

**Vaccine and Treatment Evaluation Units (VTEUs): Evaluation of Control Measures
Against Infectious Diseases Other than AIDS
STATEMENT OF WORK FOR SOLICITATION PURPOSES
RFP NIH-NIAID-DMID-08-03**

OBJECTIVE AND SCOPE

This contract provides for the design and conduct of Phase 1, Phase 2, Phase 3 and Phase 4 clinical trials and clinical studies of candidate vaccines and therapeutics, as well as for other evaluations and analyses, against infectious diseases other than human immunodeficiency virus (HIV). The Contractor shall interact with companies under contract to DMID who provide regulatory, clinical site monitoring and data management and analysis to support the VTEUs. See Appendix E attached to this RFP for more information on these companies.

Scope of Infectious Diseases: The Contractor shall evaluate candidate vaccines and therapeutics, as well as conduct other types of evaluations and analyses, for viral (other than HIV), bacterial, parasitic and fungal pathogens, including National Institute of Allergy and Infectious Diseases (NIAID) priority biodefense pathogens (http://www3.niaid.nih.gov/Biodefense/bandc_priority.htm).

Scope of Investigational Vaccine and Therapeutic Candidates: The scope of investigational candidates to be evaluated by the Contractor shall include live, attenuated, killed, vectored, DNA and combination vaccines, adjuvants, novel therapeutic agents such as immunomodulatory agents, and approaches to vaccine or therapeutic delivery, dose finding, schedule, routes and modes of delivery. The Contractor is expected to incorporate novel vaccine and therapeutic approaches as they are developed.

Scope of Clinical Research: The scope of clinical research shall include the conduct of Phase 1 and Phase 2 clinical studies and trials of candidate vaccines and therapeutics to evaluate safety, immunogenicity, reactogenicity, optimal dose and schedule, infectivity, degree of virulence or attenuations, transmissibility and genetic stability and when warranted, shall include pharmacogenomic studies. The range of characteristics to be evaluated by the Contractor will vary depending on the candidate being tested. When requested by the Project Officer, the Contractor shall initiate and maintain targeted surveillance for pathogens of interest in study populations as background information in the context of protocol development to interpret vaccine and therapeutic response, initiate clinical studies and trials at a time when the wild type pathogen is not at its peak, and determine the impact of a particular pathogen in selected high-risk populations. The scope of clinical research shall also include the conduct of Phase 3 and 4 clinical trials and studies in cases where such efficacy evaluations are feasible and includes evaluations of novel investigational product delivery systems and evaluations of current vaccines or therapeutics with new formulations, schedules or routes of delivery. Candidate vaccines and therapeutics to be evaluated by the Contractor will be provided by or through the NIAID.

Scope of Study Populations: Vaccine and therapeutic products shall be evaluated by the Contractor, as appropriate, in general populations, including pediatric, adult and elderly subjects. In order to accommodate urgent and compelling needs and opportunities as determined by the Government, the Contractor may be required to access additional populations such as women of reproductive age, pregnant women, immunocompromised populations, non-U.S. populations, and populations with underlying medical conditions.

TECHNICAL REQUIREMENTS

Independently, and not as an agent of the Government, the Contractor shall furnish all the necessary services, qualified personnel, healthy volunteer and patient populations, material, equipment, and facilities, not otherwise provided by the Government, as needed to perform the Statement of Work below:

1. STUDY POPULATIONS AND ENROLLMENT REQUIREMENTS

a. General Population

- 1) Provide subjects from pediatric, adult and elderly populations, utilizing subcontracts with affiliated clinical sites as necessary. This shall include the recruitment and enrollment in clinical trials and studies of the following minimum number of eligible healthy subjects on an annual basis:
 - 300 pediatric subjects (birth-18 years of age),
 - 1,200 adult subjects (>18-45 years of age), and
 - 300 mature adult and elderly subjects (>45 years of age and up).
- 2) Provide for the rapid expansion of enrollment of appropriate subjects to accommodate enrollment targets. Rapid expansion shall be accommodated directly by the Contractor and may include subcontracts with affiliated clinical sites to meet necessary target enrollment.

b. Additional Populations

Access, either directly or through subcontracts with affiliated clinical sites, additional study populations, including women of reproductive age, pregnant women, immunocompromised populations, non-U.S. populations, and populations with underlying medical conditions, to accommodate urgent and compelling needs and opportunities, as determined by the Government.

