U.S. Department of Health and Human Services
National Institutes of Health
National Institute of Allergy and Infectious Diseases (NIAID)

RFP-NIH-NIAID-DMID-07-05
"DEVELOPMENT OF A THIRD GENERATION ANTHRAX VACCINE"

OMB Control Number 0990-0115

1. **OFFERORS ARE RESPONSIBLE FOR ROUTINELY CHECKING THE FOLLOWING WEBSITE FOR ANY SOLICITATION AMENDMENTS. NO ADDITIONAL NOTIFICATION OF ANY AMENDMENTS WILL BE PROVIDED BY THIS OFFICE.** http://www.fedbizopps.gov/

2. **SECTION A – SOLICITATION/CONTRACT FORM -- PURCHASE AUTHORITY: FAR 1.602-1**
NOTE: The issuance of this solicitation does not commit the government to an award.

3. **Issue Date:** June 22, 2006	4. **Due Date:** September 18, 2006 **Time:** 4:00 PM, Local Time	5. **Small Bus. Set-Aside:** [ ]Yes [x] No **8(a) Set-Aside:** [ ]Yes [x] No **NAICS: 541710** (See Part IV, Section L.)

6. **Just In Time:** [x] No [ ] Yes (See Part IV, Section L.)	7. **Number of Awards:** [ ] Only 1 Award [X] Multiple Awards	8. **Technical Proposal Page Limits:** [ ] No [x] Yes **200 Pages** **See Attachment 1, Packaging and Delivery of Proposal**

9. **Issued By:** Ross Kelley Contracting Officer Office of Acquisitions, DEA, NIH, NIAID 6700-B Rockledge Drive Room 3214, MSC 7612 Bethesda, MD 20892-7612	10. [x] **NIAID reserves the right to make awards without discussion.** 11. **Options:** **[ ] No** **[X] Yes** (See Part IV, Section L.)	12. **Period of Performance:** **June 8, 2007 through June 7, 2014**

13. **Primary Point of Contact:** **Name :** Ross Kelley **Phone:** 301- 402-2234 **Fax:** 301-480-4675 **E-Mail:** RKelley@niaid.nih.gov	14. **Secondary Point of Contact:** **Name:** Barbara A. Shadrick **Phone:** 301-496-7288 **Fax:** 301-402-0972 **E-Mail:** bs92y@nih.gov	15. **Protest Officer:** Director, OA Address (see Block 9.)

16. **COLLECT CALLS WILL NOT BE ACCEPTED. FACSIMILE SUBMISSIONS ARE NOT ACCEPTABLE.**

17. Offers will be valid for 120 days unless a different period is specified by the Offeror on the form entitled "Proposal Summary and Data Record, NIH-2043" (See Part III, SECTION J – Attachments)

18. **DELIVERY ADDRESS INFORMATION**

19. **Hand Delivery or Overnight Service:** Ross Kelley Contracting Officer Office of Acquisitions DEA, NIH, NIAID 6700-B Rockledge Drive, Room 3214 Bethesda, MD 20817	20. **U.S. Postal Service or an Express Delivery Service** Ross Kelley Contracting Officer Office of Acquisitions DEA, NIH, NIAID 6700-B Rockledge Drive, Room 3214, MSC 7612 Bethesda, MD 20892-7612

21. The **Official Point of Receipt** for the purpose of determining timely delivery is the address provided in Block 19, above. The original paper copy with original signatures is the official copy for recording timely receipt. If the original paper copy of your proposal is not received by the Contracting Officer or Designee at the place and time specified, then it will be considered late and handled in accordance with FAR 15.208 entitled " Submission, Modification, Revision, and Withdrawal of Proposals." FACSIMILE OR E-MAIL SUBMISSION OF PROPOSALS IS NOT ACCEPTABLE.

DETAILED TABLE OF RFP CONTENTS

PART I - THE SCHEDULE

THE CONTRACT SCHEDULE SET FORTH IN SECTIONS B THROUGH H, HEREIN, CONTAINS CONTRACTUAL INFORMATION PERTINENT TO THIS SOLICITATION. IT IS **NOT** AN EXACT REPRESENTATION OF THE PROPOSED CONTRACT DOCUMENT. CONTRACTUAL PROVISIONS PERTINENT TO THE OFFEROR (I.E., THOSE RELATING TO THE ORGANIZATIONAL STRUCTURE [E.G., NON-PROFIT, COMMERCIAL] AND SPECIFIC COST AUTHORIZATIONS UNIQUE TO THE OFFEROR'S PROPOSAL AND REQUIRING CONTRACTING OFFICER PRIOR APPROVAL) WILL BE DISCUSSED IN THE NEGOTIATION PROCESS AND WILL BE INCLUDED IN THE RESULTANT CONTRACT. HOWEVER, THE ENCLOSED CONTRACT SCHEDULE PROVIDES ALL THE NECESSARY INFORMATION FOR THE OFFEROR TO UNDERSTAND THE TERMS AND CONDITIONS OF THE RESULTANT CONTRACT.

SECTION B - SUPPLIES OR SERVICES AND PRICES/COSTS

ARTICLE B.1. BRIEF DESCRIPTION OF SUPPLIES OR SERVICES

The contract will develop and test third generation anthrax vaccine candidates which build upon the second generation vaccine and have properties desirable for a biodefense vaccine to be stored in the Strategic National Stockpile (SNS).These properties include long-term stability at room temperature, the ability to generate a protective immune response in one or two doses, and the ability to be safely self-administered and or rapidly inoculated into large numbers of people.

ARTICLE B.2. ESTIMATED COST AND FIXED FEE

a. The estimated cost of the BASE PERIOD of this contract is $_____.

b. The fixed fee for the BASE PERIOD of this contract is $____. The fixed fee shall be paid in installments based on the percentage of completion of work, as determined by the Contracting Officer. Payment shall be subject to the withholding provisions of the clauses ALLOWABLE COST AND PAYMENT and FIXED FEE referenced in the General Clause Listing in Part II, ARTICLE I.1. of this contract. Payment of fixed fee shall not be made in less than monthly increments.

c. The Government's obligation, represented by the sum of the estimated cost plus the fixed fee for the BASE PERIOD is $_____.

d. If the Government exercises its option pursuant to ARTICLE H. . of this contract, the Government's total obligation represented by the sum of the estimated cost plus the fixed fee will be increased as follows:

	Estimated Cost ($)	**Fixed Fee ($)**	**Estimated Cost Plus Fixed Fee ($)**
Base Period Option Period(s): Total [Base Period and Option(s)]			

e. Total funds currently available for payment and allotted to this contract are $_____ of which $_____ represents the estimated costs, and of which $_____ represents the fixed fee. For further provisions on funding, see the LIMITATION OF FUNDS clause referenced in Part II, ARTICLE I.2. Authorized Substitutions of Clauses.

f. It is estimated that the amount currently allotted will cover performance of the contract through _____ .

g. The Contracting Officer may allot additional funds to the contract without the concurrence of the Contractor.

ARTICLE B. 3. PROVISIONS APPLICABLE TO DIRECT COSTS

This article will prohibit or restrict the use of contract funds, unless otherwise approved by the Contracting Officer. The following is a list of items that may be included in the resultant contract as applicable. 1) Acquisition, by purchase or lease, of any interest in real property; 2) Special rearrangement or alteration of facilities; 3) Purchase or lease of any item of general purpose office furniture or office equipment regardless of dollar value; 4) Travel Costs; 5) Consultant Costs; 6) Subcontract Costs; 7) Patient Care Costs; 8) Accountable Government Property; and 9) Research Funding.

ARTICLE B.4. ADVANCE UNDERSTANDINGS

Specific elements of cost, which normally require prior written approval of the Contracting Officer before incurrence of the cost (e.g., foreign travel, consultant fees, subcontracts) will be included in this Article if the Contracting Officer has granted his/her approval prior to contract award (Additional information is provided in Appendix C of this solicitation)

SECTION C - DESCRIPTION/SPECIFICATIONS/WORK STATEMENT

ARTICLE C.1. STATEMENT OF WORK

Independently and not as an agent 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, dated 6/19/06 , attached hereto and made a part of this Solicitation (See Section J - List of Attachments, Attachment 4).

ARTICLE C.2. REPORTING REQUIREMENTS AND DELIVERABLES

In addition to the required reports set forth elsewhere in this Schedule, the preparation and submission of regularly recurring Technical Progress Reports will be required in any contract resulting from this solicitation. These reports will require descriptive information about the activities undertaken during the reporting period and will require information about planned activities for future reporting periods. Please refer to Section J, Attachment 5, “Reporting Requirements and Deliverables.”

ARTICLE C.3. INVENTION REPORTING REQUIREMENT

All reports and documentation required by FAR CLAUSE 52.227-11 including, but not limited to, the invention disclosure report, the confirmatory license, and the government support certification, shall be directed to the Extramural Inventions and Technology Resources Branch, OPERA, NIH, 6705 Rockledge Drive, Room 1040-A, MSC 7980, Bethesda, Maryland 20892-7980 (Telephone: 301-435-1986). In addition, one copy of an annual utilization report, and a copy of the final invention statement, shall be submitted to the Contracting Officer. The final invention statement (see FAR 27.303(a)(2)(ii)) shall be submitted to the Contracting Officer on the expiration date of the contract.

The annual utilization report shall be submitted in accordance with ARTICLE F.2 . DELIVERIES of this contract. The first annual utilization report shall be due on or before _____. Thereafter, reports shall be due on or before the 30th of the month following the reporting period. The final invention statement (see FAR 27.303(a)(2)(ii)) shall be submitted on the expiration date of the contract to the following address:

Contracting Officer
OA, DEA, National Institutes of Health, NIAID
6700-B Rockledge Drive, Room 3214, MSC 7612
Bethesda, Maryland 20892-7912

If no invention is disclosed or no activity has occurred on a previously disclosed invention during the applicable reporting period, a negative report shall be submitted to the Contracting Officer at the address listed above.

To assist contractors in complying with invention reporting requirements of the clause, the NIH has developed "Interagency Edison," an electronic invention reporting system. Use of Interagency Edison is encouraged as it streamlines the reporting process and greatly reduces paperwork. Access to the system is through a secure interactive Web site to ensure that all information submitted is protected. Interagency Edison and information relating to the capabilities of the system can be obtained from the Web (http://www.iedison.gov), or by contacting the Extramural Inventions and Technology Resources Branch, OPERA, NIH.

SECTION D - PACKAGING, MARKING AND SHIPPING

All deliverables required under this contract shall be packaged, marked and shipped in accordance with Government specifications. At a minimum, all deliverables shall be marked with the contract number and contractor name. The Contractor shall guarantee that all required materials shall be delivered in immediate usable and acceptable condition.

SECTION E - INSPECTION AND ACCEPTANCE

a. The Contracting Officer or the duly authorized representative will perform inspection and acceptance of materials and services to be provided.

b. For the purpose of this SECTION, the Project Officer is the authorized representative of the Contracting Officer.

c. Inspection and acceptance will be performed at the address listed for the Project Officer in Section G, ARTICLE G.1. Acceptance may be presumed unless otherwise indicated in writing by the Contracting Officer or the duly authorized representative within 30 days of receipt.

d. This contract incorporates the following clause by reference, with the same force and effect as if it were given in full text. Upon request, the Contracting Officer will make its full text available. Also, the full text of a clause may be accessed electronically at this address: http://www.arnet.gov/far/.

FAR Clause **52.246-8, Inspection of Research and Development - Cost-Reimbursement** (May 2001).

SECTION F - DELIVERIES OR PERFORMANCE

ARTICLE F.1. PERIOD OF PERFORMANCE

a. The period of performance of this contract shall be from _____ through _____.

b. If the Government exercises its option(s), the period of performance will be increased as listed below:

Option Number	Option Period

ARTICLE F.2. DELIVERIES

Satisfactory performance of the final contract shall be deemed to occur upon performance of the work described in Article C.1. and upon delivery and acceptance by the Contracting Officer, or the duly authorized representative, of the items in Section C, ARTICLE C.2. in accordance with the stated delivery schedule.

The items described in SECTION C, ARTICLE C.2. will be required to be delivered F.o.b. Destination as set forth in FAR Clause 52.247-35, F.o.b. Destination, Within Consignees Premises (April 1984), and in accordance with and by the date(s) specified in SECTION C, ARTICLE C.2.and any specification stated in SECTION D PACKAGING MARKING AND SHIPPING of the contract.

ARTICLE F.3. CLAUSES INCORPORATED BY REFERENCE, FAR 52.252-2 (FEBRUARY 1998)

This contract incorporates the following clause by reference, with the same force and effect as if it were given in full text. Upon request, the Contracting Officer will make its full text available. Also, the full text of a clause may be accessed electronically at this address: http://www.arnet.gov/far/.

FEDERAL ACQUISITION REGULATION (48 CFR CHAPTER 1) CLAUSE:

52.242-15, Stop Work Order (August 1989) with **Alternate I** (April 1984).

SECTION G - CONTRACT ADMINISTRATION DATA

ARTICLE G.1. PROJECT OFFICER

The following Project Officer(s) will represent the Government for the purpose of this contract:

[To be specified prior to award]

The Project Officer is responsible for: (1) monitoring the Contractor's technical progress, including the surveillance and assessment of performance and recommending to the Contracting Officer changes in requirements; (2) interpreting the statement of work and any other technical performance requirements; (3) performing technical evaluation as required; (4) performing technical inspections and acceptances required by this contract; and (5) assisting in the resolution of technical problems encountered during performance.

The Contracting Officer is the only person with authority to act as agent of the Government under this contract. Only the Contracting Officer has authority to: (1) direct or negotiate any changes in the statement of work; (2) modify or extend the period of performance; (3) change the delivery schedule; (4) authorize reimbursement to the Contractor any costs incurred during the performance of this contract; or (5) otherwise change any terms and conditions of this contract.

The Government may unilaterally change its Project Officer designation.

ARTICLE G.2. KEY PERSONNEL

The personnel specified in this contract are considered to be essential to the work to be performed hereunder. Prior to diverting any of the specified individuals to other programs, the Contractor shall notify the Contracting Officer reasonably in advance and shall submit justification (including proposed substitutions) in sufficient detail to permit evaluation of the impact on the program. No diversion shall be made by the Contractor without the written consent of the Contracting Officer; provided, that the Contracting Officer may ratify in writing such diversion and such ratification shall constitute the consent of the Contracting Officer required by this article. The contract may be amended from time to time during the course of the contract to either add or delete personnel, as appropriate.

The following individuals are considered to be essential to the work being performed hereunder:

NAME	TITLE
[To be specified prior to award]	

ARTICLE G.3. INVOICE SUBMISSION/CONTRACT FINANCING REQUEST AND CONTRACT FINANCIAL REPORT

a. Invoice/Financing Request Instructions and Contract Financial Reporting for NIH Cost-Reimbursement Type Contracts NIH(RC)-4 are attached and made part of this contract. The instructions and the following directions for the submission of invoices/financing request must be followed to meet the requirements of a "proper" payment request pursuant to FAR 32.9.

These instructions also provide for the submission of financial and personnel reporting required by HHSAR 342.7002.

