BARDA Broad Agency Announcement (BAA)

(Solicitation # CBRN-BAA-13-100-SOL-00013)

Advanced Research and Development of Chemical, Biological, Radiological and Nuclear Medical Countermeasures

Topic Area of Interest No. (#1), Vaccines

MANUFACTURING AND LICENSURE OF BPSC1001/V920 (rVSVΔG-ZEBOV-GP)

Statement of Work

PREAMBLE

Independently and not as an agency of the Government, the Contractor shall be required to furnish all the necessary services, qualified personnel, material, equipment, and facilities, not otherwise provided by the Government, as needed to perform the Statement of Work submitted in response to the BARDA Broad Agency Announcement (BAA) BARDA CBRN BAA-13-100-SOL-00013.

The Government reserves the right to modify the milestones, progress, schedule, budget, or deliverables to add or delete deliverables, process, or schedules if the need arises. Because of the nature of this research and development (R&D) contract and the complexities inherent in this and prior programs, at designated milestones the Government will evaluate whether work should be redirected, removed, or whether schedule or budget adjustments should be made. The Government reserves the right to change the product, process, schedule, or events to add or delete part or all of these elements as the need arises.

CLIN 1: Base Period, "Manufacturing and Licensure of BPSC1001/V920 (rVSV ZEBOV-GP)"

Overall Objectives and Scope

The following Statement of Work (SOW) , broken into a BASE and Options, is focused on ensuring activities necessary for the long-term commercial success of the BPSC1001/V920 (rVSVΔG-ZEBOV-GP) Ebola virus vaccine can be completed, resulting in the submission of a BLA for the BPSC1001/V920 (rVSVΔG-ZEBOV-GP) program. Activities within this SOW (BASE and Options) include facility and site readiness at Merck's Burgwedel commercial facility, process simulations, validation of the commercial scale 400RB process, validation of analytical methods, stability testing for Drug Substance (DS) and Drug Product (DP) from the Process Performance Qualification (PPQ) lots, and long-term storage of both DS and DP from the PPQ lots. The SOW further includes clinical testing of BPSC1001/V920 (rVSVΔG-ZEBOV-GP) in pediatric populations, support for immunogenicity testing of samples from the NIH sponsored PREVAIL and PREPARE trials (costs not covered by NIH), and completion of the preclinical developmental and reproductive toxicity (DART) testing. Successful PPQ, analytical method validation, and facility readiness are regulatory requirements for licensure of biological products to demonstrate consistency of manufacture and compliance to current GMP regulations and are the basis for a

(b) (4)

[redacted]

Statement of Work and Work Breakdown Structure

1. Base: Facility, Site, Process Performance Qualification (PPQ) Readiness Activities, Manufacturing and Testing of Process Simulations

The BASE contract will support the necessary activities at the final commercial manufacturing facility at the expected commercial process scale (400RB process).

The SOW thus includes:

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[redacted]

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1.1.1 Program Management

The Contractor [BioProtection Systems Inc. (BPS)] shall provide for the following as outlined below and in the contract deliverables list (Article F.2):

1.1.1.1 Overall Management

The overall management, integration and coordination of all contract activities, including a technical and administrative infrastructure to ensure the efficient planning, initiation, implementation, and direction of all contract activities;

- Principal Investigator (PI) responsible for project management, communication, tracking, monitoring and reporting on status and progress, and modification to the project requirements and timelines, including projects undertaken by subcontractors; The contract deliverables list (reference), identifies all contract deliverables and reporting requirements for this contract.
- Project Manager(s) with responsibility for monitoring and tracking day to-day progress and timelines, coordinating communication and project activities; costs incurred; and program management; The contract deliverables list (reference), identifies all contract deliverables and reporting requirements for this contract.
- BARDA Liaison with responsibility for effective communication with the Project Officer and Contracting Officer. May be the PI or Project Manager.
- Administrative and legal staff to provide development of compliant subcontracts, consulting, and other legal agreements, and to ensure timely acquisition of all proprietary rights, including IP rights, and reporting all inventions made in the performance of the project.
- Administrative staff with responsibility for financial management and reporting on all activities conducted by the Contractor and any subcontractors.