2. AFFILIATED CLINICAL SITES (SUBCONTRACTORS)

- a. Solicit for, evaluate, award and manage subcontracts to provide for VTEU-affiliated clinical sites when necessary and appropriate to meet the requirements of the contract. All such subcontracts shall be approved in writing prior to protocol implementation by the Contracting Officer based on review and recommendation from the Project Officer.
- b. Affiliated clinical sites may be used for one or more of a variety of purposes in order to carry out the requirements of the contract, including providing access to and ensuring enrollment of adequate numbers of study participants in the following areas:
 - 1) Phase 1, Phase 2, Phase 3 and Phase 4 clinical trials involving general populations (i.e., pediatric, adult and elderly subjects).
 - 2) Clinical trials and studies requiring rapid expansion of enrollment.

- 3) Clinical trials and studies involving additional populations, including, women of child bearing age, pregnant women, immunocompromised populations, non-U.S. populations, and populations with underlying medical conditions.
 - 4) Clinical trials and studies determined by the Government to be necessary and important to meet urgent and compelling needs and opportunities.
- c. Ensure that all affiliated clinical sites provide the following personnel, facilities and services as necessary:
- 1) Qualified clinical investigators, nurse managers, study coordinators, data managers and data entry personnel, research pharmacy personnel, and other clinical research support staff, including staff with experience and expertise in clinical trials and studies of candidate vaccines and therapeutics for infectious diseases, including experience in complying with Good Clinical Practice (GCP) guidelines and other regulatory requirements governing the safe conduct of research involving human subjects, and experience in the screening, recruitment and retention of study participants.
 - 2) Access to necessary study populations, including both general populations and additional populations as defined in the Statement of Work.
 - 3) Clinical facilities for the screening, enrollment, treatment and follow-up of study participants.
 - 4) Research laboratory facilities, equipment and personnel for the conduct of protocol-specific laboratory tests, including cultures and/or immunologic assays. (humoral and cellular) to determine participant eligibility, baseline levels upon study entry, and response to candidate vaccines being evaluated, and for the processing and storage of clinical specimens.
 - 5) Clinical laboratory facilities/services, clinical facilities and general pharmacy services.

3. **PROTOCOL DEVELOPMENT**

a. Concept Proposal

- 1) Develop a Concept Proposal with a corresponding budget estimate for each proposed clinical study and sub-study as the initial step in the protocol development process. The development and submission of Concept Proposals and corresponding budgets shall be either at the request of the Project Officer or at the initiation of the Contractor's Principal Investigator.
- 2) All Concept Proposals shall be submitted to the Project Officer for review and determination of DMID interest in supporting the study under this contract..
- 3) All Concept Proposals require written approval by the Project Officer and the Contracting Officer prior to initiation of protocol development.

4) The Concept Proposal shall include:

a) Study Objective(s)

- indication(s) of the investigational product and stage of development,
- study population(s),
- a brief overview of the proposed study design, including estimated sample size, primary and secondary endpoints, and product information, including available risk information, and
- the stage of development of the proposed assays to be used to support the primary and secondary endpoints.

b) Rationale for the Proposed Clinical Trial or Study

- a brief description of the scientific and public health significance of the proposed study and supporting references.

c) Recruitment and Site Plan

- identification of proposed clinical site(s),
- target enrollment for each proposed clinical site including documentation of access to study populations,
- a plan for the recruitment and retention of eligible study participants, and
- a description of the capacity of the proposed clinical site(s) to undertake and complete the study successfully.

d) Protocol Timeline

A timeline and specific milestones for protocol development and initiation, including:

- completion of screening and enrollment of study participants,
- completion of the clinical trial or study, and
- analysis of study data.

e) Personnel and Percentage of Effort

A list of all personnel who will be assigned to the clinical trial or study, including:

- percentage of effort for each,
- a description of prior experience and expertise of the personnel specific to the proposed clinical trial or study, and
- prior experience with studies of a similar type, size and complexity.

f) Proposed Budget

1) A breakdown of proposed study-specific personnel by:

- function,
- position title, and
- level of effort

2) Total estimated costs for:

- supplies,
- clinical and research laboratory,
- research pharmacy,
- study participant expenses,
- study participant incentives,
- travel
- advertising costs only as they relate to recruitment from existing patient population databases
- miscellaneous costs, and
- costs for any proposed subcontracts.

b. Protocol Development

1) Protocol Development Processes and Templates

In developing protocols for clinical trials and studies to be conducted, adhere to DMID standardized protocol development processes and templates (<http://www.niaid.nih.gov/dmid/clinresearch/#resources>). Only those Concept Proposals approved for implementation by the Project Officer shall proceed to the protocol development stage. The processes and requirements delineated below shall be implemented by the Contractor during the protocol development stage. All final clinical protocols require approval by the Project Officer in order to proceed to the protocol implementation stage.

2) Protocol Team

Each protocol shall be developed by a Protocol Team, coordinated by the DMID Protocol Champion (e.g., DMID Program scientist with expertise in the area of protocol focus) and consisting of:

- the Principal Investigator;
- clinical investigators from the VTEU and any affiliated clinical sites;
- industry collaborators, when appropriate;
- DMID scientific, clinical and regulatory personnel; and
- statistical, data management, medical writing, pharmacovigilance and other personnel supplied by the DMID clinical research support services contractors.

3) Draft and Final Protocol

- a) Develop the Draft Protocol for Project Officer review, with assistance from the Protocol Team, and make any necessary revisions based on Project Officer comments. The protocol shall be considered final only upon receipt of written approval from the Project Officer.
- b) Following approval of the Final Protocol, the Case Report Forms and Manual of Operations shall be developed by either the Contractor, the DMID Data Coordinating Center, or other collaborators at the direction of the Project Officer. The Case Report Forms and Manual of Operations shall be provided by DMID to the Contractor.

4) Protocol Timeline

- a) If necessary, revise the Protocol Timeline provided in the Concept Proposal (see paragraph 4)d),above under Section 3. PROTOCOL DEVELOPMENT) to accommodate any changes with respect to protocol implementation, study completion and analysis and publication of study results, including the rationale for the proposed changes.
- b) All such modifications to the Protocol Timeline shall be subject to approval by the Project Officer prior to study implementation.

4. **PROTOCOL IMPLEMENTATION**

a. Pre-Study Initiation Requirements

Prior to study initiation, the Contractor is required to satisfy the following requirements:

1) Human Subjects Requirements

Obtain and provide to the Project Officer documentation of local Institutional Review Board (IRB) approval to conduct the clinical trial or study for all participating clinical sites;

2) Regulatory Requirements

Provide, for Project Officer approval, Essential Documentation, as defined by the International Conference on Harmonization ICH-E6-GCP, (<http://www.fda.gov/cder/guidance/959fnl.pdf>);

3) Study Initiation Meetings/Teleconferences

The Principal Investigator, clinical investigators and clinical study personnel who will be performing the clinical trial or study from both the VTEU and any affiliated clinical sites, shall participate in a study initiation meeting and/or teleconference to be organized by the CTM contractor. These meetings and/or teleconferences shall serve to review protocol specifications, requirements and procedures, target enrollment per clinical site, and protocol timelines.

b. Study Product Requirements

As requested by the Project Officer, provide documentation that all participating clinical sites have received the appropriate supply of the investigational product from the DMID repository or other entity. This shall encompass investigational product accountability, including:

- accurate records documenting receipt of test article;
- date and amount of test article dispensed to each subject;
- amount of test article used and verified during a monthly physical inventory;
- date and quantity of test article returned to DMID repository, if applicable;
- preservation and validation of cold chain for investigational and licensed products including records to verify cold chain for all materials stored at other than room temperature;
- packaging and labeling of test article in compliance with applicable labeling regulations;
- transport of investigational products to clinical area; and
- return of unused product to the DMID repository or other entity.

c. Interactions with Food and Drug Administration (FDA)

The Principal Investigator shall be available for up to six (6) teleconferences and one (1) meeting with the FDA to discuss protocols, preclinical and clinical packages, studies, and/or data resulting from studies as needed.

d. Clinical Trial Conduct

Conduct clinical trials and studies in accordance with all Federal regulations and requirements, NIAID Clinical Terms of Award (<http://www.niaid.nih.gov/ncn/pdf/clinterm.pdf>), the ICH-E6-GCP guidelines (<http://www.fda.gov/cder/guidance/959fnl.pdf>), the clinical protocol and the Manual of Operations or standard operating procedures.

