**Statement of Objectives (SOO)**
**BioMaP-Consortium OT Vehicle**

**Project Title: Monoclonal Antibody (mAb) Advanced Manufacturing Capability Improvement: Smart Manufacturing**

## 1. SCOPE

**Topic Area: BioMaP-Consortium Domain 3 – Advanced Biomanufacturing Technologies**

**1.1.** Introduction: Monoclonal Antibodies (mAbs) played a central role in the US response to the outbreaks of important human pathogens such as anthrax, Ebola, RSV or SARS-CoV-2. Building on the demonstrated manufacturing performance of mAbs for a rapid response, BARDA is seeking to improve (enhance) the speed and efficiency of mAb production. This effort is directed at developing and implementing FDA Advanced Manufacturing (Appendix 1, Reference #1) goals within the mAb therapeutic manufacturing environment. The FDA's goals for this program are to improve drug quality, address shortages of medicines, and speed time-to-market. Innovations that rapidly scale manufacturing capabilities, create a distributed network of manufacturing sites improving the cost-efficiency of manufacturing processes and new tools that can address drug shortages by improving are identified to support the emergency preparedness and response mission of the Biomedical Advanced Research and Development Authority (BARDA).

**1.2.** The types of improvements for consideration in this specific solicitation include: Application of smart manufacturing concepts that use automation, digitization, and artificial intelligence to streamline production methods, collection of more process control data, and ultimately use a smart algorithm to adaptively control or make decisions about production or release, and which can be used across all medical products.

## 2. REQUIREMENTS

### 2.1. General Objectives:

This program aims to utilize FDA Advanced Manufacturing concepts to identify, develop, and optimize qualifiable novel, as well as existing manufacturing

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technologies that will improve quality, decrease manufacturing times, improve manufacturing flexibility, and reduce cost, for mAb-based MCMs that address the BARDA threat space. Offerors must be actively developing the drug candidate and must be funded for continued development to licensure. The development effort must be post Phase 2. Offerors can also propose improvements to the manufacture of drug products that are in BARDA's mission and intended for the National Stockpile.

Results of improvements should be in the areas of Efficiency and Productivity, Cost-effectiveness, Scalability and Flexibility, Data Utilization and Insights affecting Product Quality Monitoring and Improvement, Cost Reduction, and/or Cycle Time reductions.

Technology Readiness Levels (TRL) are a type of measurement system used to assess the maturity level of a particular technology. Each technology project is evaluated against the parameters for each technology level and is then assigned a TRL rating based on the progress of the project.

For this program, the government will assess the maturity of the proposed technology and decide on the suitability for continued development under this program. The government will use TRLs 4-6 as a guideline for determining suitability. The goal is to have innovations demonstrated at a technology maturity of TRL 6 (See Appendix 1 References, #2) qualifiable for GMP[1] . A GMP run is not required.

## 2.2. Specific Objective(s):

2.2.1. Develop and implement innovations in the mAb manufacturing process to meet one or more of the goals of FDA Advanced Manufacturing, qualifiable on a scalable system, within three years of project award (See Appendix 1 References, #1). Achievement of this objective will include a GMP-qualifiable successful proof of approach, operational data showing what the improvement is and its return on investment, as well as documentation to meet all the requirements of the proposed TRL and preceding TRLs.

2.2.2. Application of smart manufacturing concepts that use automation, digitization, and artificial intelligence to streamline production methods, collect increased process control data, and ultimately use a smart algorithm to adaptively control or make decisions about production or release, which could be

1. https://www.gmp-journal.com/current-articles/details/gmp-compliant-equipment-design-the-gmp-equipment-design-guide.html

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used across all medical countermeasures within BARDA's portfolio. Considerations for success in this solicitation include the quality and the quantity of the data used, the degree of networking of the unit operation, the algorithm's adaptivity, and the level of autonomous control designed into the application.

2.2.2.1. For the purposes of this requirement, the government interprets "qualifiable" to mean that the equipment, software or other changes implemented and used in the manufacture should be of appropriate design and adequate size, and suitably located for its intended use, cleaning, sanitation (where appropriate), validation and maintenance and be supported by appropriate documentation (See Appendix 1 References, #3).

There are some general specifications in the GMP regulations that apply to every GMP compliant equipment design:

- The system may not influence the product Critical Quality Attributes in a negative way. This could include product contact surfaces, temperature control, shear force, etc., as documented with a Quality Risk Assessment
- The system must be easy to clean and sterilize. Cleanability not only includes product contact surfaces, but also the entire equipment, according to the environmental classification requirements.
- The system must comply with applicable technical rules. This includes manufacturing and quality standards for the equipment, from entities such as ASTM (E2500), ISPE or PDA.
- The system must be suitable for its purpose. The suitability of a system is proven by its qualifications. Qualification process shall be documented by the development of a user requirement specification (URS) and continues in the phases DQ, IQ, and OQ. PQ is not required unless necessary to demonstrate suitability for purpose.