1.1.1.2 Program Management Deliverables

- Contract Review Meetings including:
  - Regular Meetings

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

  - Scheduled Bi-weekly teleconferences

    The Contractor shall participate in teleconferences every two weeks between the Contractor and subcontractors (as required) and BARDA to review technical progress. Teleconferences or additional face-to-face meetings shall be more frequent at the request of BARDA

- Integrated Master Schedule

  Within 180 calendar days of the effective date of the approved COA by the CO for the subcontractor performing the work, the Contractor shall submit a first draft of an updated Integrated Master Schedule in a format agreed upon by BARDA to the Project Officer and the Contracting Officer for review and comment. The Integrated Master Schedule shall be incorporated into the contract, and will be used to monitor performance of the contract. Contractor shall include the key milestones and Go/No Go decision gates. The IMS for the period of performance will be accepted by BARDA at the PMBR.

- Integrated Master Plan

  Within 180 calendar days of the effective date of the approved COA by the CO for the subcontractor performing the work ,the Contractor shall utilize a WBS template agreed upon by BARDA for reporting on the contact. The Contractor shall expand and delineate the Contract Work Breakdown Structure (CWBS) to a level agreed upon by BARDA as part of their Integrated Master Plan for contract reporting. The CWBS shall be discernable and consistent. BARDA may require Contractor to furnish WBS data at the work package level or at a lower level if there is significant complexity and risk associated with the task.

  GO/ NO-GO Decision Gates:

The Integrated Master Plan outlines key milestones with "Go/No Go" decision criteria (entrance and exit criteria for each phase of the project). The project plan should include, but not be limited to, milestones in manufacturing, non-clinical and clinical studies, and regulatory submissions. Specific milestones will be defined that will be used to trigger subsequent Option Periods.

- Program Management Plan

  Within 90 calendar days of the effective date of the approved COA by the CO for the subcontractor performing the work, the Contractor will develop, and submit to BARDA for approval, a revised version of the Program Management Plan (PMP) that was initially submitted to HHS under contract No. HSSO100201500002C. The revised plan will detail the tools and techniques that BPS intends to employ in its management of the proposed work.

  This plan is intended to be a living document and changes to any of the individual sub-plans as well as the addition or subtraction of sub-plans will be documented and must be approved by the Program Manager and Principal Investigator. Changes to the PMP will be tracked by version number and date, and assuming changes have been made, will be submitted to BARDA for review and approval. The Program Management Plan will update the following individual sub-plans:

  - Scope/Schedule Management Plan
  - Costs Management Plan
  - Communications Management Plan
  - Stakeholder Management Plan
  - Change Management Plan
  - Quality Management Plan
  - Human Resources/Staffing Plan

- Product Development Plan

  Within 90 calendar days of the effective date of the approved COA by the CO for the subcontractor performing the work the Contractor will submit a revised version of the Integrated Product Development Plan (IPDP) that was initially submitted to HHS under contract No. HSSO100201500002C. Ultimately, this plan will require approval by BARDA's Contracting Officer's Representative and the Contracting Officer prior to initiation of any activities related to their implementation. This plan will be updated, as required.

- Subcontractor Management

  The Contractor will manage all subcontractors to oversee effective and timely execution of deliverables in the scope of work and to meet reporting requirements under this contract. (b) (4) [redacted]

(b) (4) [redacted].

- Financial Management, Accounting and Reporting

  Within 90 calendar days of the effective date of the approved COA by the CO for the subcontractor performing the work ,the Contractor will engage a subcontractor to provide specific services in Contracts and Subcontracts Management to help ensure compliance with contracts clauses and requirements, Federal Acquisition Regulations; and purchasing. Specific services will include:

  - Subcontract Requests for SOW
  - Contracts reporting and monitoring
  - Contracting Office Consent to Subcontract
  - Price Reasonableness analysis
  - Internal Controls
  - Earned Value Management support

  To the extent required by the contract, the Contractor will develop, implement, and provide ongoing support to the contract Earned Value Management (EVM) reporting. This will include the design and implementation of processes, documentation, control account plans, and the Performance Measurement Baseline (PMB) enabling the implementation of a software solution. Further, the Contractor and/or its subcontractor will support the monthly EVM processing and reporting and format 5 variance reporting. Elements of EVMS shall be applied to all CLINs as part of the Integrated Master Project Plan, the Contractor shall submit a written summary of the management procedures that it will establish, maintain and use to comply with EVMS requirements.