(1) Invoices/financing requests shall be submitted as follows:

(a) To be considered a "proper" invoice in accordance with FAR 32.9, Prompt Payment, each invoice shall clearly identify the two contract numbers that appear on the face page of the contract as follows:

Contract No. (This is the 17 digit number that appears in Block 2 of the SF-26, i.e.

HHSN266200700000C.)

ADB Contract No. (This is the 10 digit number that appears in the upper left hand corner of the SF-26, i.e. N01-AI-70000)

(b) An original and two copies to the following designated billing office:

Contracting Officer
National Institutes of Health, NIAID
DEA, Office of Acquisitions
6700-B Rockledge Drive, Room 3214, MSC 7612
BETHESDA, MD 20892-7612

(2) Inquiries regarding payment of invoices should be directed to the designated billing office, 301-496-0612.

b. The Contractor shall include the following certification on every invoice for reimbursable costs incurred with Fiscal Year funds subject to the salary rate limitation provisions as specified in SECTION H of this contract. For billing purposes, certified invoices are required for the billing period during which the applicable Fiscal Year funds were initially charged through the final billing period utilizing the applicable Fiscal Year funds:

"I hereby certify that the salaries charged in this invoice are in compliance with the applicable Public Law Number for the applicable Fiscal Year as stated in SECTION H of the above referenced contract."

ARTICLE G.4. INDIRECT COST RATES

In accordance with Federal Acquisition Regulation (FAR) (48 CFR Chapter 1) Clause 52.216-7(d)(2), "Allowable Cost and Payment" incorporated by reference in this contract in Part II, Section I, the cognizant Contracting Officer representative responsible for negotiating provisional and/or final indirect cost rates is identified as follows:

Director, Division of Financial Advisory Services
Office of Acquisition Management and Policy
National Institutes of Health
6100 Building, Room 6B05
6100 EXECUTIVE BOULEVARD, MSC 7540
BETHESDA, MD 20892-7540

These rates are hereby incorporated without further action of the Contracting Officer.

ARTICLE G.5. GOVERNMENT PROPERTY

If this RFP will result in the acquisition or use of Government Property provided by the contracting agency or if the Contracting Officer authorizes in the preaward negotiation process, the acquisition of property (other than real property), this ARTICLE will include applicable provisions and incorporate the DHHS Publication (OS) 686, entitled, **Contractor's Guide for Control of Government Property**, which can be found at:

http://knownet.hhs.gov/log/AgencyPolicy/HHSLogPolicy/contractorsguide.htm

ARTICLE G.6. POST AWARD EVALUATION OF CONTRACTOR PERFORMANCE

a. Contractor Performance Evaluations

Interim and final evaluations of contractor performance will be prepared on this contract in accordance with FAR 42.15. The final performance evaluation will be prepared at the time of completion of work. In addition to the final evaluation, interim evaluations will be prepared following Year 1 and every other year thereafter (or more frequently as determined by the Contracting Officer) to coincide with the anniversary date of the contract.

Interim and final evaluations will be provided to the Contractor as soon as practicable after completion of the evaluation. The Contractor will be permitted thirty days to review the document and to submit additional information or a rebutting statement. If agreement cannot be reached between the parties, the matter will be referred to an individual one level above the Contracting Officer, whose decision will be final.

Copies of the evaluations, contractor responses, and review comments, if any, will be retained as part of the contract file, and may be used to support future award decisions.

b. Electronic Access to Contractor Performance Evaluations

Contractors that have Internet capability may access evaluations through a secure Web site for review and comment by completing the registration form that can be obtained at the following address:

http://oamp.od.nih.gov/OD/CPS/cps.asp

The registration process requires the contractor to identify an individual that will serve as a primary contact and who will be authorized access to the evaluation for review and comment. In addition, the contractor will be required to identify an alternate contact who will be responsible for notifying the cognizant contracting official in the event the primary contact is unavailable to process the evaluation within the required 30-day time frame.

SECTION H - SPECIAL CONTRACT REQUIREMENTS

ARTICLE H.1. HUMAN SUBJECTS

Research involving human subjects shall not be conducted under this contract until the final protocol has been approved by the Project Officer. Written notice of such approval shall be provided by the Contracting Officer, after the Contractor has provided to the Contracting Officer a properly completed "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263(formerly Optional Form 310), certifying IRB review and approval of the protocol. The human subject certification can be met by submission of the Contractor's self designated form, provided that it contains the information required by the "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263(formerly Optional Form 310).

When research involving Human Subjects will take place at collaborating sites or other performance sites, the Contractor shall obtain, and keep on file, a properly completed "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263(formerly Optional Form 310) certifying IRB review and approval of the research.

ARTICLE H.2. HUMAN MATERIALS (ASSURANCE OF OHRP COMPLIANCE)

The acquisition and supply of all human specimen material (including fetal material) used under this contract shall be obtained by the Contractor in full compliance with applicable State and Local laws and the provisions of the Uniform Anatomical Gift Act in the United States, and no undue inducements, monetary or otherwise, will be offered to any person to influence their donation of human material.

The Contractor shall provide written documentation that all human materials obtained as a result of research involving human subjects conducted under this contract, by collaborating sites, or by subcontractors identified under this contract, were obtained with prior approval by the Office for Human Research Protections (OHRP) of an Assurance to comply with the requirements of 45 CFR 46 to protect human research subjects. This restriction applies to all collaborating sites without OHRP-approved Assurances, whether domestic or foreign, and compliance must be ensured by the Contractor.

Provision by the Contractor to the Contracting Officer of a properly completed "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263(formerly Optional Form 310), certifying IRB review and approval of the protocol from which the human materials were obtained constitutes the written documentation required. The human subject certification can be met by submission of a self

designated form, provided that it contains the information required by the "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263(formerly Optional Form 310).

ARTICLE H.3. REQUIRED EDUCATION IN THE PROTECTION OF HUMAN RESEARCH PARTICIPANTS

NIH policy requires education on the protection of human subject participants for all investigators receiving NIH contract awards for research involving human subjects. For a complete description of the NIH Policy announcement on required education in the protection of human subject participants, the contractor should access the NIH Guide for Grants and Contracts Announcement dated June 5, 2000 at the following website:

http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html.

The information below is a summary of the NIH Policy Announcement:

The contractor shall maintain the following information: (1) a list of the names and titles of the principal investigator and any other individuals working under the contract who are responsible for the design and/or conduct of the research; (2) the title of the education program(s) in the protection of human subjects that has been completed for each named personnel and; (3) a one sentence description of the educational program(s) listed in (2) above. This requirement extends to investigators and all individuals responsible for the design and/or conduct of the research who are working as subcontractors or consultants under the contract.

Prior to any substitution of the Principal Investigator or any other individuals responsible for the design and/or conduct of the research under the contract, the contractor shall provide the following written information to the Contracting Officer: the title of the education program and a one sentence description of the program that has been completed by the replacement.

ARTICLE H.4. DATA AND SAFETY MONITORING IN CLINICAL TRIALS

The contractor is directed to the full text of the NIH Policy regarding Data and Safety Monitoring and Reporting of Adverse Events, which may be found at the following web sites:

http://grants.nih.gov/grants/guide/notice-files/not98-084.html
http://grants.nih.gov/grants/guide/notice-files/not99-107.html
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html

The contractor must comply with the NIH Policy cited in these NIH Announcements and any other data and safety monitoring requirements found elsewhere in this contract.

Data and Safety Monitoring shall be performed in accordance with the approved Data and Safety Monitoring Plan.

The Data and Safety Monitoring [BOARD and PLAN] shall be established and approved prior to beginning the conduct of the clinical trial.

ARTICLE H.5. RESEARCH INVOLVING RECOMBINANT DNA MOLECULES (Including Human Gene Transfer Research)

All research involving Recombinant DNA Molecules shall be conducted in accordance with the NIH Guidelines for Research Involving Recombinant DNA Molecules (http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html) and the May 28, 2002 Notice, Compliance with the NIH Guidelines for Research Involving Recombinant DNA Molecules (http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-02-052.html) (and any subsequent revisions to the Guide Notice) which stipulates biosafety and containment measures for recombinant DNA research and delineates critical, ethical principles and key safety reporting requirements for human gene transfer research (See Appendix M of the Guidelines). These guidelines apply to both basic and clinical research studies.

The Recombinant DNA Advisory Committee (RAC) is charged with the safety of manipulation of genetic material through the use of recombinant DNA techniques. Prior to beginning any clinical trials involving the transfer of recombinant DNA to humans, the trial must be registered with the RAC. If this contract involves new protocols that contain unique and//or novel issues, the RAC must discuss them in a public forum and then the Institutional Biosafety Committee (IBC), the Institutional Review Board (IRB), and the project officer and contracting officer must approve the protocol prior to the start of the research.

Failure to comply with these requirements may result in suspension, limitation, or termination of the contract for any work related to Recombinant DNA Research or a requirement for contracting officer prior approval of any or all Recombinant DNA projects under this contract. This includes the requirements of the Standing Institutional Biosafety Committee (IBC) (See http://www4.od.nih.gov/oba/IBC/IBCindexpg.htm).

As specified in Appendix M-1-C-4 of the NIH Guidelines, any serious adverse event must be reported immediately to the IRB, the IBC, the Office for Human Research Protections (if applicable), and the NIH Office for Biotechnology Activities (OBA), followed by the filing of a written report with each office/group and copies to the project officer and contracting officer. (http://www4.od.nih.gov/oba/rac/guidelines_02/Appendix_M.htm#_Toc7255836).

ARTICLE H.6. CONTINUED BAN ON FUNDING OF HUMAN EMBRYO RESEARCH

a. Pursuant to Public Law(s) cited in paragraph b. , below, NIH is prohibited from using appropriated funds to support human embryo research. Contract funds may not be used for (1) the creation of a human embryo or embryos for research purposes; or (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 CFR 46.204(b) and Section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b)). The term "human embryo or embryos" includes any organism, not protected as a human subject under 45 CFR 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells.

   Additionally, in accordance with a March 4, 1997 Presidential Memorandum, Federal funds may not be used for cloning of human beings.

b. **Public Law and Section No.** **Fiscal Year** **Period Covered**

[Applicable information to be included at award]

ARTICLE H.7. NEEDLE EXCHANGE

a. Pursuant to Public Law(s) cited in paragraph b., below, contract funds shall not be used to carry out any program of distributing sterile needles or syringes for the hypodermic injection of any illegal drug.

b. **Public Law and Section No.** **Fiscal Year** **Period Covered**

[Applicable information to be included at award]

ARTICLE H.8. PRIVACY ACT

This procurement action requires the Contractor to do one or more of the following: design, develop, or operate a system of records on individuals to accomplish an agency function in accordance with the Privacy Act of 1974, Public Law 93-579, December 31, 1974 (5 USC 552a) and applicable agency regulations. Violation of the Act may involve the imposition of criminal penalties.

The Privacy Act System of Records applicable to this project is Number 09-25-0200 (see http://oma.od.nih.gov/ms/privacy/pa-files/0200.htm).

ARTICLE H.9. OMB CLEARANCE or CLINICAL EXEMPTION

In accordance with HHSAR 352.270-7, Paperwork Reduction Act, the Contractor shall not proceed with surveys or interviews until such time as Office of Management and Budget (OMB) Clearance or for conducting interviews has been obtained by the Project Officer and the Contracting Officer has issued written approval to proceed. In addition, in accordance with 5 CFR 1320.3(h)(5), this requirement may be eligible for a Clinical Exemption to OMB Clearance requirements subject to the approval of the NIH Clinical Exemption Review Committee (CERC). The clinical exemption must be obtained and written approval to proceed received from the Project Officer and Contracting Officer before data is collected under this contract or any subcontract.

ARTICLE H.10. ANIMAL WELFARE

All research involving live, vertebrate animals shall be conducted in accordance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals. This policy may be accessed at:
http://grants1.nih.gov/grants/olaw/references/phspol.htm

ARTICLE H.11. PROTECTION OF PERSONNEL WHO WORK WITH NONHUMAN PRIMATES

All contractor personnel who work with nonhuman primates or enter rooms or areas containing nonhuman primates shall comply with the procedures set forth in NIH Policy Manual 3044-2, entitled, "Protection of NIH Personnel Who Work with Nonhuman Primates," located at the following URL:
http://www1.od.nih.gov/oma/manualchapters/intramural/3044-2/

ARTICLE H.12. OPTION PROVISION

Unless the Government exercises its option pursuant to the Option Clause set forth in ARTICLE I.3., the contract will consist only of items 1 through 7 of the Statement of Work as defined in Sections C and F of the contract. Pursuant to clause 52.217- 7 set forth in ARTICLE I.3. of this contract, the Government may, by unilateral contract modification, require the Contractor to perform items 8 and 9 of the Statement of Work as also defined in Sections C and F of this contract. If the Government exercises this option, notice must be given at least 60 days prior to the expiration date of this contract, and the estimated cost [plus fixed fee] of the contract will be increased as set forth in Article [B.2./B.3].

ARTICLE H.13. SUBCONTRACTING PROVISIONS

a. Small Business Subcontracting Plan

(1) The Small Business Subcontracting Plan, dated _____ is attached hereto and made a part of this contract.

(2) The failure of any Contractor or subcontractor to comply in good faith with FAR Clause 52.219-8, entitled "Utilization of Small Business Concerns" incorporated in this contract and the attached Subcontracting Plan, will be a material breach of such contract or subcontract and subject to the remedies reserved to the Government under FAR Clause 52.219-16 entitled, "Liquidated Damages-Subcontracting Plan."

b. Subcontracting Reports

The Contractor shall submit the following Subcontracting reports electronically via the "electronic Subcontracting Reporting System (eSRS) at http://www.esrs.gov.

(1) Individual Subcontract Reports (ISR)

Regardless of the effective date of this contract, the Report shall be submitted on the following dates for the entire life of this contract:

April 30th
October 30th

(2) Summary Subcontract Report (SSR)

Regardless of the effective date of this contract, the Summary Subcontract Report shall be submitted annually on the following date for the entire life of this contract:

October 30th

For both the Individual and Summary Subcontract Reports, the [Contracting Officer/Contract Specialist/or title of alternate designee] shall be included as a contact for notification purposes at the following e-mail address:

Contracting Officer/Contract Specialist
[e-mail address will be provided at time of award]

ARTICLE H.14. SALARY RATE LIMITATION LEGISLATION PROVISIONS

[NOTE: This requirement will be revised in the resultant contract subject to the implementation of a FY07 Public Law covering the period of 10/01/2006 through 09/30/2007.]

a. Pursuant to the P.L.(s) cited in paragraph b., below, no NIH Fiscal Year funds may be used to pay the direct salary of an individual through this contract at a rate in excess of the applicable amount shown or the applicable Executive Level for the fiscal year covered. Direct salary is exclusive of fringe benefits, overhead and general and administrative expenses (also referred to as "indirect costs" or "facilities and administrative (F&A) costs"). Direct salary has the same meaning as the term "institutional base salary." An individual's direct salary (or institutional base salary) is the annual compensation that the contractor pays for an individual's appointment whether that individual's time is spent on research, teaching, patient care or other activities. Direct salary (or institutional base salary) excludes any income that an individual may be permitted to earn outside of duties to the contractor. The per year salary rate limitation also applies to individuals proposed under subcontracts. It does not apply to fees paid to consultants. If this is a multiple year contract, it may be subject to unilateral modifications by the Government if an individual's salary rate used to establish contract funding exceeds any salary rate limitation subsequently established in future HHS appropriation acts.

b.

