance with the instructions provided in Part VI Proposal Instructions of the BAA.

Learn more about BARDA's IEID Therapeutics Program.

Technical POC for AOI 9.1, 9.2, and 9.3: Dr. Peter Adams; Peter.Adams@hhs.gov

Technical POC for AOI 9.4: Sabrina Stronsky; Sabrina.Stronsky@hhs.gov

Contracting POC: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI 9 (IEID Therapeutics): <brief description>"

Note: *Development programs at a maturity level less than TRL 6 should consider funding opportunities offered by NIAID or other Federal agencies that fund earlier-stage R&D projects.*

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

Technical inquiries about funding through NIAID programs can be directed to: DMIDResources@niaid.nih.gov.

Area of Interest #10: ImmuneChip+

Accurately modeling human tissues under homeostatic and pathologic conditions in vitro is a key step to accelerating the pace of MCM 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 toward comprehensive, histologically accurate approaches that include components of the human immune system, these MPSs 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 CBRN 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. Ideally, 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 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 MCMs.

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

Submission Requirements and Desired Attributes:

<u>Biological attributes:</u>

1) Human tissue models are highly desired. Projects specifically focusing on platform optimization and comparing with known preclinical 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 (d) 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. GLP capabilities
   c. Laboratory QMS(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 to this AOI.

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; sources of primary cells; 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.

Chem MCM Program Interest Areas:

- 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.
- NOTE: Respondents proposing studies of Organisation for the Prohibition of Chemical Weapons (OPCW) scheduled chemicals must have appropriate facilities and licensure to handle such chemicals.

Rad/Nuc MCM Program Interest Areas:

- Natural history studies of acute radiation syndrome (ARS) 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.
- NOTE: 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 awardees are expected to share project updates and results in a quarterly program meeting, with representatives from multiple federal agencies and other contractors present.

Learn more about BARDA's ImmuneChip+ Program**.**

Technical POC: immunechipbarda@hhs.gov with the subject line: "[Company Name] [ImmuneChip+]".

***Note**: Questions should not contain proprietary or classified information.*

Contracting POC: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI10 (ImmuneChip+): <brief description>"

Area of Interest #11: [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 R&D activities for novel immunogenicity assays (herein immune assays).

A) Offerors shall develop assay(s) to analyze clinical study samples to evaluate immune responses to COVID-19 vaccines, licensed or under development and to SARS-CoV-2 infection. 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 multiparameter intracellular staining (ICS) assays to identify and quantify SARS-CoV-2 -specific T cell subsets in peripheral blood mononuclear cell (PBMC) samples. Offerors shall also address the following requirements in the development of assay:
      - Focus on markers that define T cell lineage, Th1, Th2 and Th17 response, memory, regulatory, and cytotoxicity, as well as 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 U.S. Government request (and availability of appropriate reagents).
      - Validation studies shall be performed for each of the markers that define 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 development should describe quality systems and statistical analyses capabilities.
      - Offerors should provide a plan for technology transfer to a qualified testing laboratory designated by the U.S. Government to support funded clinical trials.

B) Offerors shall establish laboratory testing capability using the assays developed under A) (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 to be used as primary, secondary, and exploratory endpoint analyses for vaccine clinical studies. Data may be used to support a U.S. FDA EUA or BLA.
   i. Establish laboratory testing capability for multiparameter ICS assay to identify and quantify SARS-CoV-2 -specific T cells for PBMC samples. Offerors shall address the following requirements in the establishment of testing capacity:
      - When appropriate, establish assay equivalence for the required assay via technology transfer from the laboratory that developed and validated the assay.
      - Perform vaccine-product specific partial validation, if required by the FDA.
      - Sample throughput of 200 samples/week with appropriate trending quality controls.
      - Offerors proposing to perform laboratory assay testing should describe quality systems, data management and statistical analyses capabilities.

Note that an initial Quad Chart/Market Research Abstract will not be sought for this AOI. Offerors must submit Proposals in accordance with the instructions provided in Part VI Proposal Instructions of the BAA. The submission cutoff date for AOI 11 is **November 8, 2023, at 4:30 PM Eastern Time**.

Technical POC: Dr. Lakshmi Jayashankar; Lakshmi.Jayashankar@hhs.gov

Contracting POC: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI 11 (COVID-19 Immune Assays): <brief description>"

Area of Interest #12: 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. Offerors must justify how common aspects of the platform's development, manufacturing, and/or safety from the development of one product may be leveraged to accelerate regulatory review of subsequent products against distinct priority pathogens. Platforms focusing on botulinum neurotoxin with a potential to also be effective for viral infections will be considered.