  The Contractor and/or its subcontractor will provide Project Accounting and Finance Management to help ensure compliance with contracts clauses and requirements, Federal Acquisition Regulations; and cost accounting and billing.

  Specific services will include:

  - Monthly Job Cost reporting and billing
  - Time Reporting
  - Indirect Rate calculations
  - Internal Controls and training
  - QA/QC Plans and Ongoing activity

- Decision Gate Reporting

  On completion of a stage of the product development, as defined in the agreed upon Integrated Master Schedule and Integrated Master Plan, the Contractor shall prepare and submit to the Project Officer and the Contracting Officer a Decision Gate Report that contains (i) sufficient detail, documentation and analysis to support successful completion of the stage according to the predetermined qualitative and quantitative criteria that were established for Go/No Go decision making; and (ii) a description of the next stage of product development to be initiated and a request for approval to proceed to the next stage of product development.

- Risk Management Plan

  Within 90 calendar days of the effective date of the approved COA by the CO for the subcontractor performing the work, the Contractor shall develop a risk management plan within highlighting potential problems and/or issues that may arise during the life of the contract, their impact on cost, schedule and performance, and appropriate remediation plans. This plan should reference relevant WBS elements where appropriate. Updates to this plan shall be included every three months (quarterly) in the monthly Project Status Report.

- Quality Management Plan

  Within 90 calendar days of the effective date of the approved COA by the CO for the subcontractor performing the work ,the Contractor will update, and submit to BARDA for approval, a revised quality plan for the program to ensure compliance with specified requirements, guidance documents and GCP/GMP/GLP regulations; and to ensure continual improvement.

  The quality plan will:

  - Describe the quality planning process;
  - Establish quality objectives;
  - Identify quality system changes in alignment with compliance requirements, contractual requirements and operational requirements; and
  - Ensure comprehensive quality oversight of the subcontractors through documentation reviews and quality system compliance audits.

  This quality plan will be maintained by the BPS quality lead who will be responsible for assuring that all quality objectives are appropriately documented and accomplished. This quality plan may be supplemented with additional, separate implementation plans and schedules.

  The Contractor will manage the program's quality activities according to the approved quality plan.

- Deviation Request:

  During the course of contract performance, in response to a need to change IMS activities as baselined at the PMBR, the Contractor shall submit a Deviation Report. This report shall request a change in the agreed-upon IMS and timelines. This report shall include: (i) discussion of the justification/rationale for the proposed change; (ii) options for addressing the needed changes from the agreed upon timelines, including a cost-benefit analysis of each option; and (iii) recommendations for the preferred option that includes a full analysis and discussion of the effect of the change on the entire product development program, timelines, and budget.

- Monthly and Annual Reports

  The Contractor shall deliver Project Status Reports on a monthly basis. The reports shall address the items below cross referenced to the WBS, SOW, IMS, and EVM:

  - Executive summary highlighting the progress, issues, and relevant activities in manufacturing, non-clinical, clinical, and regulatory;
  - Progress in meeting contract milestones, detailing the planned progress and actual progress during the reporting period, explaining any differences between the two and corrective steps;
  - Updated IMS;
  - Updated EVM;
  - Updated Risk Management Plan (Every 3 months);
  - Three month rolling forecast of planned activities;
  - Progress of regulatory submissions;
  - Estimated and actual expenses;

- Data Management

  The Contractor shall develop and implement appropriate data management and quality control systems/procedures, including transmission, storage, confidentiality, and retrieval of all contract data; Provide for the statistical design and analysis of data resulting from the research;

- Performance Measurement Baseline Review (PMBR):

  Within 180 calendar days of the effective date of the approved COA by the CO for the subcontractor performing the work, The Contractor shall engage a subcontractor to submit a plan for a PMBR. At the PMBR, the Contractor and BARDA shall mutually agree upon the budget, schedule and technical plan baselines (Performance Measurement Baseline). These baselines shall be the basis for monitoring and reporting progress throughout the life of the contract.