Public Law No.	**Fiscal Year**	**Dollar Amount of Salary Limitation***

[Applicable information to be included at award]

c. Payment of direct salaries is limited to the Executive Level I rate which was in effect on the date(s) the expense was incurred.

For the period 10/1/05 - 12/31/05, the Executive Level I rate is $180,100. Effective January 1, 2006, the Executive Level I rate increased to $183,500 and will remain at that rate until it is revised. See the web site listed below for the Executive Schedule rates of pay:

FOR FY-06 EXECUTIVE LEVEL SALARIES EFFECTIVE JANUARY 1, 2006:
http://www.opm.gov/oca/06tables/html/ex.asp
(Note: This site shows the FY-06 rates. For previous years, click on "salaries and wages" and then scroll down to the bottom of the page and click on the year to locate the desired Executive Level salary rates.)

ARTICLE H.15. ELECTRONIC AND INFORMATION TECHNOLOGY STANDARDS

Pursuant to Section 508 of the Rehabilitation Act of 1973 (29 U.S.C. 794d) as amended by P.L.105-220 under Title IV (Rehabilitation Act Amendments of 1998) all Electronic and Information Technology (EIT) developed, procured, maintained and/or used under this contract shall be in compliance with the "Electronic and Information Technology Accessibility Standards" set forth by the Architectural and Transportation Barriers Compliance Board (also referred to as the "Access Board") in 36 CFR Part 1194. The complete text of Section 508 Final Standards can be accessed at http://www.access-board.gov/.

ARTICLE H.16. INFORMATION SECURITY

The Statement of Work (SOW) requires the contractor to develop or access Federal automated information systems; therefore, the contractor shall comply with the "DHHS Information Security Program Policy" (http://www.hhs.gov/read/irmpolicy/FINALHHSInformationSecurityProgramP.doc) as set forth below. The contractor shall include this provision in any subcontract awarded under this contract.

a. Information Type

**** *(NOTE: The resultant contract will include the Information Type(s), however for the purposes of this RFP, the Information Type(s) is specified in SECTION L.2.b. Technical Proposal Instructions of this RFP.)* ****

[ ] Administrative, Management and Support Information:

[ ] Mission Based Information:

b. Security Categories and Levels

**** *(NOTE: The resultant contract will include the Security Categories and Levels, however for the purposes of this RFP, the Security Categories and Levels are specified in SECTION L.2.b. Technical Proposal Instructions of this RFP.)* ****

Confidentiality	Level:	[ ] Low	[ ] Moderate	[ ] High
Integrity	Level:	[ ] Low	[ ] Moderate	[ ] High
Availability	Level:	[ ] Low	[ ] Moderate	[ ] High
Overall	Level:	[ ] Low	[ ] Moderate	[ ] High

c. Position Sensitivity Designations

(1) The following position sensitivity designations and associated clearance and investigation requirements apply under this contract:

**** *(NOTE: The resultant contract will include the Position Sensitivity Designations, however for the purposes of this RFP, the Position Sensitivity Designations applicable to this RFP are specified in SECTION L.2.b. Technical Proposal Instructions of this RFP.)* ****

[ ] Level 6: Public Trust - High Risk (Requires Suitability Determination with a BI). Contractor employees assigned to a Level 6 position are subject to a Background Investigation (BI).

[ ] Level 5: Public Trust - Moderate Risk (Requires Suitability Determination with NACIC, MBI or LBI). Contractor employees assigned to a Level 5 position with no previous investigation and approval shall undergo a National Agency Check and Inquiry Investigation plus a Credit Check (NACIC), a Minimum Background Investigation (MBI), or a Limited Background Investigation (LBI).

[ ] Level 1: Non Sensitive (Requires Suitability Determination with an NACI). Contractor employees assigned to a Level 1 position are subject to a National Agency Check and Inquiry Investigation (NACI).

(2) The contractor shall submit a roster, by name, position and responsibility, of all IT staff working under the contract. The roster shall be submitted to the Project Officer, with a copy to the Contracting Officer, within 14 days of the effective date of the contract. Any revisions to the Roster as a result of staffing changes shall be submitted within fifteen (15) calendar days of the change. The Contracting Officer shall notify the contractor of the appropriate level of suitability investigations to be performed. An electronic template, "Roster of Employees Requiring Suitability Investigations," is available for contractor use at:
http://ais.nci.nih.gov/forms/Suitability-roster.xls

Upon receipt of the Government's notification of applicable Suitability Investigation required, the contractor shall complete and submit the required forms within 30 days of the notification. Additional submission instructions can be found at the "NCI Information Technology Security Policies, Background Investigation Process" website: http://ais.nci.nih.gov.

Contractor employees who have had a background investigation conducted by the U.S. Office of Personnel Management (OPM) within the last five years may only require an updated or upgraded investigation.

(3) Contractor employees shall comply with the DHHS criteria for the assigned position sensitivity designations prior to performing any work under this contract. The following exceptions apply:

Levels 5 and 1: Contractor employees may begin work under the contract after the contractor has submitted the name, position and responsibility of the employee to the Project Officer, as described in paragraph c.(2) above.

Level 6: In special circumstances the Project Officer may request a waiver of the preappointment investigation. If the waiver is granted, the Project Officer will provide written authorization for the contractor employee to work under the contract.

d. Systems Security Plan

The contractor shall protect Federal automated information systems that are developed or accessed by the contractor. System security shall be accomplished in accordance with the contractor's System Security Plan dated _____. The plan must:]

(1) Include a detailed plan of present and proposed systems security programs commensurate with the size and complexity of the requirements of the Statement of Work. The contractor shall use the NIH Systems Security Plan Template (detailed) at http://irm.cit.nih.gov/security/secplantemp.doc or NIH Systems Security Plan Outline (outline only) at http://irm.cit.nih.gov/nihsecurity/Security_Plan_Outline.doc.

[OR (To be determined during negotiations)]

(1) Include a plan of present and proposed systems security programs commensurate with the size and complexity of the requirements of the Statement of Work. The minimum areas to be addressed include, but are not limited to administrative, technical, and physical security as follows:

(i) Security Awareness Training
(ii) Logical Access Control
-Network (ex: firewall)
-System (ex: network OS, tcp wrappers, SSH)
-Application (ex: S-LDAP, SSL)
-Remote Access (ex: VPN)
-Monitoring and support (ex: IDS, pager, NOC)
(iii) Protection against data loss
-OS security (ex: patch management, configuration)

-Application security (ex: patch management)
-Database security
-Back-up and recovery
-Fault tolerance, high availability

(iv) Malicious Code Protection (ex: Antivirus, filtering of e-mail attachments, etc)

(v) Physical Security

-Access control (ex: locks, guards)
-Power conditioning and/or UPS
-Air conditioning
-Fire protection

Include an acknowledgment of its understanding of the security requirements.

Provide similar information for any proposed subcontractor developing or accessing an AIS.

e. Rules of Behavior

The contractor shall comply with the the NIH Information Technology General Rules of Behavior at: http://irm.cit.nih.gov/security/nihitrob.html.

f. Information Security Training

Each contractor employee shall complete the NIH Computer Security Awareness Training (http://irtsectraining.nih.gov/) prior to performing any contract work, and on an annual basis thereafter, during the period of performance of this contract.

The contractor shall maintain a listing by name and title of each individual working under this contract that has completed the NIH required training. Any additional security training completed by contractor staff shall be included on this listing.

Contractor staff shall complete the following additional training prior to performing any work under this contract:

**** *[Additional courses will be listed here in the resultant contract, if applicable.]* ****

g. Personnel Security Responsibilities

The contractor shall perform and document the actions identified in the "Employee Separation Checklist", attached and made a part of this contract, when a contractor employee terminates work under this contract. All documentation shall be made available to the Project Officer and/or Contracting Officer upon request.

h. Commitment to Protect Departmental Information Systems and Data

(1) Contractor Agreement

The Contractor shall not release, publish, or disclose Departmental information to unauthorized personnel, and shall protect such information in accordance with provisions of the following laws and any other pertinent laws and regulations governing the confidentiality of sensitive information:

-18 U.S.C. 641 (Criminal Code: Public Money, Property or Records)
-18 U.S.C. 1905 (Criminal Code: Disclosure of Confidential Information)
-Public Law 96-511 (Paperwork Reduction Act)

(2) Contractor-Employee Non-Disclosure Agreements

Each contractor employee who may have access to sensitive Department information under this contract shall complete Commitment To Protect Non-Public Information - Contractor Agreement. A copy of each signed and witnessed Non-Disclosure agreement shall be submitted to the Project Officer prior to performing any work under the contract.

i. References

1. DHHS Information Security Program Policy: http://www.hhs.gov/ohr/manual/pssh.pdf
2. DHHS Personnel Security/Suitability Handbook: http://www.hhs.gov/ohr/manual/pssh.pdf
3. NIST Special Publication 800-16, Information Technology Security Training Requirements: http://csrc.nist.gov/publications/nistpubs/800-16/800-16.pdf
   Appendix A-D: http://csrc.nist.gov/publications/nistpubs/800-16/AppendixA-D.pdf
4. NIST SP 800-18, Guide for Developing Security Plans for Information Technology Systems: http://csrc.nist.gov/publications/nistpubs/index.html
5. NIST SP 800-60, Guide for Mapping Types of Information and Information Systems to Security Categories, Volume I: http://csrc.nist.gov/publications/nistpubs/800-60/SP800-60V1-final.pdf
6. NIST SP 800-60, Guide for Mapping Types of Information and Information Systems to Security Categories, Volume II: http://csrc.nist.gov/publications/nistpubs/800-60/SP800-60V2-final.pdf
7. NIST SP 800-64, Security Considerations in the Information System Development Life Cycle: http://csrc.nist.gov/publications/nistpubs/800-64/NIST-SP800-64.pdf
8. NIH Computer Security Awareness Training Course: http://irtsectraining.nih.gov/
9. Roster of Employees Requiring Suitability Investigations: http://ais.nci.nih.gov/forms/Suitability-roster.xls
10. NCI Information Technology Security Policies, Background Investigation Process: http://ais.nci.nih.gov/
11. NIH Systems Security Plan Template (detailed): http://irm.cit.nih.gov/security/secplantemp.doc
12. NIH Systems Security Plan Outline (outline only): http://irm.cit.nih.gov/nihsecurity/Security_Plan_Outline.doc
13. NIH Information Technology General Rules of Behavior: http://irm.cit.nih.gov/security/nihitrob.html
14. Commitment To Protect Non-Public Information - Contractor Agreement: http://irm.cit.nih.gov/security/Nondisclosure.pdf

ARTICLE H.17. ENERGY STAR REQUIREMENTS

Executive Order 13123, “Greening the Government Through Efficient Energy Management” and FAR 23.203 require that when Federal Agencies acquire energy using products, they select, where life-cycle cost-effective, and available, ENERGY STAR® or other energy efficient products.

Unless the Contracting Officer determines otherwise, all energy-using products acquired under this contract must be either an ENERGY STAR® or other energy efficient product designated by the Department of Energy’s Federal Energy Management Program (FEMP).

For more information about ENERGY STAR® see http://www.energystar.gov/
For more information about FEMP see http://www.eere.energy.gov/

ARTICLE H.18. PUBLICATION AND PUBLICITY

The contractor shall acknowledge the support of the National Institutes of Health whenever publicizing the work under this contract in any media by including an acknowledgment substantially as follows:

"This project has been funded in whole or in part with Federal funds from the National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, under Contract No.HHSN2662007XXXXX.

ARTICLE H.19. PRESS RELEASES

a. Pursuant to Public Law(s) cited in paragraph b., below, the contractor shall clearly state, when issuing statements, press releases, requests for proposals, bid solicitations and other documents describing projects or programs funded in whole or in part with Federal money: (1) the percentage of the total costs of the program or project which will be financed with Federal money; (2) the dollar amount of Federal funds for the project or program; and (3) the percentage and dollar amount of the total costs of the project or program that will be

financed by nongovernmental sources.

b. **Public Law and Section No.** **Fiscal Year** **Period Covered**

[Applicable information to be included at award]

ARTICLE H.20. REPORTING MATTERS INVOLVING FRAUD, WASTE AND ABUSE

Anyone who becomes aware of the existence or apparent existence of fraud, waste and abuse in NIH funded programs is encouraged to report such matters to the HHS Inspector General's Office in writing or on the Inspector General's Hotline. The toll free number is **1-800-HHS-TIPS** (**1-800-447-8477).** All telephone calls will be handled confidentially. The e-mail address is **Htips@os.dhhs.gov** and the mailing address is:

Office of Inspector General
Department of Health and Human Services
TIPS HOTLINE
P.O. Box 23489
Washington, D.C. 20026

ARTICLE H.21. ANTI-LOBBYING

a. Pursuant to Public Law(s) cited in paragraph c., below, contract funds shall only be used for normal and recognized executive-legislative relationships. Contract funds shall not be used, for publicity or propaganda purposes; or for the preparation, distribution, or use of any kit, pamphlet, booklet, publication, radio, television, or video presentation designed to support or defeat legislation pending before the Congress or any State legislature, except in presentation to the Congress or any State legislature itself.

b. Contract funds shall not be used to pay salary or expenses of the contractor or any agent acting for the contractor, related to any activity designed to influence legislation or appropriations pending before the Congress or any State legislature.

c. **Public Law and Section No.** **Fiscal Year** **Period Covered**

[Applicable information to be included at award]

ARTICLE H.22. OBTAINING AND DISSEMINATING BIOMEDICAL RESEARCH RESOURCES

Unique research resources arising from NIH-funded research are to be shared with the scientific research community. NIH provides guidance, entitled, "Sharing Biomedical Research Resources: Principles and Guidelines for Recipients of NIH Research Grants and Contracts," (Federal Register Notice, December 23, 1999 [64 FR 72090]), concerning the appropriate terms for disseminating and acquiring these research resources. This guidance, found at : http://ott.od.nih.gov/NewPages/64FR72090.pdf. is intended to help contractors ensure that the conditions they impose and accept on the transfer of research tools will facilitate further biomedical research, consistent with the requirements of the Bayh-Dole Act and NIH funding policy.

Note: For the purposes of this Article, the terms, "research tools," "research materials," and "research resources" are used interchangeably and have the same meaning.

ARTICLE H.23. POSSESSION USE AND TRANSFER OF SELECT BIOLOGICAL AGENTS OR TOXINS

The contractor shall not conduct work involving select agents or toxins under this contract until it and any associated subcontractor(s) comply with the following:

For prime or subcontract awards to ***domestic institutions*** that possess, use, and/or transfer Select Agents

under this contract, the institution must comply with the provisions of 42 CFR part 73, 7 CFR part 331, and/or 9 CFR part 121 (http://www.aphis.usda.gov/programs/ag_selectagent/FinalRule3-18-05.pdf), as required, before using NIH funds for research involving Select Agents. No NIH funds can be used for research involving Select Agents if the final registration certificate is denied.