e. Protocol Amendments and Other Clinical Trial Modifications

- 1) Recommend to the Project Officer amendments to the clinical protocol, the Manual of Operations and the informed consent documents, including a written description of the proposed amendments/modifications and their rationale.
- 2) All amendments and modifications shall require approval by the Project Officer prior to implementation.
- 3) Obtain and provide documentation of IRB approval for protocol amendments for the Contractor and all affiliated clinical sites prior to implementation.

f. Data Management and Quality Control

- 1) Develop and implement standards and procedures for the entry and quality control of study data for all clinical trials and studies conducted under the contract, including those conducted at any affiliated clinical site.
- 2) Ensure that clinical data are accurate, complete and entered in a timely fashion.
- 3) The Contractor and all affiliated clinical sites shall transfer study data to the data management system, operated by the DMID Data Coordinating Center contractor, within seventy-two (72) hours of study activity to maintain up-to-date information of all clinical and laboratory data.
- 4) Training in the use of the data management system for clinical site personnel will be provided by the DMID Data Coordinating Center contractor prior to study implementation.
- 5) Perform data management activities in collaboration with the DMID Data Coordinating Center contractor or the data coordinating center of an industry collaborator.
- 6) Manage data and address queries in accordance with DMID source document guidelines in collaboration with the DMID Data Coordinating Center contractor (www.niaid.nih.gov/dmid/clinresearch/sourcedocumentationstandards.pdf), or the data management center of an industry collaborator.
- 7) Upon approval of the Project Officer, provide clinical study data to the Investigational New Drug (IND) sponsor for use in the Annual IND Report to the FDA. This data shall also be used in the Final Clinical Study Report prepared by DMID which shall follow the International Conference on Harmonization (ICH) Guidelines on Structure and Content of Clinical Study Reports E3 to be submitted to the FDA by DMID within one (1) year of closure of activity on study (link for annual report: <http://a257.g.akamaitech.net/7/257/2422/01apr20051500/edocket.access.gpo.gov/cfr/2005/aprqr/21cfr312.23.htm> and link for final report: <http://a257.g.akamaitech.net/7/257/2422/01apr20051500/edocket.access.gpo.gov/cfr/2005/aprqr/21cfr312.64.htm>).

g. Study Analysis

The Principal Investigator shall collaborate and coordinate with the DMID Protocol Team and DMID Data Coordinating Center contractor or the data management center of an industry collaborator in the analysis of final study data including submission, receipt, collation and interpretation of study data.

5. **PROTOCOL OVERSIGHT**

- a. Oversee the safety of all clinical trials and studies conducted, including those conducted at affiliated clinical sites. Oversee adherence to all Federal regulations and to the DMID, NIAID, NIH policies and guidelines, including the NIAID Clinical Terms of Award governing research involving human subjects (<http://www.niaid.nih.gov/dmid/clinresearch>).
- b. The specific protocol safety oversight responsibilities of the Principal Investigator include coordination of oversight functions in collaboration with the existing DMID Clinical Trials Management (CTM) contractor and with the Safety Oversight Structure, as delineated below.

1) Safety Oversight Structure

- a) For each clinical trial and study, DMID will establish a Safety Oversight Structure, independent of the Principal Investigator and coordinated by the CTM contractor. All Safety Oversight Structures shall operate in a manner consistent with DMID Safety Oversight Guidances (<http://www.niaid.nih.gov/dmid/clinresearch>). The Contractor shall be responsible for presenting the study and study data to the Safety Oversight Structure.
- b) The Safety Oversight Structure will accommodate the risk and complexity of the clinical trial or study. For clinical trials and other trials for which the risks and complexities justify it, the Safety Oversight Structure shall be a Data and Safety Monitoring Board (DSMB); for most Phase 1 and Phase 2 clinical trials, the Safety Oversight Structure shall be a Safety Monitoring Committee (SMC). In all cases, the DSMB or the SMC shall be established by DMID and coordinated by the CTM contractor. Some small early phase studies of low risk may be overseen by an Independent Safety Monitor and designated back-up monitor.
- c) The Independent Safety Monitor and back-up monitor shall be identified by the Contractor for all affiliated clinical sites and must be approved by the Project Officer.
- d) At the Project Officer's request, nominate individuals to serve on Safety Oversight Structures, and all such nominations shall require approval by the Project Officer based on DMID Safety Oversight Guidances.
- e) Collaborate with the Data Coordinating Center contractor or industry data coordinating center to provide both interim and final analyses when appropriate.