The PMBR is conducted to achieve confidence that the baselines accurately capture the entire technical scope of work, are consistent with contract schedule requirements, are reasonably and logically planned, and have adequate resources assigned. The goals of the PMBR are as follows:

- Jointly assess areas such as the Contractor's planning for complete coverage of the SOW, logical scheduling of the work activities, adequate resources, and identification of inherent risks
- Confirm the integrity of the Performance Measurement Baseline (PMB)
- Foster the use of EVM as a means of communication
- Provide confidence in the validity of Contractor reporting
- Identify risks associated with the PMB
- Present any revised PMBs for mutual agreement
- Present an Integrated Master Schedule: The Contractor shall deliver an initial program level Integrated Master Schedule (IMS) that rolls up all time-phased WBS elements down to the activity level. This IMS shall include the dependencies that exist between tasks. This IMS will be agreed to and finalized at the PMBR. DIMGMT-81650 may be referenced as guidance in creation of the IMS (see http://www.acq.osd.mil/pm/).
- Present the Risk Management Plan

1.1.1.3 Long-term Storage and Stability Testing, 90 Roller Bottle Drug Product Lots Produced Under Contract HHS0100201500002C

The Contractor has previously stored Final Drug Product from lots produced at the 90 RB scale (b) (4) [redacted]

(b) (4) [redacted]

1.1.2. Process Performance Qualification (PPQ) and Site Readiness Activities

The contractor and/or its subcontractor(s) shall complete the necessary facility upgrades and implementation of quality systems to support cGMP production of the Ebola Zaire Vaccine BPSC1001/V920 (rVSVΔG-ZEBOV-GP).

In addition, the contractor and/or its subcontractor(s)will conduct PPQ readiness activities to generate necessary documents and data to support process validation and to support a Biological License Application (BLA) for BPSC1001/V920 (rVSVΔGZEBOV- GP manufacturing.

(b) (4) [redacted]

- (b) (4) [redacted]

(b) (4) [redacted]

- [redacted]
- [redacted]

1.1.3 Manufacture and Testing of Process Simulations

Complete the necessary up to three consecutive end-to-end Process Simulations for DS and DP product with the expected commercial process.

Activities include:

- (b) (4) [redacted]
- [redacted]
- [redacted]
- [redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

1.1.5 Non-Clinical: Reproductive Toxicology Studies

(b) (4)

(b) (4)

1.1.6. Clinical Study: Immunogenicity for PREVAIL and PREPARE Studies

(b) (4)

Option 1: Manufacturing and Testing of PPQ Lots, BLA Preparation and Pre-PAI Activities

(b) (4)

The Contractor and/or its subcontractor(s) shall carry out the following tasks and subtasks and in accordance with the agreed upon Integrated Master Schedule and Integrated Master Plan

(defined in 4.1.1.2 and 4.1.1.3) which shall further detail the conduct of the specific tasks and subtasks.

2.1 Program Management (consistent with section 1.1.1) (WBS 2.1)

Program management scope in BASE year is consistent with program management scope in each option year.

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The contractor and/or its subcontractor(s) shall carry out the following tasks and subtasks and in accordance with agreed upon Integrated Master Schedule and Integrated Master Plan

(defined in 4.1.1.2 and 4.1.1.3) which shall further detail the conduct of the specific tasks and subtasks.

(b) (4)

[redacted]