For prime or subcontract awards to ***foreign institutions*** that possess, use, and/or transfer Select Agents under this contract, before using NIH funds for any work directly involving the Select Agents, the foreign institution must provide information satisfactory to the NIAID, NIH that safety, security, and training standards equivalent to those described in 42 CFR part 73, 7 CFR part 331, and/or 9 CFR part 121 at:
(http://www.aphis.usda.gov/programs/ag_selectagent/FinalRule3-18-05.pdf)
are in place and will be administered on behalf of all Select Agent work sponsored by these funds. The process for making this determination includes inspection of the foreign laboratory facility by an NIAID representative. During this inspection, the foreign institution must provide the following information: concise summaries of safety, security, and training plans; names of individuals at the foreign institution who will have access to the Select Agents and procedures for ensuring that only approved and appropriate individuals, in accordance with institution procedures, will have access to the Select Agents under the contract; and copies of or links to any applicable laws, regulations, policies, and procedures applicable to that institution for the safe and secure possession, use, and/or transfer of select agents. An NIAID-chaired committee of U.S. federal employees (including representatives of NIH grants/contracts and scientific program management, CDC, Department of Justice and other federal intelligence agencies, and Department of State) will ultimately assess the results of the laboratory facility inspection, and the regulations, policies, and procedures of the foreign institution for equivalence to the U.S. requirements described in 42 CFR part 73, 7 CFR part 331, and/or 9 CFR part 121 (http://www.aphis.usda.gov/programs/ag_selectagent/FinalRule3-18-05.pdf). The committee will provide recommendations to the DEA Director, NIAID. The DEA Director will make the approval decision and notify the Contracting Officer. The Contracting Officer will inform the prime contractor of the approval status of the foreign institution. No NIH funds can be used for research involving Select Agents at a foreign institution until NIAID grants this approval.

Listings of HHS select agents and toxins, and overlap select agents or toxins as well as information about the registration process for domestic institutions, are available on the Select Agent Program Web site at http://www.cdc.gov/od/sap/ and http://www.cdc.gov/od/sap/docs/salist.pdf. Listings of USDA select agents and toxins as well as information about the registration process for domestic institutions are available on the APHIS/USDA website at:http://www.aphis.usda.gov/programs/ag_selectagent/index.html and: http://www.aphis.usda.gov/programs/ag_selectagent/ag_bioterr_forms.html.
For foreign institutions, see the NIAID Select Agent Award information:
(http://www.niaid.nih.gov/ncn/clinical/default_biodefense.htm).

ARTICLE H.24. PROHIBITION ON CONTRACTOR INVOLVEMENT WITH TERRORIST ACTIVITIES

The contractor acknowledges that U.S. Executive Orders and Laws, including but not limited to E.O. 13224 and P.L. 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.

ARTICLE H.25. NIH POLICY ON ENHANCING PUBLIC ACCESS TO ARCHIVED PUBLICATIONS RESULTING FROM NIH-FUNDED RESEARCH

The Policy requests that beginning May 2, 2005, NIH-funded investigators submit to the NIH National Library of Medicine's (NLM) PubMed Central (PMC) an electronic version of the author's final manuscript, upon acceptance for publication, resulting from research supported in whole or in part with direct costs from NIH. NIH defines the author's final manuscript as the final version accepted for journal publication, and includes all modifications from the publishing peer review process. The PMC archive will preserve permanently these manuscripts for use by the public, health care providers, educators, scientists, and NIH. The Policy directs electronic submissions to the NIH/NLM/PMC: http://www.pubmedcentral.nih.gov.

Additional information is available at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-022.html.

ARTICLE H.26. CONSTITUTION DAY

Each educational institution that receives Federal funds for a fiscal year shall hold an educational program on the United States Constitution on September 17 of such year for the students serviced by the educational institution in accordance with Public Law 108-447.

PART II - CONTRACT CLAUSES

SECTION I - CONTRACT CLAUSES

THE FOLLOWING **ARTICLE I.1 GENERAL CLAUSE LISTING(S)** WILL BE APPLICABLE TO MOST CONTRACTS RESULTING FROM THIS RFP. HOWEVER, THE ORGANIZATIONAL STRUCTURE OF THE SUCCESSFUL OFFEROR(S) WILL DETERMINE THE SPECIFIC GENERAL CLAUSE LISTING TO BE CONTAINED IN THE CONTRACT(S) AWARDED FROM THIS RFP:

General Clauses for a Cost-Reimbursement Research and Development Contract

The complete listing of these clauses may be accessed at:
http://rcb.cancer.gov/rcb-internet/appl/general-clauses/clauses.jsp

ARTICLE I.2. AUTHORIZED SUBSTITUTIONS OF CLAUSES

Any authorized substitutions and/or modifications other than the General Clauses which will be based on the type of contract/Contractor will be determined during negotiations.

It is expected that the following clause(s) will be made part of the resultant contract:

FAR Clauses **52.215-15, Pension Adjustments And Asset Reversions** (October 2004); **52.215-18, Reversion Or Adjustment Of Plans For Post Retirement Benefits (PRB) Other Than Pensions** (July 2005); and, **52.215-19, Notification Of Ownership Changes** (October 1997), are deleted in their entirety.

Alternate IV (October 1997) of FAR Clause **52.215-21, Requirements For Cost Or Pricing Data Or Information Other Than Cost Or Pricing Data--Modifications** (October 1997) is added.

Alternate II (October 2001) of FAR Clause **52.219-9, Small Business Subcontracting Plan** (July 2005) is added.

FAR Clause **52.232-20, Limitation Of Cost** (April 1984), is deleted in its entirety and FAR Clause **52.232-22, Limitation Of Funds** (April 1984) is substituted therefor. ***[NOTE: When this contract is fully funded, FAR Clause 52.232-22, LIMITATION OF FUNDS will no longer apply and FAR Clause 52.232-20, LIMITATION OF COST will become applicable.]***

Alternate I (February 2002) of FAR Clause **52.232-25, Prompt Payment** (February 2002), is deleted.

ARTICLE I.3. ADDITIONAL CONTRACT CLAUSES

Additional clauses other than those listed below which are based on the type of contract/Contractor shall be determined during negotiations. Any contract awarded from this solicitation will contain the following:

This contract incorporates the following clauses by reference, (unless otherwise noted), with the same force and effect as if they were given in full text. Upon request, the Contracting Officer will make their full text available.

a. FEDERAL ACQUISITION REGULATION (FAR) (48 CFR CHAPTER 1) CLAUSES

(1) FAR Clause **52.216-15, Predetermined Indirect Cost Rates** (April 1998).

(2) FAR Clause **52.217-7**, **Option for Increased Quantity - Separately Priced Line Item** (March 1989)

(3) FAR Clause **52.219-4, Notice of Price Evaluation Preference for HUBZone Small Business Concerns** (July 2005).

(4) FAR Clause **52.219-25, Small Disadvantaged Business Participation Program--Disadvantaged Status and Reporting** (October 1999).

(5) FAR Clause **52.224-1, Privacy Act Notification** (April 1984).

(6) FAR Clause **52.224-2, Privacy Act** (April 1984).

(7) FAR Clause **52.227-2**, **Notice and Assistance Regarding Patent and Copyright Infringement** (August 1996)

(8) FAR Clause **52.227-14, Rights in Data - General** (June 1987) with Alternates III and V.

(9) FAR Clause **52-227-15, Representation of Limited Rights Data and Restricted Software** (May 1999).

(10) FAR Clause **52.227-16, Additional Data Requirements** (June 1987).

(11) FAR Clause **52.230-3, Disclosure and Consistency of Cost Accounting Practices** (April 1998).

(12) FAR Clause **52.230-6, Administration of Cost Accounting Standards** (April 2005).

(13) FAR Clause **52.239-1, Privacy or Security Safeguards** (August 1996).

(14) **FAR Clause 52.242-3, Penalties for Unallowable Costs** (May 2001).

b. DEPARTMENT OF HEALTH AND HUMAN SERVICES ACQUISITION REGULATION (HHSAR) (48 CHAPTER 3) CLAUSES:

(1) HHSAR Clause **352.223-70**, **Safety and Health** (January 2001).

(2) HHSAR Clause **352.270-1, Accessibility of Meetings, Conferences and Seminars to Persons with Disabilities** (January 2001).

(3) HHSAR Clause **352.270-8, Protection of Human Subjects** (March 2005).

(4) HHSAR Clause **352.270-9, Care of Live Vertebrate Animals** (March 2005).

c. NATIONAL INSTITUTES OF HEALTH (NIH) RESEARCH CONTRACTING (RC) CLAUSES:

The following clauses are attached and made a part of this contract:

(1) **NIH (RC)-7, Procurement of Certain Equipment** (April 1984) (OMB Bulletin 81-16)

(2) **NIH(RC)-11, Research Patient Care Costs** (4/1/84).

ARTICLE I.4. ADDITIONAL FAR CONTRACT CLAUSES INCLUDED IN FULL TEXT

Additional clauses other than those listed below which are based on the type of contract/Contractor shall be determined during negotiations. Any contract awarded from this solicitation will contain the following:

This contract incorporates the following clauses in full text.

FEDERAL ACQUISITION REGULATION (FAR)(48 CFR CHAPTER 1) CLAUSES:

a. FAR Clause **52.222-39, Notification Of Employee Rights Concerning Payment Of Union Dues Or Fees** (December 2004)

(a) Definition. As used in this clause--

United States means the 50 States, the District of Columbia, Puerto Rico, the Northern Mariana Islands, American Samoa, Guam, the U.S. Virgin Islands, and Wake Island.

(b) Except as provided in paragraph (e) of this clause, during the term of this contract, the Contractor shall post a notice, in the form of a poster, informing employees of their rights concerning union membership and payment of union dues and fees, in conspicuous places in and about all its plants and offices, including all places where notices to employees are customarily posted. The notice shall include the following information (except that the information pertaining to National Labor Relations Board shall not be included in notices posted in the plants or offices of carriers subject to the Railway Labor Act, as amended (45 U.S.C. 151-188)).

Notice to Employees

Under Federal law, employees cannot be required to join a union or maintain membership in a union in order to retain their jobs. Under certain conditions, the law permits a union and an employer to enter into a union-security agreement requiring employees to pay uniform periodic dues and initiation fees. However, employees who are not union members can object to the use of their payments for certain purposes and can only be required to pay their share of union costs relating to collective bargaining, contract administration, and grievance adjustment.

If you do not want to pay that portion of dues or fees used to support activities not related to collective bargaining, contract administration, or grievance adjustment, you are entitled to an appropriate reduction in your payment. If you believe that you have been required to pay dues or fees used in part to support activities not related to collective bargaining, contract administration, or grievance adjustment, you may be entitled to a refund and to an appropriate reduction in future payments.

For further information concerning your rights, you may wish to contact the National Labor Relations Board (NLRB) either at one of its Regional offices or at the following address or toll free number:

National Labor Relations Board
Division of Information
1099 14th Street, N.W.
Washington, DC 20570
1-866-667-6572
1-866-316-6572 (TTY)

To locate the nearest NLRB office, see NLRB's website at http://www.nlrb.gov.

(c) The Contractor shall comply with all provisions of Executive Order 13201 of February 17, 2001, and related implementing regulations at 29 CFR part 470, and orders of the Secretary of Labor.

(d) In the event that the Contractor does not comply with any of the requirements set forth in paragraphs (b), (c), or (g), the Secretary may direct that this contract be cancelled, terminated, or suspended in whole or in part, and declare the Contractor ineligible for further Government contracts in accordance with procedures at 29 CFR part 470, Subpart B--Compliance Evaluations, Complaint Investigations and Enforcement Procedures. Such other sanctions or remedies may be imposed as are provided by 29 CFR part 470, which implements Executive Order 13201, or as are otherwise provided by law.

(e) The requirement to post the employee notice in paragraph (b) does not apply to--

(1) Contractors and subcontractors that employ fewer than 15 persons;

(2) Contractor establishments or construction work sites where no union has been formally recognized by the Contractor or certified as the exclusive bargaining representative of the Contractor's employees;

(3) Contractor establishments or construction work sites located in a jurisdiction named in the definition of the United States in which the law of that jurisdiction forbids enforcement of union-security agreements;

(4) Contractor facilities where upon the written request of the Contractor, the Department of Labor Deputy Assistant Secretary for Labor-Management Programs has waived the posting requirements with respect to any of the Contractor's facilities if the Deputy Assistant Secretary finds that the Contractor has demonstrated that--

(i) The facility is in all respects separate and distinct from activities of the Contractor related to the performance of a contract; and
(ii) Such a waiver will not interfere with or impede the effectuation of the Executive order; or

(5) Work outside the United States that does not involve the recruitment or employment of workers within the United States.

(f) The Department of Labor publishes the official employee notice in two variations; one for contractors covered by the Railway Labor Act and a second for all other contractors. The Contractor shall--

(1) Obtain the required employee notice poster from the Division of Interpretations and Standards, Office of Labor-Management Standards, U.S. Department of Labor, 200 Constitution Avenue, NW, Room N-5605, Washington, DC 20210, or from any field office of the Department's Office of Labor-Management Standards or Office of Federal Contract Compliance Programs;

(2) Download a copy of the poster from the Office of Labor-Management Standards website at http://www.olms.dol.gov; or

(3) Reproduce and use exact duplicate copies of the Department of Labor's official poster.

(g) The Contractor shall include the substance of this clause in every subcontract or purchase order that exceeds the simplified acquisition threshold, entered into in connection with this contract, unless exempted by the Department of Labor Deputy Assistant Secretary for Labor-Management Programs on account of special circumstances in the national interest under authority of 29 CFR 470.3(c). For indefinite quantity subcontracts, the Contractor shall include the substance of this clause if the value of orders in any calendar year of the subcontract is expected to exceed the simplified acquisition threshold. Pursuant to 29 CFR part 470, Subpart B--Compliance Evaluations, Complaint Investigations and Enforcement Procedures, the Secretary of Labor may direct the Contractor to take such action in the enforcement of these regulations, including the imposition of sanctions for noncompliance with respect to any such subcontract or purchase order. If the Contractor becomes involved in litigation with a subcontractor or vendor, or is threatened with such involvement, as a result of such direction, the Contractor may request the United States, through the Secretary of Labor, to enter into such litigation to protect the interests of the United States.

b. FAR Clause **52.222-50, Combating Trafficking in Persons** (April 2006)

(a) *Definitions*. As used in this clause-- *Coercion* means--

(1) Threats of serious harm to or physical restraint against any person;
(2) Any scheme, plan, or pattern intended to cause a person to believe that failure to perform an act would result in serious harm to or physical restraint against any person; or
(3) The abuse or threatened abuse of the legal process.

Commercial sex act means any sex act on account of which anything of value is given to or received by any person.

Debt bondage means the status or condition of a debtor arising from a pledge by the debtor of his or her personal services or of those of a person under his or her control as a security for debt, if the value of those services as reasonably assessed is not applied toward the liquidation of the debt or the length and nature of those services are not respectively limited and defined.

Employee means an employee of a Contractor directly engaged in the performance of work under a Government contract, including all direct cost employees and any other Contractor employee who has other than a minimal impact or involvement in contract performance.

Individual means a Contractor that has no more than one employee including the Contractor. Involuntary servitude includes a condition of servitude induced by means of--

(1) Any scheme, plan, or pattern intended to cause a person to believe that, if the person did not enter into or continue in such conditions, that person or another person would suffer serious harm or physical restraint; or
(2) The abuse or threatened abuse of the legal process.