2) Clinical Site Monitoring

- a) Accommodate clinical site monitoring/auditing, at the request of the Project Officer, to verify that the rights and well-being of the study participants are protected, the study data are accurate, complete and verifiable, and the conduct of the study is in compliance with Good Clinical Practices (GCP), the clinical protocol and applicable regulatory requirements.
- b) Make available for clinical site monitoring purposes, all necessary facilities, personnel and records to support monitoring requirements during the active recruitment, dosing, follow-up and close-out phases of all clinical trials and studies.
- c) When NIAID is the IND sponsor, clinical site monitoring for all clinical trials and studies conducted by the Contractor and affiliated clinical sites shall be carried out by the CTM contractor. In those limited cases when DMID is not the IND sponsor, appropriate monitoring staff designated by the IND sponsor shall carry out this function.
- d) The Principal Investigator shall be responsible for developing and implementing remedial actions to address site performance problems and issues identified through the clinical site monitoring process.

3) System of Records

Design, implement and maintain a system of records for each clinical trial and study undertaken. This system of records shall be in accordance with the Privacy Act and the Confidentiality of Information Clauses contained within the contract.

6. ADDITIONAL EVALUATIONS AND ANALYSES

- a. Design and conduct additional evaluations and analyses. Such additional studies may be requested by the Project Officer or proposed by the Contractor. These include:
 - pharmacogenomic studies;
 - targeted surveillance for pathogens of interest in study populations as background information in the context of protocol development;
 - evaluations of novel investigational product delivery systems; and
 - evaluations of current vaccine formulations, schedules and modes of delivery.
- b. For each of these additional evaluations and analyses, develop and submit, for Project Officer approval, a proposed plan covering the following:
 - 1) a description of the scope and design of the proposed research;
 - 2) the rationale for the additional work based on need, opportunity and public health importance;
 - 3) a description of potential risks and problems and proposed approaches to reducing risk and overcoming problems;

- 4) a timeline for study implementation, reporting of interim data, study completion and analysis of final study data;
 - 5) any proposed affiliated clinical sites and personnel and a brief description of the qualifications and experience of all proposed personnel;
 - 6) a proposed budget to include a breakdown of proposed study specific personnel by:
 - function,
 - position title,
 - level of effort proposed for the study;
 - 7) total estimated costs for:
 - supplies,
 - clinical and research laboratory,
 - research pharmacy,
 - participant expenses,
 - participant incentives,
 - travel,
 - advertising costs only as they relate to recruitment from existing patient population databases, and
 - miscellaneous costs.
- c. Upon written approval by the Project Officer and the Contracting Officer, conduct evaluations/analyses in accordance with the approved plan.

7. STORAGE, SHIPPING AND TRACKING OF CLINICAL SAMPLES

- a. Ship clinical specimens for further testing to laboratories or repositories designated by the Project Officer.
- b. Ensure that blood and other body fluids and tissue samples are classified, labeled, documented, packaged, shipped, and tracked according to Federal regulations and the International Air Transport Association (IATA) requirements for the shipment of dangerous goods (<http://www.iata.org/ps/publications/9065.htm>).
- c. Samples shall be shipped under temperature monitored conditions and within the time frame specified in the clinical protocols or other documents.
- d. Confirm receipt of specimens in the appropriate condition for further testing by the DMID-designated laboratory or repository to which the specimens are shipped.

8. QUALITY ASSURANCE/QUALITY CONTROL (QA/QC)

- a. Quality Assurance/Quality Control Plan
 - 1) Develop and implement a Quality Assurance/Quality Control plan to standardize contract research processes to ensure that the conduct of any clinical trial and all data generated meet all regulatory standards and other standards (see http://www.niaid.nih.gov/dmid/clinresearch/OP_QM001Rev0.pdf for guidance). This plan shall include standard operating procedures for establishing and maintaining the QA/QC process. It shall also include a description of the process for internal quality

audits of site protocols and a description of remediation procedures for addressing issues when identified.