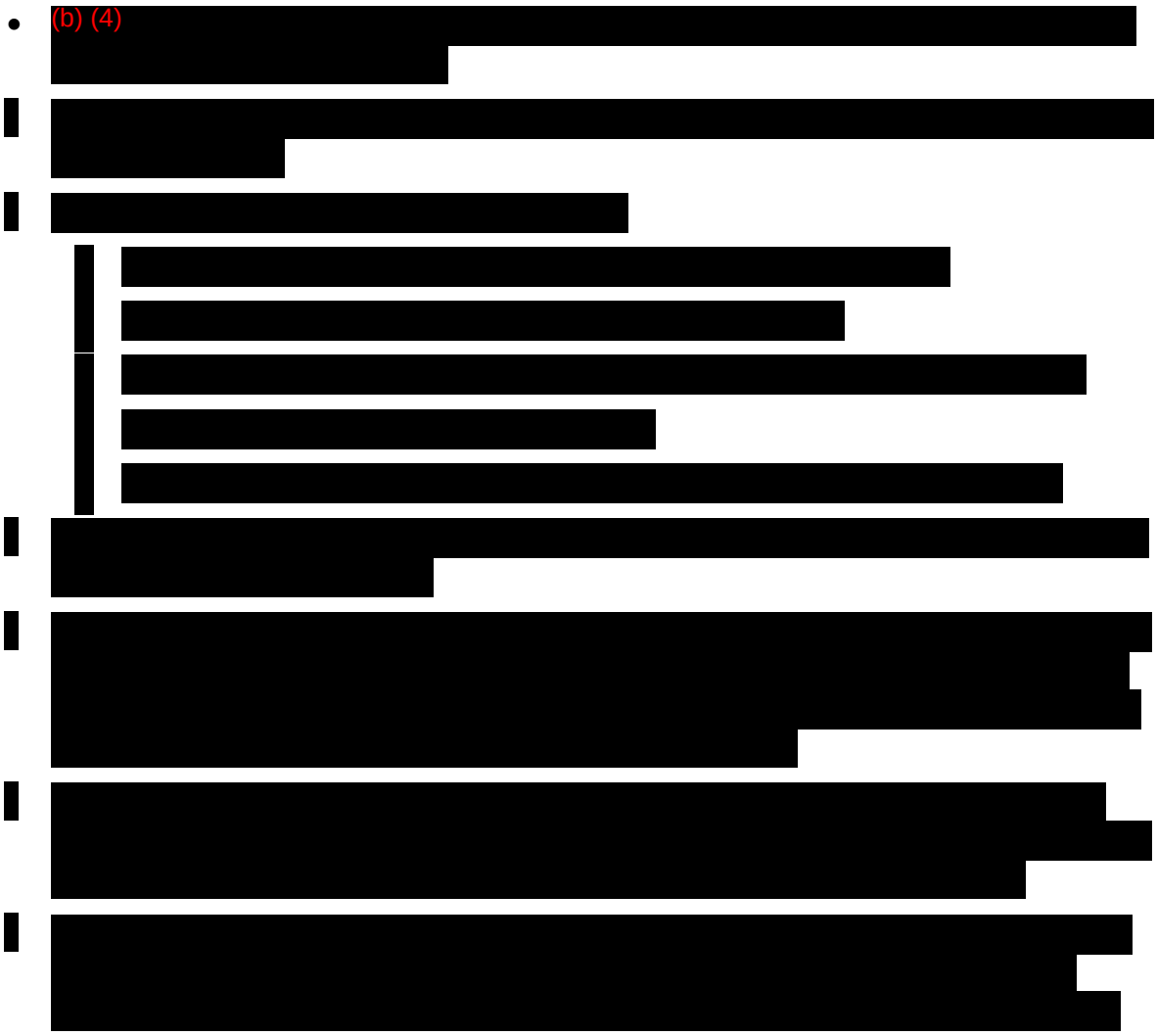
3.1 Program Management (Consistent with section 4.1.1.1) (WBS 4.1)

Program management scope in BASE year is consistent with program management scope in each option year.

(b) (4)

[redacted]

- (b) (4) [redacted]



Option 3: Additional Process Simulations and Manufacturing of PPQ Lots

Go/No Go Decision Criteria: Option 3 will be considered if additional process simulation and/or Process Performance Qualification Lots are needed. This decision will be considered after completion of all milestones under WBS 1.1.3, and again after all milestones under WBS 2.2 (if Option 2 should be exercised).

The contractor and/or its subcontractor(s) shall carry out the following tasks and subtasks and in accordance with an agreed upon Integrated Master Schedule and Integrated Master Plan (defined in 4.1.1.2 and 4.1.1.3) which shall further detail the conduct of the specific tasks and subtasks.

4.1 Program Management (Consistent with section 1.1.1) (WBS 6.1)

Program management scope in BASE year is consistent with program management scope in each option year.

(b) (4)

[redacted]

- (b) (4) [redacted]