Platforms may include, but are not limited to, bi- or multi-specific antibodies, nucleic acid expressed antibodies, Vhh/single-domain antibodies (sdAbs), double-stranded RNA-mediated interference (RNAi), antisense oligonucleotides (ASOs), and clustered regular interspaced short palindromic repeat-associated proteins (CRISPR-Cas).

Initial viral targets for the proposed platform **must** be one of the following priority pathogens: filoviruses (Ebola, Marburg, Sudan viruses), orthomyxoviruses (influenza), Variola virus (smallpox), botulinum neurotoxins, or sarbecoviruses (SARS-CoV-2 and SARS-CoV) (see note below for SARS-CoV-2).

Competitive Proposals Will Include the Following Parameters:

- All activities necessary to support an MCM candidate for one of the priority pathogens/toxins through Phase 1 studies, including proposed manufacturing plan and scale.
- Option period(s) to advance a candidate product on the same therapeutic platform against a secondary target(s) to be agreed upon by the Offeror and U.S. Government. Target preference is for respiratory viruses and viruses causing hemorrhagic fever.
    - Ideal viral/toxin targets must have a well-defined animal model and a defined path for regulatory approval.
- Analysis of risks and gaps in the therapeutic platform technology and proposed efforts to mitigate those risks. Consideration should be given to how the Offeror will improve regulatory and safety aspects of the platform; reduce cost of goods; and improve development timelines, including manufacturing approach.
    - Priority will be given to proposals that aim to develop a platform with the ability to go from discovery (utilizing only nucleic acid sequence of target pathogen) to IND in no more than 6 months, with potential to accelerate to 3 months.
- Timeline with description of required activities for advancement of any candidate product on the platform, starting from threat identification through IND submission. A timeline based on current technology capabilities should be provided as well as an anticipated optimal timeline based on proposed process improvements.
- Feedback from FDA or other stringent regulatory authorities in support of the proposed platform and developmental plan.
- If proposing a therapeutic indication, evidence that products developed on the platform have the potential to be used to treat acute viral infections or exposures. Evidence may include efficacy studies or pharmacokinetics/ pharmacodynamics of products developed on the platform. Further priority will

be given to platforms achieving those endpoints without a requirement for intravenous administration.

- Proposals directed at host targets and proposals for broad-spectrum antivirals are **not** responsive to this AOI.
- 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 U.S. taxpayer support for the development program. U.S.-based manufacturing is preferred.

Guidance for proposals pursuing a PEP or PrEP indication:

Post-exposure prophylaxis (PEP) indications will only be considered for filovirus targets, and only candidates requiring a single dose administration and a non-intravenous route of administration will be considered for a filovirus PEP indication.

Pre-exposure prophylaxis (PrEP) indications will only be considered for influenza and SARS-CoV-2, and candidates meeting the following criteria will be prioritized:

- 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- and SARS-)

Guidance for proposals pursuing a mAb platform:

Monoclonal antibody (mAb) approaches are not a priority for this AOI. Offerors must submit a Market Research Abstract prior to submitting a proposal for a mAb product, and Offerors are encouraged to reach out to the Technical POC below prior to submitting either a Proposal or Market Research Abstract so as to receive feedback on their planned submission. Proposals for monoclonal antibodies should substantially and demonstrably reduce development timelines; propose an innovative manufacturing approach to substantially and demonstrably reduce cost of goods and subsequent per dose cost (i.e. cost of goods at less than $250/gram); offer non-intravenous routes of administration for treatment of acute viral infection; and/or propose delivery to immune-privileged sites and/or ability to target mAbs to specific organs (for example the lungs or airways).

Important guidance for proposals for SARS-CoV-2:

Funding for SARS-CoV-2 is dependent on specific funding availability. Offerors must submit a Market Research Abstract prior to submitting a proposal for a SARS-CoV-2 product, and Offerors are strongly encouraged to reach out to the Technical POC below prior to submitting either a Proposal or Market Research Abstract so as to receive feedback on their planned submission. Proposals should include all available efficacy data against the latest viral variants.

Technical POC: FASTxBAA@hhs.gov

Contracting POC: BARDA-BAA@hhs.gov with the subject line "Contracting questions: AOI 12 (FASTx): <brief description>"

Part IX: Appendix

Appendix 1: 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).

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

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

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;

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;

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

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.

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.)

Appendix 2: 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.