Severe forms of trafficking in persons means--

(1) Sex trafficking in which a commercial sex act is induced by force, fraud, or coercion, or in which the person induced to perform such act has not attained 18 years of age; or
(2) The recruitment, harboring, transportation, provision, or obtaining of a person for labor or services, through the use of force, fraud, or coercion for the purpose of subjection to involuntary servitude, peonage, debt bondage, or slavery. Sex trafficking means the recruitment, harboring, transportation, provision, or obtaining of a person for the purpose of a commercial sex act.

(b) *Policy.* The United States Government has adopted a zero tolerance policy regarding Contractors and Contractor employees that engage in or support severe forms of trafficking in persons, procurement of commercial sex acts, or use of forced labor. During the performance of this contract, the Contractor shall ensure that its employees do not violate this policy.

(c) *Contractor requirements*. The Contractor, if other than an individual, shall establish policies and procedures for ensuring that its employees do not engage in or support severe forms of trafficking in persons, procure commercial sex acts, or use forced labor in the performance of this contract. At a minimum, the Contractor shall--

(1) Publish a statement notifying its employees of the United States Government's zero tolerance policy described in paragraph (b) of this clause and specifying the actions that will be taken against employees for violations of this policy. Such actions may include, but are not limited to, removal from the contract, reduction in benefits, or termination of employment;

(2) Establish an awareness program to inform employees about--

(i) The Contractor's policy of ensuring that employees do not engage in severe forms of trafficking in persons, procure commercial sex acts, or use forced labor;
(ii) The actions that will be taken against employees for violation of such policy;
(iii) Regulations applying to conduct if performance of the contract is outside the U.S., including--

(A) All host country Government laws and regulations relating to severe forms of trafficking in persons, procurement of commercial sex acts, and use of forced labor; and
(B) All United States laws and regulations on severe forms of trafficking in persons, procurement of commercial sex acts, and use of forced labor which may apply to its employees' conduct in the host nation, including those laws for which jurisdiction is established by the Military Extraterritorial Jurisdiction Act of 2000 (18 U.S.C. 3261-3267),

and 18 U.S.C 3271, Trafficking in Persons Offenses Committed by Persons Employed by or Accompanying the Federal Government Outside the United States;

(3) Provide all employees directly engaged in performance of the contract with a copy of the statement required by paragraph (c)(1) of this clause and obtain written agreement from the employee that the employee shall abide by the terms of the statement; and

(4) Take appropriate action, up to and including termination, against employees or subcontractors that violate the policy in paragraph (b) of this clause.

(d) *Notification.* The Contractor shall inform the contracting officer immediately of--

(1) Any information it receives from any source (including host country law enforcement) that alleges a contract employee has engaged in conduct that violates this policy; and
(2) Any actions taken against employees pursuant to this clause.

(e) *Remedies.* In addition to other remedies available to the Government, the Contractor's failure to comply with the requirements of paragraphs (c) or (d) of this clause may render the Contractor subject to--

(1) Required removal of a Contractor employee or employees from the performance of the contract;
(2) Required subcontractor termination;
(3) Suspension of contract payments;
(4) Loss of award fee for the performance period in which the Government determined Contractor non-compliance;
(5) Termination of the contract for default, in accordance with the termination clause of this contract; or
(6) Suspension or debarment.

(f) *Subcontracts*. The Contractor shall include the substance of this clause, including this paragraph (f), in all subcontracts for the acquisition of services.

PART III - LIST OF DOCUMENTS, EXHIBITS AND OTHER ATTACHMENTS

SECTION J - LIST OF ATTACHMENTS

The following documents are incorporated into this RFP:

SOLICITATION ATTACHMENTS:

Attachment No.	Title	Location
Attachment 1:	Packaging and Delivery of Proposal	Linked to the Attachment Title
Attachment 2:	Proposal Intent Response Sheet	Linked to the Attachment Title
Attachment 3:	Background	Linked to the Attachment Title
Attachment 4:	Statement of Work	Linked to the Attachment Title
Attachment 5:	Reporting Requirement and Deliverables	Linked to the Attachment Title
Attachment 6	Appendix A - Additional Technical Proposal Instructions	Linked to the Attachment Title
Attachment 7	Appendix B - Additional Business Proposal Instructions	Linked to the Attachment Title
Attachment 8	Appendix C - Advance Understandings	Linked to the Attachment Title

TECHNICAL PROPOSAL ATTACHMENTS: (The following attachments must be completed, where applicable, and submitted with the Technical Proposal.)

Title	Location
Targeted/Planned Enrollment Table	http://rcb.cancer.gov/rcb-internet/forms/enroll-table.pdf
Technical Proposal Cost Summary	http://www.niaid.nih.gov/contract/forms.htm
Summary of Related Activities	http://www.niaid.nih.gov/contract/forms.htm
Government Notice for Handling Proposals	http://www.niaid.nih.gov/contract/forms/form7.pdf
Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption, OMB Form No. 0990-0263 (formerly Optional Form 310	http://rcb.cancer.gov/rcb-internet/forms/of310.pdf
Project Objectives, NIH 1688-1	http://rcb.cancer.gov/rcb-internet/forms/nih1688-1.pdf

BUSINESS PROPOSAL ATTACHMENTS: (The following attachments must be completed, where applicable, and submitted with the Business Proposal.)

Title	Location
Proposal Summary and Data Record, NIH-2043	http://www.niaid.nih.gov/contract/forms.htm
Small Business Subcontracting Plan	http://rcb.cancer.gov/rcb-internet/forms/sb-subplan-nci.pdf
Breakdown of Proposed Estimated Costs (plus Fee) with Excel Spreadsheet	http://oamp.od.nih.gov/contracts/BUSCOST.HTM http://oamp.od.nih.gov/Division/DFAS/spshexcl.xls
Offeror's Points of Contact	http://www.niaid.nih.gov/contract/forms.htm
Disclosure of Lobbying Activities, OMB Form SF-LLL	http://rcb.cancer.gov/rcb-internet/forms/sflllin.pdf

INFORMATIONAL ATTACHMENTS: (The following Attachments and Reports will become part of any contract resulting from this RFP and will be required during contract performance.)

Title	Location
Invoice/Financing Request and Contract Financial Reporting Instructions--Cost Reimbursement, NIH(RC)-4	http://rcb.cancer.gov/rcb-internet/forms/rc4.pdf
Privacy Act System of Records *System of Records No. 09-25-0200 is applicable to this RFP.*	http://oma.od.nih.gov/ms/privacy/pa-files/read02systems.htm
Safety and Health, HHSAR Clause 352.223-70	http://www.niaid.nih.gov/contract/forms/form10.pdf
Procurement of Certain Equipment, NIH(RC)-7	http://www.niaid.nih.gov/contract/forms/NIH-RC-7.pdf
Research Patient Care Costs, NIH(RC)-11	http://www.niaid.nih.gov/contract/forms/nih-rc-11.pdf
Inclusion Enrollment Report	http://rcb.cancer.gov/rcb-internet/forms/inclusion-enrollment.pdf
Disclosure of Lobbying Activities, OMB Form SF-LLL	http://rcb.cancer.gov/rcb-internet/forms/sflllin.pdf
Commitment To Protect Non-Public Information Contractor Agreement	http://irm.cit.nih.gov/security/Nondisclosure.pdf
Roster of Employees Requiring Suitability Investigations	http://ais.nci.nih.gov/forms/Suitability-roster.xls
Employee Separation Checklist	http://rcb.cancer.gov/rcb-internet/forms/Emp-sep-checklist.pdf

PART IV - REPRESENTATIONS AND INSTRUCTIONS

SECTION K - REPRESENTATIONS, CERTIFICATIONS AND OTHER STATEMENTS OF OFFERORS

SECTION K can be accessed electronically from the INTERNET at the following address:

http://rcb.cancer.gov/rcb-internet/wkf/sectionk.pdf

If you are unable to access this document electronically, you may request a copy from the Contracting Officer identified on the cover page of this solicitation.

IF YOU INTEND TO SUBMIT A PROPOSAL, YOU MUST COMPLETE SECTION K AND SUBMIT IT AS PART OF YOUR BUSINESS PROPOSAL.

SECTION L - INSTRUCTIONS, CONDITIONS AND NOTICES TO OFFERORS

1. GENERAL INFORMATION

a. **INSTRUCTIONS TO OFFERORS--COMPETITIVE ACQUISITION** [FAR Provision 52.215-1 (January 2004)]

(a) *Definitions*. As used in this provision--

Discussions are negotiations that occur after establishment of the competitive range that may, at the Contracting Officer's discretion, result in the offeror being allowed to revise its proposal.

"In writing", *"writing"*, or *"written"* means any worded or numbered expression that can be read, reproduced, and later communicated, and includes electronically transmitted and stored information.

"*Proposal modification*" is a change made to a proposal before the solicitation's closing date and time, or made in response to an amendment, or made to correct a mistake at any time before award.

"*Proposal revision*" is a change to a proposal made after the solicitation closing date, at the request of or as allowed by a Contracting Officer as the result of negotiations.

"*Time,*" if stated as a number of days, is calculated using calendar days, unless otherwise specified, and will include Saturdays, Sundays, and legal holidays. However, if the last day falls on a Saturday, Sunday, or legal holiday, then the period shall include the next working day.

(b) *Amendments to solicitations*. If this solicitation is amended, all terms and conditions that are not amended remain unchanged. Offerors shall acknowledge receipt of any amendment to this solicitation by the date and time specified in the amendment(s).

(c) *Submission, modification, revision, and withdrawal of proposals*. (1) Unless other methods (*e.g.*, electronic commerce or facsimile) are permitted in the solicitation, proposals and modifications to proposals shall be submitted in paper media in sealed envelopes or packages (i) addressed to the office specified in the solicitation, and (ii) showing the time and date specified for receipt, the solicitation number, and the name and address of the offeror. Offerors using commercial carriers should ensure that the proposal is marked on the outermost wrapper with the information in paragraphs (c)(1)(i) and (c)(1)(ii) of this provision.

(2) The first page of the proposal must show--
- (i) The solicitation number;
- (ii) The name, address, and telephone and facsimile numbers of the offeror (and electronic address if available);
- (iii) A statement specifying the extent of agreement with all terms, conditions, and provisions included in the solicitation and agreement to furnish any or all items upon which prices are offered at the price set opposite each item;
- (iv) Names, titles, and telephone and facsimile numbers (and electronic addresses if available) of persons authorized to negotiate on the offeror's behalf with the Government in connection with this solicitation; and
- (v) Name, title, and signature of person authorized to sign the proposal. Proposals signed by an agent shall be accompanied by evidence of that agent's authority, unless that evidence has been previously furnished to the issuing office.

(3) *Submission, modification, revision, and withdrawal of proposals*. (i) Offerors are responsible for submitting proposals, and any modifications or revisions, so as to reach the Government office designated in the solicitation by the time specified in the solicitation. If no time is specified in the solicitation, the time for receipt is 4:30 p.m., local time, for the designated Government office on the date that proposal or revision is due.

(ii) (A) Any proposal, modification, or revision received at the Government office designated in the solicitation after the exact time specified for receipt of offers is "late" and will not be

considered unless it is received before award is made, the Contracting Officer determines that accepting the late offer would not unduly delay the acquisition; and--

(*1*) If it was transmitted through an electronic commerce method authorized by the solicitation, it was received at the initial point of entry to the Government infrastructure not later than 5:00 p.m. one working day prior to the date specified for receipt of proposals; or

(*2*) There is acceptable evidence to establish that it was received at the Government installation designated for receipt of offers and was under the Government's control prior to the time set for receipt of offers; or

(*3*) It is the only proposal received.

(B) However, a late modification of an otherwise successful proposal that makes its terms more favorable to the Government, will be considered at any time it is received and may be accepted.

(iii) Acceptable evidence to establish the time of receipt at the Government installation includes the time/date stamp of that installation on the proposal wrapper, other documentary evidence of receipt maintained by the installation, or oral testimony or statements of Government personnel.

(iv) If an emergency or unanticipated event interrupts normal Government processes so that proposals cannot be received at the office designated for receipt of proposals by the exact time specified in the solicitation, and urgent Government requirements preclude amendment of the solicitation, the time specified for receipt of proposals will be deemed to be extended to the same time of day specified in the solicitation on the first work day on which normal Government processes resume.

(v) Proposals may be withdrawn by written notice received at any time before award. Oral proposals in response to oral solicitations may be withdrawn orally. If the solicitation authorizes facsimile proposals, proposals may be withdrawn via facsimile received at any time before award, subject to the conditions specified in the provision at 52.215-5, Facsimile Proposals. Proposals may be withdrawn in person by an offeror or an authorized representative, if the identity of the person requesting withdrawal is established and the person signs a receipt for the proposal before award.

(4) Unless otherwise specified in the solicitation, the offeror may propose to provide any item or combination of items.

(5) Offerors shall submit proposals in response to this solicitation in English, unless otherwise permitted by the solicitation, and in U.S. dollars, unless the provision at FAR 52.225-17, Evaluation of Foreign Currency Offers, is included in the solicitation.

(6) Offerors may submit modifications to their proposals at any time before the solicitation closing date and time, and may submit modifications in response to an amendment, or to correct a mistake at any time before award.

(7) Offerors may submit revised proposals only if requested or allowed by the Contracting Officer.

(8) Proposals may be withdrawn at any time before award. Withdrawals are effective upon receipt of notice by the Contracting Officer.

(d) *Offer expiration date*. Proposals in response to this solicitation will be valid for the number of days specified on the solicitation cover sheet (unless a different period is proposed by the offeror).

(e) *Restriction on disclosure and use of data.* (1) The proposal submitted in response to this request may contain data (trade secrets; business data, e.g., commercial information, financial information, and cost and pricing data; and technical data) which the offeror, including its prospective subcontractor(s), does not want used or disclosed for any purpose other than for evaluation of the proposal. The use and disclosure

of any data may be so restricted; provided, that the Government determines that the data is not required to be disclosed under the Freedom of Information Act, 5 U.S.C. 552, as amended, and the offeror marks the cover sheet of the proposal with the following legend, specifying the particular portions of the proposal which are to be restricted in accordance with the conditions of the legend. The Government's determination to withhold or disclose a record will be based upon the particular circumstances involving the record in question and whether the record may be exempted from disclosure under the Freedom of Information Act. The legend reads:

> Unless disclosure is required by the Freedom of Information Act, 5 U.S.C. 552, as amended, (the Act) as determined by Freedom of Information (FOI) officials of the Department of Health and Human Services, data contained in the portions of this proposal which have been specifically identified by page number, paragraph, etc. by the offeror as containing restricted information shall not be used or disclosed except for evaluation purposes.
>
> The offeror acknowledges that the Department may not be able to withhold a record (data, document, etc.) nor deny access to a record requested pursuant to the Act and that the Department's FOI officials must make that determination. The offeror hereby agrees that the Government is not liable for disclosure if the Department has determined that disclosure is required by the Act.
>
> If a contract is awarded to the offeror as a result of, or in connection with, the submission of this proposal, the Government shall have right to use or disclose the data to the extent provided in the contract. Proposals not resulting in a contract remain subject to the Act.
>
> The offeror also agrees that the Government is not liable for disclosure or use of unmarked data and may use or disclose the data for any purpose, including the release of the information pursuant to requests under the Act. The data subject to this restriction are contained in pages (insert page numbers, paragraph designations, etc. or other identification).