- 2) Submit a draft of this plan within ninety (90) calendar days of contract award.
- 3) The Project Officer will provide comments to the Contractor within two (2) weeks of receipt of the draft plan.
- 4) Submit a final plan that incorporates the Project Officer's comments within two (2) weeks after comments are received.

b. Independent Audits

- 1) Arrange for independent audits, as needed or as requested by the Project Officer with concurrence by the Contracting Officer. Audits may be requested to assure that Contractor and/or affiliated clinical site facilities and all planned procedures meet FDA regulations and guidance for GCP standards.
- 2) Ensure that all Contractor and/or affiliated clinical site records and staff are available for independent audits.
- 3) Provide interim and final audit reports to the Project Officer and the Contracting Officer within thirty (30) calendar days after audit completion.

9. **SCIENTIFIC AND TECHNICAL PERSONNEL**

a. Principal Investigator

- 1) The Contractor's Principal Investigator shall be licensed as a physician and shall ensure that active licensure is maintained for the entire period of contract performance.
- 2) The Principal Investigator shall possess experience in the design and conduct of clinical trials and studies for infectious diseases.

b. Other Scientific/Technical Personnel

- 1) Provide and maintain appropriately trained personnel to carry out the clinical research requirements of the contract. This shall include:
 - a) Physician investigators as required per protocol. Physician investigators conducting clinical trials shall be licensed physicians and shall ensure that active licensure is maintained for the entire period of contract performance. In addition, all such protocol-specific physician investigators shall be experienced in the design and conduct of studies of infectious diseases and in the assessment of participants for study eligibility and safety post enrollment.
 - b) Clinical Research Study Staff as required per protocol, including: nurse managers, study coordinators, clinical support staff, laboratory personnel, personnel with regulatory expertise, and data managers. All clinical research study staff shall be trained and experienced in Good Clinical Practices.

- c) A Research Pharmacist proficient in all aspects of investigational product management as needed to meet the requirements of each protocol.
- d) Collaborating clinical investigators in other medical specialties when necessary to meet protocol-specific requirements.
- e) Qualified personnel necessary to package, label, and transport under appropriate conditions clinical specimens to DMID-designated laboratories or DMID-supported repositories in cases where laboratory tests are not to be performed at the Contractor's facility.
- f) Qualified personnel, such as microbiologists with specialized expertise, necessary for the processing of investigational products in accordance with protocol-specific requirements.
- g) Qualified personnel necessary to meet emerging, high priority public health needs.
- h) Protocol-related training opportunities for designated scientists to learn techniques and methods relevant to the conduct of studies or clinical trials under this contract.

10. CLINICAL RESEARCH FACILITIES AND RESOURCES

a. Outpatient Clinical Research Facilities

The Contractor, as well as all affiliated clinical sites participating as subcontractors, shall provide outpatient clinical facilities to accommodate enrollment, administration of investigational products, and follow-up of subjects in accordance with the specific requirements of the clinical protocols approved for implementation. These facilities shall include the following:

- 1) Areas which allow for temporary subject waiting, check-in and discharge.
- 2) Examination rooms which allow for full physical examinations and privacy for discussions with subjects, including counseling, obtaining medical histories and informed consent, and administration of investigational products.
- 3) Outpatient laboratory facilities for the collection, processing and temporary storage of clinical specimens.
- 4) Computers with broadband secure internet access for randomization, remote data entry and transmission of digitalized test results including electrocardiograms and other diagnostic test results and digital photographs.
- 5) Emergency care and accommodations in the event a study subject requires such services.

b. Inpatient Clinical Research Facilities

Provide inpatient facilities for the implementation of protocols requiring inpatient care, utilizing affiliated clinical sites as necessary. These inpatient clinical research facilities shall meet the requirements of the Joint Commission on Accreditation of Healthcare Organizations (www.jcaho.org). Facilities shall include:

- 1) Clinical research facilities to accommodate overnight clinical care of subjects as specified in protocols approved for implementation.
- 2) Availability of standard clinical support services for inpatient care, twenty four (24) hours/day, seven (7) days/week, to include nursing, emergency, respiratory, dietary, laboratory, radiology and laundry services for active inpatient protocols.
- 3) Computers with broadband secure internet access for randomization, remote data entry and transmission of digitalized test results including electrocardiograms and other diagnostic test results and digital photographs.
- 4) Emergency care and accommodations in the event a study subject requires such services.