2.2.2.2. The offeror must provide data driven evidence to support claims of process improvement relative to a baseline process. In addition, the offeror must provide baseline data from which improvements have been demonstrated.

2.2.2.3. Focus areas for improvement can be (but not limited to):

2.2.2.3.1. Efficiency and Productivity (Cycle time, Throughput and Overall effectiveness)

2.2.2.3.2. Cost-effectiveness (ROI, Cost per gm, maintenance)

2.2.2.3.3. Scalability and Flexibility (Changeover time, Capacity utilization, Adaptability to process change)

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2.2.2.3.4. Data Utilization and Insights (Predictive analytics, Decision making speed and Data accuracy)

2.2.2.3.5. Regulatory Compliance (Audit findings, Deviation rates, CAPA timelines)

2.2.2.4. The government reserves the right to decide on best value to the government.

## 3. PROGRAM MANAGEMENT

The Awardee is responsible for overall management and execution of the work to achieve the objectives of the agreement. The Awardee must provide the overall management, integration, and coordination of all agreement activities to ensure the efficient planning, initiation, implementation, and direction of all agreement activities.

The Awardee will be responsible for establishing and managing project milestones for the effort. The Awardee will ensure that any changes or deviations planned or incurred by the Awardee in pursuing the objectives of any resulting agreement are reported to the USG. While primary responsibility for management and execution of the effort resides with the Awardee, the USG will provide input to the milestone review process and any changes to the objectives of any resulting agreement.

## 4. DELIVERABLES

See Appendix 2.

## 5. PHYSICAL PROPERTY

Title or interest in equipment acquired by Recipient under this Agreement will vest with the Recipient.

## 6. REQUIRED TERMS RELATED TO USG INVESTMENT

*Consider whether the following four (4) regulatory flow downs are required for the proposed project. Each project may require All, None, or a Combination. Please work with your BioMaP-Consortium Sponsor Liaison to mark those that apply or provide additional regulatory requirements as necessary for final submission.*

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☐Needle Exchange

☐Product Licensure

☐Final Distribution

☐Manufacturing Standards

☐All of these

☒None of these

☐Other, please provide additional information:

## 7. SCHEDULE OBJECTIVES

To be determined. The schedule for performance under the specific project agreements will be variable depending on the specific circumstances of the agreements.

## 8. RISK MANAGEMENT OBJECTIVES

The Awardee will establish a Risk Management program that includes development of a Risk Management Plan, Risk Register, and risk mitigation strategies. See Risk Management Requirements in the Deliverables Table. The Awardee must manage all project risks and report changes to all identified risks to the USG as they occur/arise. The USG must be permitted to participate in the risk management and mitigation processes associated with this project.

## 9. INTELLECTUAL PROPERTY

The Government requires not less than Government Purpose Rights to any intellectual property developed under this effort with USG funds.

## 10. REFERENCES

See Appendix 1

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**APPENDIX 1. REFERENCES**


1. Advanced Manufacturing: https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/advanced-manufacturing
2. Technology Readiness Levels: https://medicalcountermeasures.gov/trl/integrated-trls/
3. Qualifiable: GMP-compliant equipment design: The GMP Equipment Design Guide - GMP Journal


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## APPENDIX 2. Project Agreement Deliverables

| Deliverable Description | Content Requirements and Instructions | Reporting Frequency |
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| Kick Off Meeting | Recipient to develop Agenda and host an in-person or virtual kick-off meeting to discuss overall project objectives, key personnel, deliverables, risks, schedule and funding/payment procedures.<br><br>Provide meeting minutes. | Kickoff meeting conducted within 5 days of award.<br><br>Minutes to be submitted within 3 business days of meeting. |
| Ad-hoc Project Team Meetings | Recipient to schedule and create and agenda. Follows Agenda mutually agreed upon in advance of meeting. RECIPIENT to provide meeting minutes within 3 business days from date of meeting. | As needed for special topics, when specifically requested by the OTAO or OTTR. |
| Monthly Project Team Meetings | Purpose is to review monthly progress report findings, any changes since last month and any projected issues or challenges. | Virtual. Monthly, 5 business days after the monthly report deliverable. 1 hour duration, hosted by the recipient.<br><br>Minutes to be submitted within 3 business days of meeting. |
| Monthly Project Progress Report | Monthly report of overall status including cost, performance and schedule progress and variance from plan. Include discussion of important design considerations and milestones, such as Process Flow Diagrams complete, P&IDs Issued for Design, Process Description complete, etc. Include status of other engineering disciplines, project delays, risk management, funding issues, Construction, Startup, Commissioning/Validation, Regulatory progress, and deviations from proposed Return on Investment. Level of detail for various aspects of project may decrease or increase in detail as the project moves through the various phases of execution. | Monthly. Due 15th of the month. Contractor format acceptable, in PDF. |