(2) In addition, the offeror should mark each page of data it wishes to restrict with the following statement:

> "Use or disclosure of data contained on this page is subject to the restriction on the cover sheet of this proposal or quotation."

(3) Offerors are cautioned that proposals submitted with restrictive legends or statements differing in substance from the above legend may not be considered for award. The Government reserves the right to reject any proposal submitted with a nonconforming legend.

(f) *Contract award*. (1) The Government intends to award a contract or contracts resulting from this solicitation to the responsible offeror(s) whose proposal(s) represents the best value after evaluation in accordance with the factors and subfactors in the solicitation.

(2) The Government may reject any or all proposals if such action is in the Government's interest.

(3) The Government may waive informalities and minor irregularities in proposals received.

(4) The Government intends to evaluate proposals and award a contract without discussions with offerors (except clarifications as described in FAR 15.306(a)). Therefore, the offeror's initial proposal should contain the offeror's best terms from a cost or price and technical standpoint. The Government reserves the right to conduct discussions if the Contracting Officer later determines them to be necessary. If the Contracting Officer determines that the number of proposals that would

otherwise be in the competitive range exceeds the number at which an efficient competition can be conducted, the Contracting Officer may limit the number of proposals in the competitive range to the greatest number that will permit an efficient competition among the most highly rated proposals.

(5) The Government reserves the right to make an award on any item for a quantity less than the quantity offered, at the unit cost or prices offered, unless the offeror specifies otherwise in the proposal.

(6) The Government reserves the right to make multiple awards if, after considering the additional administrative costs, it is in the Government's best interest to do so.

(7) Exchanges with offerors after receipt of a proposal do not constitute a rejection or counteroffer by the Government.

(8) The Government may determine that a proposal is unacceptable if the prices proposed are materially unbalanced between line items or subline items. Unbalanced pricing exists when, despite an acceptable total evaluated price, the price of one or more contract line items is significantly overstated or understated as indicated by the application of cost or price analysis techniques. A proposal may be rejected if the Contracting Officer determines that the lack of balance poses an unacceptable risk to the Government.

(9) If a cost realism analysis is performed, cost realism may be considered by the source selection authority in evaluating performance or schedule risk.

(10) A written award or acceptance of proposal mailed or otherwise furnished to the successful offeror within the time specified in the proposal shall result in a binding contract without further action by either party.

(11) If a post-award debriefing is given to requesting offerors, the Government shall disclose the following information, if applicable:

(i) The agency's evaluation of the significant weak or deficient factors in the debriefed offeror's offer.
(ii) The overall evaluated cost or price and technical rating of the successful and debriefed offeror and past performance information on the debriefed offeror.
(iii) The overall ranking of all offerors, when any ranking was developed by the agency during source selection;
(iv) A summary of the rationale for award.
(v) For acquisitions of commercial items, the make and model of the item to be delivered by the successful offeror.
(vi) Reasonable responses to relevant questions posed by the debriefed offeror as to whether source-selection procedures set forth in the solicitation, applicable regulations, and other applicable authorities were followed by the agency.

(End of Provision)

b. **NAICS CODE AND SIZE STANDARD**

Note: The following information is to be used by the offeror in preparing its Representations and Certifications (See Section K of this RFP), specifically in completing the provision entitled, SMALL BUSINESS PROGRAM REPRESENTATION, FAR Clause 52.219-1.

(1) The North American Industry Classification System (NAICS) code for this acquisition is 541710.

(2) The small business size standard is 500.

THIS REQUIREMENT IS NOT SET-ASIDE FOR SMALL BUSINESS. However, the Federal Acquisition Regulation (FAR) requires in EVERY solicitation, (except for foreign acquisitions) the inclusion of the

North American Industry Classification (NAICS) Code and corresponding size standard which best describes the nature of the requirement in the solicitation.

c. **TYPE OF CONTRACT AND NUMBER OF AWARDS**

It is anticipated that Multiple Award(s) will be made from this solicitation and that the award(s) will be made on/about June 8, 2007.

It is anticipated that the award(s) from this solicitation will be a multiple-year cost reimbursement type contract completion with a 3 year base period of performance and options which could extend the period of performance up to 4 additional years. Incremental funding will be used [see Section L.2.c. Business Proposal Instructions].

d. **ESTIMATE OF EFFORT**

It is expected that a completion type contract will be awarded as a result of this RFP. To assist you in the preparation of your proposal, the Government considers the effort to be approximately as follows:

Base and Option Years	Full Time Equivalent
Base Years 1 and 2	13 per year
Base Year 3	Reduced to 7.55
Option 1 (Year 3)	2.1
Option 2 (Years 4-7)	2.1 each year

This information is furnished for the offeror's information only and is not to be considered restrictive for proposal purposes.

e. **COMMITMENT OF PUBLIC FUNDS**

The Contracting Officer is the only individual who can legally commit the Government to the expenditure of public funds in connection with the proposed procurement. Any other commitment, either explicit or implied, is invalid.

f. **COMMUNICATIONS PRIOR TO CONTRACT AWARD**

Offerors shall direct all communications to the attention of the Contract Specialist or Contracting Officer cited on the face page of this RFP. Communications with other officials may compromise the competitiveness of this acquisition and result in cancellation of the requirement.

g. **RELEASE OF INFORMATION**

Contract selection and award information will be disclosed to offerors in accordance with regulations applicable to negotiated acquisition. Prompt written notice will be given to unsuccessful offerors as they are eliminated from the competition, and to all offerors following award.

h. **COMPARATIVE IMPORTANCE OF PROPOSALS**

You are advised that paramount consideration shall be given to the evaluation of technical proposals. All evaluation factors other than cost or price, when combined, are significantly more important than cost or price. The relative importance of the evaluation factors are specified in SECTION M of this solicitation. However, the Government reserves the right to make an award to the best advantage of the Government, cost and other factors considered.

i. **PREPARATION COSTS**

This RFP does not commit the Government to pay for the preparation and submission of a proposal.

j. **SERVICE OF PROTEST** (AUGUST 1996) - FAR 52.233-2

(a) Protests, as defined in section 33.101 of the Federal Acquisition Regulation, that are filed directly with an agency, and copies of any protests that are filed with the Government Accountability Office (GAO), shall be served on the Contracting Officer (addressed as follows) by obtaining written and dated acknowledgment of receipt from:

Contracting Officer
Office of Acquisitions, DEA
NIAID,NIH,DHHS
6700-B Rockledge Drive, Room 3214, MSC 7612
Bethesda MD 20892-7612

(b) The copy of any protest shall be received in the office designated above within one day of filing a protest with the GAO.

(End of Provision)

k. **LATE PROPOSALS AND REVISIONS**, HHSAR 352.215-70

Notwithstanding the procedures contained in FAR 52.215-1(c)(3) of the provision of this solicitation entitled Instructions to Offerors-Competitive Acquisition, a proposal received after the date specified for receipt may be considered if it offers significant cost or technical advantages to the Government; and it was received before proposals were distributed for evaluation, or within five calendar days after the exact time specified for receipt, whichever is earlier.

(End of provision)

2. INSTRUCTIONS TO OFFERORS

a. GENERAL INSTRUCTIONS

INTRODUCTION

The following instructions will establish the acceptable minimum requirements for the format and contents of proposals. Special attention is directed to the requirements for technical and business proposals to be submitted in accordance with these instructions.

(1) **Contract Type and General Clauses**

It is contemplated that a cost-reimbursement completion type contract will be awarded. (See General Information) Any resultant contract shall include the clauses applicable to the selected offeror's organization and type of contract awarded as required by Public Law, Executive Order, or acquisition regulations in effect at the time of execution of the proposed contract.

(2) **Authorized Official and Submission of Proposal**

The proposal must be signed by an official authorized to bind your organization and must stipulate that it is predicated upon all the terms and conditions of this RFP. Your proposal shall be submitted in the number of copies, to the addresses, and marked as indicated in the Attachment entitled, PACKAGING AND DELIVERY OF PROPOSAL, Part III, Section J hereof. Proposals will be typewritten, paginated, reproduced on letter size paper and will be legible in all required copies. To expedite the proposal evaluation, all documents required for responding to the RFP should be placed in the following order:

I. COVER PAGE

Include RFP title, number, name of organization, DUNS No., identification of the proposal part, and indicate whether the proposal is an original or a copy.

II. TECHNICAL PROPOSAL

It is recommended that the technical proposal consist of a cover page, a table of contents, and the information requested in the Technical Proposal Instructions and as specified in SECTION J, List of Attachments. (See also, Appendix A - Additional Technical Proposal Instructions).

III. BUSINESS PROPOSAL

It is recommended that the business proposal consist of a cover page, a table of contents, and the information requested in the Business Proposal Instructions and as specified in SECTION J, List of Attachments. (See also, Appendix B - Additional Business Proposal Instructions.)

(3) **Proposal Summary and Data Record (NIH-2043)**

The Offeror must complete the Form NIH-2043, attached, with particular attention to the length of time the proposal is firm and the designation of those personnel authorized to conduct negotiations. (See Section J, Attachment entitled, PROPOSAL SUMMARY AND DATA RECORD.)

(4) **Separation of Technical and Business Proposals**

The proposal must be prepared in two parts: a "Technical Proposal" and a "Business Proposal." Each of the parts shall be separate and complete in itself so that evaluation of one may be accomplished independently of, and concurrently with, evaluation of the other. The technical proposal must include direct cost and resources information, such as labor-hours and categories and applicable rates, materials, subcontracts, travel, etc., and associated costs so that the offeror's understanding of the project may be evaluated (See Attachment entitled, TECHNICAL PROPOSAL COST SUMMARY). However, the technical

proposal should **not** include pricing data relating to individual salary information, indirect cost rates or amounts, fee amounts (if any), and total costs. The technical proposal should disclose your technical approach in as much detail as possible, including, but not limited to, the requirements of the technical proposal instructions.

(5) **Alternate Proposals**

You may, at your discretion, submit alternate proposals, or proposals which deviate from the requirements; provided, that you also submit a proposal for performance of the work as specified in the statement of work. Such proposals may be considered if overall performance would be improved or not compromised and if they are in the best interests of the Government. Alternative proposals, or deviations from any requirements of this RFP, shall be clearly identified.

(6) **Evaluation of Proposals**

The Government will evaluate technical proposals in accordance with the criteria set forth in Part IV, Section M of this RFP.

(7) **Potential Award Without Discussions**

The Government reserves the right to award a contract without discussions if the Contracting Officer determines that the initial prices are fair and reasonable and that discussions are not necessary.

(8) **Use of the Metric System of Measurement**

It is the policy of the Department of Health and Human Services to support the Federal transition to the metric system and to use the metric system of measurement in all procurement, grants, and other business related activities unless such use is impracticable or is likely to cause significant inefficiencies.

The offeror is encouraged to prepare their proposal using either "Hard Metric," "Soft Metric," or "Dual Systems" of measurement. The following definitions are provided for your information:

Hard Metric - The replacement of a standard inch-pound size with an accepted metric size for a particular purpose. An example of size substitution might be: selling or packaging liquids by the liter instead of by the pint or quart (as for soft drinks), or instead of by the gallon (as for gasoline).

Soft Metric - The result of a mathematical conversion of inch-pound measurements to metric equivalents for a particular purpose. The physical characteristics are not changed.

Dual Systems - The use of both inch-pound and metric systems. For example, an item is designed, produced, and described in inch-pound values with soft metric values also shown for information or comparison purposes.

(9) **Standards for Privacy of Individually Identifiable Health Information**

The Department of Health and Human Services (DHHS) issued final modifications to the “Standards for Privacy of Individually Identifiable Health Information,” the “Privacy Rule,” on August 14, 2002. The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information and is administered and enforced by the DHHS Office for Civil Rights (OCR). Those who must comply with the Privacy Rule (classified under the Rule as “covered entities” must do so by April 14, 2003 (with the exception of small health plans which have an extra year to comply.

Decisions about the applicability and implementation of the Privacy Rule reside with the contractor and his/her institution. The OCR Web site (http://www.hhs.gov/ocr/) provides information of the Privacy Rule, including a complete Regulation Text and a set of decision tools on “Am I a covered entity?” Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, award, and administration of grants, cooperative agreements and contracts can be found at:

http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html.

(10) **Privacy Act - Treatment of Proposal Information**

The Privacy Act of 1974 (P.L. 93-579) requires that a Federal agency advise each individual whom it asks to supply information, the authority which authorizes the solicitation, whether disclosure is voluntary or mandatory, the principal purpose or purposes for which the information is intended to be used, the uses outside the agency which may be made of the information, and the effects on the individual, if any, of not providing all or any part of the requested information.

The NIH is requesting the information called for in this RFP pursuant to the authority provided by Sec. 301(a)(7) of the Public Health Service Act, as amended, and P.L. 92-218, as amended.

Providing the information requested is entirely voluntary. The collection of this information is for the purpose of conducting an accurate, fair, and adequate review prior to a discussion as to whether to award a contract.

Failure to provide any or all of the requested information may result in a less than adequate review.

In addition, the Privacy Act of 1974 (P.L. 93-579, Section 7) requires that the following information be provided when individuals are requested to disclose their social security number.

Provision of the social security number is voluntary. Social security numbers are requested for the purpose of accurate and efficient identification, referral, review and management of NIH contracting programs. Authority for requesting this information is provided by Section 301 and Title IV of the PHS Act, as amended.

The information provided by you may be routinely disclosed for the following purposes:

- to the cognizant audit agency and the General Accounting Office for auditing.
- to the Department of Justice as required for litigation.
- to respond to congressional inquiries.
- to qualified experts, not within the definition of Department employees, for opinions as a part of the review process.

(11) **Selection of Offerors**

a) The acceptability of the [scientific and] technical portion of each [research] contract proposal will be evaluated by a technical review committee. The committee will evaluate each proposal in strict conformity with the evaluation criteria of the RFP, utilizing point scores and written critiques. The committee may suggest that the Contracting Officer request clarifying information from an offeror.

b) The business portion of each contract proposal will be subjected to a cost and price analysis, management analysis, etc.

c) If award will be made without conducting discussions, offerors may be given the opportunity to clarify certain aspects of their proposal (e.g., the relevance of an offeror's past performance information and adverse past performance information to which the offeror has not previously had an opportunity to respond) or to resolve minor or clerical errors.

d) If the Government intends to conduct discussions prior to awarding a contract-

(1) Communications will be held with offerors whose past performance information is the determining factor preventing them from being placed within the competitive range. Such communications shall address adverse past performance information to which an offeror has not had a prior opportunity to respond. Also, communications may be held with any other offerors whose exclusion from, or inclusion in, the competitive range is uncertain.

Such communications shall not be used to cure proposal deficiencies or omissions that alter the technical or cost elements of the proposal, and/or otherwise revise the proposal, but may be considered in rating proposals for the purpose of establishing the competitive range.

(2) The Contracting Officer will, in concert with program staff, decide which proposals are in the competitive range. The competitive range will be comprised of all of the most highly rated proposals. Oral or written discussions will be conducted with all offerors in the competitive range.