c. Clinical Laboratory Facilities

Provide the following clinical laboratory facilities and services, utilizing affiliated clinical sites as necessary:

- 1) Process and store clinical specimens and conduct protocol-required tests to determine participant eligibility and safety evaluations.
- 2) Qualified personnel and other resources necessary to maintain current Clinical Laboratory Improvement Amendment certification (www.cms.hhs.gov/clia) and Joint Commission on Accreditation of Healthcare Organizations approval (www.jcaho.org).
- 3) Clinical laboratory support services which are available twenty four (24) hours/day, seven (7) days/week.
- 4) Prepare and submit a Semiannual Laboratory Report that includes all laboratory work performed to support clinical protocols, laboratory work performed at the request of the Project Officer and a discussion of technical and administrative problems encountered, their resolutions or proposed corrective action, and an explanation of differences between planned and actual progress.

d. Research Laboratory Facilities

Provide research laboratory facilities and resources as follows, utilizing affiliated clinical sites as necessary:

- 1) Process and store specimens and conduct protocol relevant cultures and/or immunologic assays (humoral and cellular) to determine participant eligibility, baseline levels on entry into a study, and response to the candidate vaccines.
- 2) Ensure that work conforms to standards acceptable for IND and/or Biological Licensing Application (BLA) submission (see <http://www.niaid.nih.gov/dmid/clinresearch/#resources> for guidance).
- 3) Prepare and submit a Semiannual Laboratory Report that includes all laboratory work performed to support clinical protocols, laboratory work performed at the request of the Project Officer and a discussion of technical and administrative problems encountered, their resolutions or proposed corrective action, and an explanation of differences between planned and actual progress.

e. Research Pharmacy Facilities

The Contractor, as well as all affiliated clinical sites, shall provide research pharmacy facilities and resources for the management of investigational products according to protocol-specific requirements. This includes:

- 1) The development and implementation of Standard Operating Procedures (SOPs) for research pharmacy functions.
- 2) The development and implementation of appropriate procedures and policies to provide for, store appropriately, and monitor controlled access to investigational products.
- 3) The receipt of investigational products from the DMID Regulatory Support contractor repository or other supplier, and the returning of investigational products to this repository or disposing of investigational products as specified in the protocol or Manual of Operations

f. General Clinical Research Facilities

The Contractor and all affiliated clinical sites shall provide general clinical research facilities and other resources for the conduct of clinical trials and studies approved for implementation. This includes:

- 1) Non-clinical space for contract management, data management and study coordination.
- 2) Computers with broadband secure internet access.
- 3) Dedicated space for clinical site monitoring staff to include access to site computers with broadband secure internet access and access to regulatory and subject records.
- 4) Areas for secure storage of confidential study documents with controlled access.

11. PROJECT MANAGEMENT

a. Overall Project Management

- 1) Provide for the overall management, integration and coordination of all contract activities, including the management and coordination of activities carried out under subcontracts.
- 2) Provide a technical and administrative infrastructure to ensure the planning, initiation, implementation, management and timely completion of all projects carried out under this contract and effective communications with the Project Officer and the Contracting Officer.
- 3) Include a Principal Investigator with responsibility for overall project management and communications, tracking, monitoring and reporting on project status and progress, and recommending modifications to project requirements and timelines, including projects undertaken by subcontractors.
- 4) Include personnel to coordinate contract and study specific activities conducted and administrative staff with responsibility for financial management and financial reporting on all activities conducted by the Contractor and subcontractors.

b. Affiliated Clinical Site Subcontract Management and Reporting

The Contractor shall carry out the following for each project to be conducted under a subcontract:

- 1) Solicit, evaluate, award and manage subcontracts, including overseeing the technical, administrative and operational activities of subcontractors; auditing subcontractor facilities, services, and financial expenditures; and tracking deliverables and reporting requirements.
- 2) Assess and provide quarterly technical reports on subcontractor performance and progress toward achievement of defined milestones; and identify and resolve problems with subcontractor performance.
- 3) Ensure that subcontractor personnel, equipment and facilities are compliant with regulatory requirements in effect throughout the contract period.
- 4) Ensure the complete and effective transfer of technology by the subcontractors to the Contractor, the United States Government, or a third party as designated by the Project Officer.
- 5) Perform all necessary transition and closeout functions on each subcontract as specified in each protocol.