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| Bi-Annual In-Process Review (IPR) | Organized, scheduled and hosted by Recipient. May be virtual or physical at the Recipient's facilities based on USG preference. High level project progress review of overall objectives. | Every 6 months from start of project.<br><br>Recipient to send brief 3 working days in advance of meeting. |
| Integrated Master Project Schedule | MS Project Detailed Project Schedule, full detailed schedule for entire Project, including all major activities, critical path, and milestones. Status updated regularly. | Status updated monthly and when milestones and/or major events change. Submitted with the Monthly Project Progress Report. |
| Project Budget | Excel Detailed Project Budget, full detailed budget for entire Project | Notify USG via e-mail whenever Project Budget is revised/updated and post to shared documents site |
| Project Documentation | Project Design and other related project execution related documents | Included in the Monthly Project Progress Report |
| Project Risk Register | Project risks identified throughout the project shall be tracked via a Risk Register Log (or similar list/tracking vehicle). Log should contain information regarding identification date, severity of risk, mitigation plan(s) and dates for implementation, risk owner, etc. | Updated monthly and submitted with Monthly Project Progress Report. |
| Project Action Items List | Actions identified throughout the project, which are not tracked by some other project management tool, and which require follow up and monitoring for completion, will be captured in an Action Items List. (Or similar list/tracking tool.) List should contain information regarding identification date, target completion, responsible individuals/groups, etc. | Submitted if/as required with monthly technical progress report. |
| Site Visits | Host visits from USG following agenda/schedule mutually agreed upon with USG in advance of visits. Provide visit notes within 3 business days from date of visit. | Typically, quarterly, commensurate with quarterly IPR, at the Agreements Officer's discretion. |
| Annual Project Progress Report | High level project progress review of overall objectives. Updated projections against project expectations, including risks and mitigation plans, should be | Annually from award. To review progress over the previous 12 months. A Draft to be submitted 30 days after the |

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| | reported with respect to the previous annual report. Summary of critical changes that took place over the year. Recommended to not exceed 20 pages. | completion of each year of performance. Within 15 days of receipt, the Government will provide review comments. The Respondent shall respond within 15 days of receipt of comments.<br>Report format: Microsoft Word and PDF |
| Final Report | Final report summarizing stated objectives and the progress that was achieved in meeting those objectives; summary of risks incurred, impacts and mitigation; quantitative discussion of production improvements achieved; financial summary of project; schedule summary for project, comparing original schedule to final schedule; recommendations for path forward as applicable.<br>A section shall be included that details the effort, any changes made from initial processes, and reduction to practical evidence. Include any changes to training requirements necessitated by implementing the process changes conducted in this program.<br>A section shall be included that details any improvements realized by implementation of the project. Report shall include improvements in terms of dollar savings, flexibility, speed, output, and/or any other areas | Initial submission to be submitted 30 days prior to the end of the period of performance. Within 15 days of receipt, the Government will provide review comments. The Respondent shall respond within 15 days of receipt of comments. |
| Security Plan | The Security Plan must detail how the RECIPIENT will adhere to established ASPR Informational Technology (IT) and Operational Security (OPSEC) policies and requirements.<br><br>The Security Plan must include but is not limited to; | Initial submission 30 Days after Award, updated as necessary<br><br>See BARDA Security Plan checklist |

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| | • Internal management security measures that meet the ASPR, IT, and OPSEC security requirements<br>• Plan to ensure Project Agreement security compliance, to include roles and responsibilities<br>• Plan to manage Consortium member physical, IT, and OPSEC security compliance as a contingency of Consortium membership | |
| Quality Management Plan | The recipient shall develop and submit a Quality Management Plan that details the approach to regulatory compliance appropriate to the proposed innovations. | Initial submission 30 Days after Award, updated as necessary<br>Report format: Microsoft Word and PDF |
| Infrastructure and Management Structure Organizational Chart | The recipient shall complete description of the infrastructure and management structure (organizational chart) including but not limited to addressing all elements that will accomplish the program's goals and milestones. The recipient shall propose a workforce management plan, e.g., how workforce will train, maintain, etc., that reflects the ability to meet the requirements. | Initial submission 30 Days after Award, updated as necessary<br>Report format: Microsoft Word and PDF |

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