While it is NIAID's policy to conduct discussions with all offerors in the competitive range, NIAID reserves the right, in special circumstances, to limit the number of proposals included in the competitive range to the greatest number that will permit an efficient competition. All aspects of the proposals are subject to discussions, including cost, technical approach, past performance, and contractual terms and conditions. At the conclusion of discussions, each offeror still in the competitive range shall be given an opportunity to submit a written Final Proposal Revision (FPR) with the reservation of the right to conduct finalization of details with the selected source in accordance with HHSAR 315.370.

e) The process described in FAR 15.101-1 will be employed, which permits the Government to make tradeoffs among cost or price and non-cost factors and to consider award to other than the lowest price offeror or other than the highest technically rated offeror. This process will take into consideration the results of the technical evaluation, the past performance evaluation (if applicable) and the cost analysis.

f) The NIAID reserves the right to make a single award, multiple awards, or no award at all to the RFP. In addition, the RFP may be amended or canceled as necessary to meet NCI requirements. Synopses of awards exceeding $25,000 will be published in FedBizOpps.

(12) **Institutional Responsibility Regarding Conflicting Interests of Investigators**

EACH INSTITUTION MUST:

(a) Maintain an appropriate written, enforced policy on conflict of interest that complies with 42 CFR Part 50 Subpart F and/or 45 CFR Part 94 as appropriate and inform each investigator of the Institution's policy, the Investigator's reporting responsibilities, and the applicable regulations. If the Institution carries out the NIH funded research through subgrantees, contractors or collaborators, the Institution must take reasonable steps to ensure that Investigators working for such entities comply with the regulations, either by requiring those investigators to comply with the Institution's policy or by requiring the entities to provide assurances to the Institution that will enable the Institution to comply with the regulations.

(b) Designate an Institutional official(s) to solicit and review financial disclosure statements from each Investigator who is planning to participate in NIH-funded research.

(c) Require that by the time an application/proposal is submitted to the NIH each investigator who is planning to participate in the NIH-funded research has submitted to the designated official(s) a listing of his/her known Significant Financial Interests (and those of his/her spouse and dependent children): (i) that would reasonably appear to be affected by the research for which the NIH funding is sought; and (ii) in entities whose financial interests would reasonably appear to be affected by the research. All financial disclosures must be updated during the period of the award, either on an annual basis or as new reportable Significant Financial Interests are obtained.

(d) Provide guidelines consistent with the regulations for the designated official(s) to identify conflicting interests and take such actions as necessary to ensure that such conflicting interests will be managed, reduced, or eliminated.

(e) Maintain records, identifiable to each award, of all financial disclosures and all actions taken by the institution with respect to each conflicting interest for: (1) in the case of grants, at least three years

from the date of submission of the final expenditures report or, where applicable, from other dates specified in 45 CFR Part 74.53(b) and (2) in the case of contracts, 3 years after final payment or, where applicable, for the other time period specified in 48 CFR Part 4 Subpart 4.7, Contract Records Retention.

(f) Establish adequate enforcement mechanisms and provide for sanctions where appropriate.

(g) Certify, in each application/proposal for funding to which the regulations applies, that:

1) there is in effect at the Institution a written and enforced administrative process to identify and manage, reduce or eliminate conflicting interests with respect to all research projects for which funding is sought from the NIH;

2) prior to the Institution's expenditure of any funds under the award, the Institution will report to the awarding component the existence of a conflicting interest (but not the nature of the interest or other details) found by the Institution and assure that the interest has been managed, reduced or eliminated in accord with the regulations; and for any interest that the Institution identifies as conflicting subsequent to the expenditure of funds after award, the report will be made and the conflicting interest managed, reduced, or eliminated, at least on a temporary basis within sixty days of that identification;

3) the Institution agrees to make information available, upon request, to the awarding component regarding all conflicting interests identified by the Institution and how those interested have been managed, reduced, or eliminated to protect the research from bias; and

4) the Institution will otherwise comply with the regulations.

Institutional Management of Conflicting Interests

(a) The designated official(s) must: (1) review all financial disclosures; and (2) determine whether conflict of interest exists, and if so, determine what actions should be taken by the Institution to manage, reduce or eliminate such conflict of interest. **A conflict of interest exists when the designated official(s) reasonably determines that a Significant Financial Interest could directly and significantly affect the design, conduct, or reporting of the NIH-funded research**.

Examples of conditions or restrictions that might be imposed to manage actual or potential conflicts of interests include, but are not limited to:

(i) public disclosure of significant financial interests;
(ii) monitoring of research by independent reviewers;
(iii) modification of the research plan;
(iv) disqualification of the Investigator(s) from participation in all or a portion of the research funded by the awarding component;
(v) divestiture of significant financial interests; or
(vi) severance of relationships that create actual or potential conflicts of interests.

(b) An Institution may require the management of other conflicting financial interests in addition to those described in paragraph (a) of this section, as the Institution deems appropriate.

(13) **Past Performance Information**

a) Offerors shall submit the following information as part of their **business** proposal.

A list of the last 5 contracts completed during the past 3 years and the last 3 contracts contracts awarded that are similar in nature to the solicitation workscope. Contracts listed may include those entered into by the Federal Government, agencies of state and local governments and commercial concerns. Offerors that are newly formed entities without prior contracts should list contracts and subcontracts as required above for all key personnel.

Include the following information for each contract or subcontract:

1. Name of Contracting Organization
2. Contract Number (for subcontracts, provide the prime contract number and the subcontract number)
3. Contract Type
4. Total Contract Value
5. Description of Requirement
6. Contracting Officer's Name and Telephone Number
7. Program Manager's Name and Telephone Number
8. Standard Industrial Code

The offeror shall submit comparable information on all subcontractors that the offeror proposes to perform a major subcontract under this effort. For the purpose of this solicitation, a "major subcontract" is defined as .

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

b) Each offeror will be evaluated on its performance under existing and prior contracts for similar products or services. 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.

(14) **Electronic and Information Technology Accessibility**

Section 508 of the Rehabilitation Act of 1973 (29 U.S.C. 794d), as amended by P.L.105-220 under Title IV (Rehabilitation Act Amendments of 1998) and the Architectural and Transportation Barriers Compliance Board Electronic and Information Technology (EIT) Accessibility Standards (36 CFR part 1194) require that all EIT acquired must ensure that:

a. Federal employees with disabilities have access to and use of information and data that is comparable to the access and use by Federal employees who are not individuals with disabilities; and

b. Members of the public with disabilities seeking information or services from an agency have access to and use of information and data that is comparable to the access to and use of information and data by members of the public who are not individuals with disabilities.

This requirement includes the development, maintenance, and/or use of EIT products/services, therefore, any proposal submitted in response to this solicitation must demonstrate compliance with the established EIT Accessibility Standards.

Further information about Section 508 is available via the Internet at http://www.section508.gov .

(15) **Prohibition on Contractor Involvement with Terrorist Activities**

The contractor acknowledges that U.S. Executive Orders and Laws, including but not limited to E.O. 13224 and P.L. 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.

(16) **Solicitation Provisions Incorporated by Reference, FAR 52.252-1 (February 1998)**

This Solicitation incorporates one or more solicitation provisions by reference, with the same force and effect as if they were given in full text. Upon request, the Contracting Officer will make their full text

available. The offeror is cautioned that the listed provisions may include blocks that must be completed by the offeror and submitted with its quotation or offer. In lieu of submitting the full text provisions, the offeror may identify the provision by paragraph identifier and provide the appropriate information with its quotation or offer. Also, the full text of a solicitation provision may be accessed electronically at this address: http://www.arnet.gov/far/.

FEDERAL ACQUISITION REGULATION (48 CFR CHAPTER 1):

a) Data Universal Numbering System (DUNS) Number, FAR Clause 52.204-6 (October 2003).

b) Facilities Capital Cost of Money, FAR Clause 52.215-16, (October 1997).

c) Order of Precedence-Uniform Contract Format, FAR Clause 52.215-8, (October 1997).

d) Preaward On-Site Equal Opportunity Compliance Evaluation, (Over $10,000,000), FAR Clause 52.222-24, (February 1999).

b. TECHNICAL PROPOSAL INSTRUCTIONS

A detailed work plan must be submitted indicating how each aspect of the statement of work is to be accomplished. Your technical approach should be in as much detail as you consider necessary to fully explain your proposed technical approach or method. The technical proposal should reflect a clear understanding of the nature of the work being undertaken. The technical proposal must include information on how the project is to be organized, staffed, and managed. Information should be provided which will demonstrate your understanding and management of important events or tasks.

(1) Technical Discussions

The technical discussion included in the technical proposal should respond to the items set forth below:

a) Project Objectives, NIH-1688-1

The offeror shall insert a completed NIH Form 1688-1, Project Objective, as provided in Section J, Attachments, behind the Title Page of each copy of the proposal, along with the "Government Notice for Handling Proposals." The NIH Form 1688-1 is to be completed as follows:

- For an **Institution of Higher Education:** The form MUST be completed in its entirety.
- For **OTHER** than an Institution of Higher Education: The starred items (Department, Service, Laboratory or Equivalent, and Major Subdivision) should be left blank.

The information required under the "Summary of Objectives" portion of the form MUST meet the requirements set forth in the section of the form entitled, **"INSTRUCTIONS:"**

b) Statement of Work

(1) Objectives

State the overall objectives and the specific accomplishments you hope to achieve. Indicate the rationale for your plan, and relation to comparable work in progress elsewhere. Review pertinent work already published which is relevant to this project and your proposed approach. This should support the scope of the project as you perceive it.

(2) Approach

Use as many subparagraphs, appropriately titled, as needed to clearly outline the general plan of work. Discuss phasing of research and, if appropriate, include experimental design and possible or probable outcome of approaches proposed.

(3) Methods

Describe in detail the methodologies you will use for the project, indicating your level of experience with each, areas of anticipated difficulties, and any unusual expenses you anticipate.

(4) Schedule

Provide a schedule for completion of the work and delivery of items specified in the statement of work. Performance or delivery schedules shall be indicated for phases or segments, as applicable, as well as for the overall program. Schedules shall be shown in terms of calendar months from the date of authorization to proceed or, where applicable, from the date of a stated event, as for example, receipt of a required approval by the Contracting Officer. Unless the request for proposal indicates that the stipulated schedules are mandatory, they shall be treated as desired or recommended schedules. In this event, proposals based upon the offeror's best alternative schedule, involving no overtime, extra shift or other premium, will be accepted for consideration.

c) **Personnel**

Describe the experience and qualifications of personnel who will be assigned for direct work on this program. Information is required which will show the composition of the task or work group, its general qualifications, and recent experience with similar equipment or programs. Special mention shall be made of direct technical supervisors and key technical personnel, and the approximate percentage of the total time each will be available for this program.

OFFERORS SHOULD ASSURE THAT THE PRINCIPAL INVESTIGATOR, AND ALL OTHER PERSONNEL PROPOSED, SHALL NOT BE COMMITTED ON FEDERAL GRANTS AND CONTRACTS FOR MORE THAN A TOTAL OF 100% OF THEIR TIME. IF THE SITUATION ARISES WHERE IT IS DETERMINED THAT A PROPOSED EMPLOYEE IS COMMITTED FOR MORE THAN 100% OF HIS OR HER TIME, THE GOVERNMENT WILL REQUIRE ACTION ON THE PART OF THE OFFEROR TO CORRECT THE TIME COMMITMENT.

(1) Principal Investigator/Project Director

List the name of the Principal Investigator/Project Director responsible for overall implementation of the contract and key contact for technical aspects of the project. Even though there may be co-investigators, identify the Principal Investigator/Project Director who will be responsible for the overall implementation of any awarded contract. Discuss the qualifications, experience, and accomplishments of the Principal Investigator/Project Director. State the estimated time to be spent on the project, his/her proposed duties, and the areas or phases for which he/she will be responsible.

(2) Other Investigators

List all other investigators/professional personnel who will be participating in the project. Discuss the qualifications, experience, and accomplishments. State the estimated time each will spend on the project, proposed duties on the project, and the areas or phases for which each will be responsible.

(3) Additional Personnel

List names, titles, and proposed duties of additional personnel, if any, who will be required for full-time employment, or on a subcontract or consultant basis. The technical areas, character, and extent of subcontract or consultant activity will be indicated and the anticipated sources will be specified and qualified. For all proposed personnel who are not currently members of the offeror's staff, a letter of commitment or other evidence of availability is required. A resume does not meet this requirement. Commitment letters for use of consultants and other personnel

to be hired must include:

-The specific items or expertise they will provide.

-Their availability to the project and the amount of time anticipated.

-Willingness to act as a consultant.

-How rights to publications and patents will be handled.

(4) Resumes

Resumes of all key personnel are required. Each must indicate educational background, recent experience, specific or technical accomplishments, and a listing of relevant publications.

(2) **Technical Evaluation**

Proposals will be technically evaluated in accordance with the factors, weights, and order of relative importance as described in the Technical Evaluation Criteria (See Section M of this solicitation).

(3) **Additional Technical Proposal Information**

a) Proposals which merely offer to conduct a program in accordance with the requirements of the Government's scope of work will not be eligible for award. The offeror must submit an explanation of the proposed technical approach in conjunction with the tasks to be performed in achieving the project objectives.

b) The technical evaluation is conducted in accordance with the weighted technical evaluation criteria by an initial review panel. This evaluation produces a numerical score (points) which is based upon the information contained in the offeror's proposal only.

(4) **Other Considerations**

Record and discuss specific factors not included elsewhere which support your proposal. Using specifically titled subparagraphs, items may include:

a) Any agreements and/or arrangements with subcontractor(s). Provide as much detail as necessary to explain how the statement of work will be accomplished within this working relationship.

b) Unique arrangements, equipment, etc., which none or very few organizations are likely to have which is advantageous for effective implementation of this project.

c) Equipment and unusual operating procedures established to protect personnel from hazards associated with this project.

d) Other factors you feel are important and support your proposed research.

e) Recommendations for changing reporting requirements if such changes would be more compatible with the offeror's proposed schedules.

<u>IMPORTANT NOTE TO OFFERORS</u>: The following 12 paragraphs (5) through (16) shall be addressed in a SEPARATE SECTION of the Technical Proposal entitled, "HUMAN SUBJECTS."

(5) **Human Subjects**

The following notice is applicable when contract performance is expected to involve risk to human subjects:

Notice to Offerors of Requirements of 45 CFR Part 46, Protection of Human Subjects (MARCH 2005)

(a) Copies of the Department of Health and Human Services (Department) regulations for the protection of human subjects, 45 CFR Part 46, are available from the Office for Human Research Protections (OHRP), Bethesda, Maryland 20892. The regulations provide a systematic means, based on established ethical principles, to safeguard the rights and welfare of individuals who participate as subjects in research activities supported or conducted by the Department.

(b) The regulations define a human subject as a living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with the individual, or identifiable private information. The regulations extend to the use of human organs, tissue, and body fluids from individually identifiable human subjects as well as to graphic, written, or recorded information derived from individually identifiable human subjects. The use of autopsy materials is governed by applicable State and local law and is not directly regulated by 45 CFR Part 46.

(c) Activities in which the only involvement of human subjects will be in one or more of the categories set forth in 45 CFR 46.101(b)(1-6) are exempt from coverage.

(d) Inappropriate designations of the noninvolvement of human subjects or of exempt categories of research in a project may result in delays in the review of a proposal. The OpDiv will make a final determination of whether the proposed activities are covered by the regulations or are in an exempt category, based on the information provided in the proposal. In doubtful cases, prior consultation with OHRP, (telephone: 301-496-7005), is recommended.