c. Coordination with DMID Clinical Research Support Services Contracts

Ensure the effective and efficient coordination of specified functions in collaboration with the DMID clinical research support services contractors identified in the Statement of Work. These functions include:

- clinical site monitoring;
- clinical trial/study statistical design and analysis;
- preparation of case report forms;
- data collection, management, quality assurance and entry;
- safety monitoring;
- auditing; and
- clinical agent repository functions for distribution and tracking of IND products.

d. Technology Transfer

- 1) The Contractor and any subcontractor(s) may be required to transfer assays or other techniques developed or improved under the contract to specified DMID/NIAID contracts. These contract-generated resources shall include complete protocols and critical reagents for products developed and/or improved with contract funding and must be submitted at the request of the Project Officer.
- 2) The Contractor shall also have the capability to transfer in assays or other technologies needed to support clinical trials.

e. Meetings

1) Contract Initiation Meeting

Within three (3) months of contract award, participate in a one-day contract initiation meeting with the Project Officer, the Contracting Officer, other key NIAID staff and key contract scientific, technical and administrative personnel, to be held in Bethesda, Maryland. The purpose of this initiation meeting is to orient the Contractor to NIAID contract procedures.

2) Annual VTEU Meetings

Key personnel shall participate in one (1) meeting per year for two (2) days, to be held in the Bethesda, Maryland area.

The purpose of this meeting is to:

- organize, facilitate and plan clinical trial and study coordination;
- address regulatory issues related to clinical trials and studies proposed and approved for implementation.

review:

- status of ongoing clinical trials and studies,
- risks and obstacles,
- proposed approaches to reducing risk and overcoming obstacles, and
- interim and final clinical trial/study results.

3) Annual Site Visits

- a) Host an annual site visit for NIAID contract and program staff. These site visits shall be attended by the Principal Investigator, the Contractor's business representative, all key personnel and investigators and coordinators of active projects from the previous twelve months, including affiliated clinical site key personnel.
- b) The Contractor shall be responsible for:
 - agenda planning,
 - development of written and oral presentation materials, and
 - logistical arrangements for all non-Government site visit participants.
- c) Presentations and discussions shall focus on:
 - summaries of all goals and milestones reached during the review period;
 - all problems encountered that impact the completion of approved clinical trials and studies;
 - the submission of contract deliverables;
 - proposed modifications to established milestones and timelines; and
 - the rationale for proposed future plans for effectively and efficiently carrying out the requirements of the contract.
- d) A report of each annual site visit shall be prepared by the Contractor and submitted to the Project Officer and the Contracting Officer within thirty (30) calendar days of completion of each site visit.

4) Protocol Specific Meetings

Participate in study initiation meetings, Protocol Team meetings, scientific planning meetings, as needed. These meetings may be conducted in person at the Contractor's site or another designated site, web-based or via teleconference.

f. Publications and Presentations of Contract-Generated Data and Findings

- 1) Develop and implement policies and procedures for authorship, preparation, review, and final approval of publications, abstracts and oral presentations resulting from contract-sponsored studies, and for submission of manuscripts for publication in peer reviewed journals. During the publication review and approval process, the respective roles and responsibilities of pharmaceutical/biotechnology companies providing experimental products for evaluation in clinical trials and studies shall be addressed in specific Clinical Trial Agreements (CTA) between DMID and the company.

- 2) The Contractor shall not publish, present or disseminate any information from work performed under this contract without submission of the materials to the Project Officer for review.
- 3) The Project Officer shall have seven (7) calendar days from receipt of materials to review and provide comments on an abstract and thirty (30) calendar days from receipt of materials to review and provide comments on other publications and presentations. If the Project Officer does not respond within these time frames, the Contractor may proceed with such publications or presentations.

12. TRANSITION

a. Transition Plan

Three (3) months prior to the completion date of this contract, the Contractor shall provide a plan for an orderly transition of data and materials, including stored participant specimens and records, to the Government. This plan will be subject to the approval of the Project Officer and the Contracting Officer.

b. Transition of Data and Materials

On or before the completion date of the contract, the Contractor shall deliver data and materials, including participant specimens and records, to locations specified by the Project Officer and in accordance with the approved transition plan.