(e) In accordance with 45 CFR Part 46, prospective Contractors being considered for award shall be required to file with OHRP an acceptable Assurance of Compliance with the regulations, specifying review procedures and assigning responsibilities for the protection of human subjects. The initial and continuing review of a research project by an institutional review board shall assure that the rights and welfare of the human subjects involved are adequately protected, that the risks to the subjects are reasonable in relation to the potential benefits, if any, to the subjects and the importance of the knowledge to be gained, and that informed consent will be obtained by methods that are adequate and appropriate. The contracting officer will direct the offeror/contractor to the OHRP IRB Registration and Assurance Filing website, found at http://www.hhs.gov/ohrp/ or to the physical address if the offeror/contractor cannot access the Internet. HHS regulations for the protection of human subjects may be found at:

http://www.access.gpo.gov/nara/cfr/waisidx_01/45cfr46_01.html

(f) It is recommended that OHRP be consulted for advice or guidance concerning either regulatory requirements or ethical issues pertaining to research involving human subjects.

(End of provision)

(6) **Instructions to Offerors Regarding Protection of Human Subjects**

Offerors must address the following human subjects protections issues if this contract will be for research involving human subjects (note: under each of the following points below, the offeror should indicate whether the information provided relates to the primary research site, or to a collaborating performance site(s), or to all sites:

(a) Risks to the subjects

Human Subjects Involvement and Characteristics:

- Describe the proposed involvement of human subjects in response to the solicitation.

- Describe the characteristics of the subject population, including their anticipated number, age range, and health status.

- Identify the criteria for inclusion or exclusion of any subpopulation. Explain the rationale for the involvement of special classes of subjects, such as fetuses, pregnant women, children, prisoners, institutionalized individuals, or others who are likely to be vulnerable populations.

Sources of Materials:

- Identify the sources of research material obtained from individually identifiable living human subjects in the form of specimens, records, or data. Indicate whether the material or data will be obtained specifically for research purposes or whether use will be made of existing specimens, records, or data.

Potential Risks:

- Describe the potential risks to subjects (physical, psychological, social, legal, or other) and assess their likelihood and seriousness to the subjects.

- Describe alternative treatments and procedures, including the risks and benefits of the alternative treatments and procedures, to participants in the proposed research, where appropriate.

(b) Adequacy of Protection Against Risks

Recruitment and Informed Consent:

- Describe plans for the recruitment of subjects and the procedures for obtaining informed consent. Include a description of the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. The informed consent document for the contractor and any collaborating sites should be submitted only if requested elsewhere in the solicitation. Be aware that an IRB-approved informed consent document for the contractor and any participating collaborative sites must be provided to the Government prior to patient accrual or participant enrollment.

Protection Against Risk:

- Describe the procedures for protecting against or minimizing potential risks, including risks to confidentiality, and assess their likely effectiveness.

- Discuss provisions for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects where appropriate.

- In studies that involve interventions, describe the provisions for data and safety monitoring of the research to ensure the safety of subjects.

(c) Potential Benefits of the Proposed Research to the Subjects and Others

- Discuss the potential benefits of the research to the subjects and others.

- Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and others.

- Describe treatments and procedures that are alternatives to those provided to the participants by the proposed research, where appropriate.

(d) Importance of the Knowledge to be Gained

- Discuss the importance of the knowledge gained or to be gained as a result of the proposed research.

- Discuss why the risks to subjects are reasonable in relation to the importance of the knowledge that may reasonably be expected to result.

Note: If a test article (investigational new drug, device, or biologic) is involved, name the test article and state whether the 30-day interval between submission of offeror's certification to the Food and Drug Administration (FDA) and its response has elapsed or has been waived and/or whether the FDA has withheld or restricted use of the test article.

Collaborating Site(s)

When research involving human subjects will take place at collaborating site(s) or other performance site(s), the offeror must provide in this section of its proposal a list of the collaborating sites and their assurance numbers. Further, if you are awarded a contract, you must obtain in writing, and keep on file, an assurance from each site that the previous points have been adequately addressed at a level of attention that is at least as high as that documented at your organization. Site(s) added after an award is made must also adhere to the above requirements.

(7) **Required Education in the Protection of Human Research Participants**

NIH policy requires education on the protection of human subject participants for all investigators submitting NIH proposals for contracts for research involving human subjects. This policy announcement is found in the NIH Guide for Grants and Contracts Announcement dated June 5, 2000 at the following website: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html. Offerors should review the policy announcement prior to submission of their offers. The following is a summary of the Policy Announcement:

For any solicitation for research involving human subjects, the offeror shall provide in its technical proposal the following information: (1) a list of the names of the principal investigator and any other individuals proposed under the contract who are responsible for the design and/or conduct of the research; (2) the title of the education program completed (or to be completed prior to the award of the contract) for each named personnel; (3) a one sentence description of the program(s) listed in (2) above. This requirement extends to investigators and all individuals responsible for the design and/or conduct of the research who are working as subcontractors or consultants under the contract.

Curricula that are readily available and meet the educational requirement include the NIH on-line tutorial, titled "Protection of Human Research Subjects: Computer-Based Training for Researchers," available at http://ohsr.od.nih.gov/cbt/. You may download the information at this site at no cost and modify it, if desired. The University of Rochester has made its training program available for individual investigators. Completion of this program will also satisfy the educational requirement. The University of Rochester manual can be obtained through Centerwatch, Inc. at
http://www.centerwatch.com/order/pubs_profs_protect.html.
In addition, the NCI sponsors an online training course at:
http://cme.cancer.gov/clinicaltrials/learning/humanparticipant-protections.asp.
If an institution already has developed educational programs on the protection of research participants, completion of these programs also will satisfy the educational requirement.

In addition, prior to the substitution of the principal investigator or any other individuals responsible for the design and/or conduct of the research under the contract, the contractor shall provide the contracting officer with the title of the education program and a one sentence description of the program that the replacement has completed.

(8) **Inclusion of Women and Minorities in Research Involving Human Subjects**

It is NIH policy that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects involving human subjects, unless a clear and compelling

rationale and justification establishes to the satisfaction of the relevant Institute/Center Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. The Director, NIH, may determine that exclusion under other circumstances is acceptable, upon the recommendation of an Institute/Center Director, based on a compelling rationale and justification. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be routinely excluded from participation in clinical research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43), ***and applies to research subjects of all ages***.

All investigators proposing research involving human subjects should read the UPDATED "NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research, Amended October 2001," published in the NIH Guide for Grants and Contracts on October 9, 2001 at the following web site:
http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm

These guidelines contain a definition of **clinical research** adopted in June 2001, as: "(1) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Excluded from this definition are in vitro studies that utilize human tissues that cannot be linked to a living individual. Patient-oriented research includes (a) mechanisms of human disease, (b) therapeutic interventions, (c) clinical trials, and (d) development of new technologies; (2) Epidemiologic and behavioral studies; and (3) Outcomes research and health services research," at:
(http://www.nih.gov/news/crp/97report/execsum.htm).

Information Required for ALL Clinical Research Proposals

This solicitation contains a review criterion addressing the adequacy of: (1) the offeror's plans for inclusion of women and minorities in the research proposed; or (2) the offeror's justification(s) for exclusion of one or both groups from the research proposed.

Provide information on the composition of the proposed study population in terms of sex/gender and racial/ethnic groups and provide a rationale for selection of such subjects in response to the requirements of the solicitation. The description may include (but is not limited to) information on the population characteristics of the disease or condition being studied in the planned research, and/or described in the statement of work, national and local demography, knowledge of the racial/ethnic/cultural characteristics of the population, prior experience and collaborations in recruitment and retention of the populations and subpopulations to be studied, and the plans, arrangements and letters of commitment from relevant community groups and organizations for the planned research.

The proposal must include the following information:

- A description of the subject selection criteria
- The proposed dates of enrollment (beginning and end)
- A description of the proposed outreach programs for recruiting women and minorities as subjects
- A compelling rationale for proposed exclusion of any sex/gender or racial/ethnic group
- The proposed sample composition using the "Targeted/Planned Enrollment Table"(see Section J, Attachments)

NOTE 1: *For all proposals, use the ethnic and racial categories and complete the "Targeted/Planned Enrollment Table in accordance with the Office of Management and Budget (OMB) Directive No. 15, which may be found at: http://www.whitehouse.gov/OMB/fedreg/ombdir15.html.*

Standards for Collecting Data. When you, as a contractor, are planning data collection items on race and ethnicity, you shall use, at a minimum, the categories identified in OMB Directive No. 15. The collection of greater detail is encouraged. However, you should design any additional, more detailed items so that they can be aggregated into these required categories. Self-reporting or self-identification using two separate questions is the preferred method for collecting data on race and ethnicity. When you collect race and ethnicity separately, you must collect ethnicity first. You shall offer respondents the option of selecting one or more racial designations. When you collect data on race and ethnicity separately, you

shall also make provisions to report the number of respondents in each racial category who are Hispanic or Latino. When you present aggregate data, you shall provide the number of respondents who selected only one category, for each of the five racial categories. If you collapse data on multiple responses, you shall make available, at a minimum, the total number of respondents reporting "more than one race." Federal agencies shall not present data on detailed categories if doing so would compromise data quality or confidentiality standards.

In addition to the above requirements, solicitations for **NIH defined Phase III clinical trials**[1] require that: a) all proposals and/or protocols provide a description of plans to conduct analyses, as appropriate, to detect significant differences in intervention effect (see NIH Guide: http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm, Definitions - Significant Difference), by sex/gender, racial/ethnic groups, and relevant subpopulations, if applicable; and b) all contractors to report annually cumulative subject accrual, and progress in conducting analyses for sex/gender and race/ethnicity differences.

Offerors may obtain copies of the Updated Guidelines from the sources above or from the contact person listed in the solicitation.

Also, the proposal must include one of the following plans:

- Plans to conduct valid analysis to detect significant differences in intervention effect among sex/gender and/or racial/ethnic subgroups when prior studies strongly support these significant differences among subgroups, OR

- Plans to include and analyze sex/gender and/or racial/ethnic subgroups when prior studies strongly support no significant differences in intervention effect between subgroups, OR

- Plans to conduct valid analyses of the intervention effect in sex/gender and/or racial/ethnic subgroups (without requiring high statistical power for each subgroup) when the prior studies neither support nor negate significant differences in intervention effect between subgroups.

Use the form entitled, "Targeted/Planned Enrollment Table," when preparing your response to the solicitation requirements for inclusion of women and minorities. (See Section J-List of Documents, Exhibits and Other Attachments of the RFP)

Unless otherwise specified in this solicitation, the Government has determined that the work required by this solicitation does not involve a sex/gender specific study or a single or limited number of minority population groups. Therefore, the NIH believes that the inclusion of women and minority populations is appropriate for this project. (See Section M of this RFP for more information about evaluation factors for award.)

Use the form entitled, "Inclusion Enrollment Report," for reporting in the resultant contract.

(9) **Inclusion of Children in Research Involving Human Subjects**

It is NIH policy that children (defined below) must be included in all human subjects research, including, but not limited to, clinical trials, conducted under a contract funded by the NIH, unless there are *clear and compelling* reasons not to include them. (See examples of Justifications for Exclusion of Children below). For the purposes of this policy, contracts involving human subjects include categories that would otherwise be exempt from the DHHS Policy for Protection of Human Research Subjects (sections 101(b) and 401(b) of 45 CFR 46), such as surveys, evaluation of educational interventions, and studies of existing data or specimens that should include children as participants. This policy applies to both domestic and foreign research contracts.

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1 See NIH Guide http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm, for the Definition of an "NIH-Defined Phase III clinical trial.

For purposes of this policy, a child is defined as an individual under the age of 21 years.

All offerors proposing research involving human subjects should read the "NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects" which was published in the NIH Guide for Grants and Contracts on March 6, 1998 and is available at the following URL address:
http://www.nih.gov/grants/guide/notice-files/not98-024.html

Offerors also may obtain copies from the contact person listed in the RFP.

Inclusion of children as participants in research must be in compliance with all applicable subparts of 45 CFR 46 as well as other pertinent laws and regulations whether or not such research is otherwise exempted from 45 CFR 46. Therefore, any proposals must include a description of plans for including children, unless the offeror presents clear and convincing justification for an exclusion. The "Human Subjects" section of your technical proposal should provide either a description of the plans to include children and a rationale for selecting or excluding a specific age range of child, or an explanation of the reason(s) for excluding children as participants in the research. This solicitation contains a review criterion addressing the adequacy of: (1) the plans for including children as appropriate for the scientific goals of the research; and/or (2) the justification of exclusion of children or exclusion of a specific age range of children.

When children are included, the plan also must include a description of: (1) the expertise of the investigative team for dealing with children at the ages included; (2) the appropriateness of the available facilities to accommodate the children; and, (3) the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose/objective of the solicitation.

Justifications for Exclusion of Children

It is expected that children will be included in all research involving human subjects unless one or more of the following exclusionary circumstances can be fully justified:

- The objective of the solicitation is not relevant to children.

- There are laws or regulations barring the inclusion of children in the research to be conducted under the solicitation.

- The knowledge being sought in the research is already available for children or will be obtained from another ongoing study, and an additional study will be redundant. You should provide documentation of other studies justifying the exclusion.

- A separate, age-specific study in children is warranted and preferable. Examples include:
- The relative rarity of the condition in children, as compared with adults (in that extraordinary effort would be needed to include children); or
- The number of children is limited because the majority are already accessed by a nationwide pediatric disease research network; or
- Issues of study design preclude direct applicability of hypotheses and/or interventions to both adults and children (including different cognitive, developmental, or disease stages of different age-related metabolic processes); or
- Insufficient data are available in adults to judge potential risk in children (in which case one of the research objectives could be to obtain sufficient adult data to make this judgment). While children usually should not be the initial group to be involved in research studies, in some instances, the nature and seriousness of the illness may warrant their participation earlier based on careful risk and benefit analysis; or
- Study designs aimed at collecting additional data on pre-enrolled adult study subjects (e.g., longitudinal follow-up studies that did not include data on children);
- Other special cases justified by the offeror and found acceptable to the review group and the Institute Director

Definition of a Child

For the purpose of this solicitation, a child is defined as an individual under the age of 21 years. The definition of child described above will pertain to this solicitation (notwithstanding the FDA definition of a child as an individual from infancy to 16 years of age, and varying definitions employed by some states). Generally, State laws define what constitutes a "child," and such definitions dictate whether or not a person can legally consent to participate in a research study. However, State laws vary, and many do not address when a child can consent to participate in research. Federal Regulations (45 CFR 46, subpart D, Sec.401-409) address DHHS protections for children who participate in research, and rely on State definitions of "child" for consent purposes. Consequently, the children included in this policy (persons under the age of 21) may differ in the age at which their own consent is required and sufficient to participate in research under State law. For example, some states consider a person age 18 to be an adult and therefore one who can provide consent without parental permission.

(10) **Research Involving Prisoners as Subjects**

a. HHS Regulations at 45 CFR Part 46, Subpart C provide additional protections pertaining to biomedical and behavioral research involving prisoners or those individuals who, during the period of the contract become prisoners, as subjects. These regulations also set forth the duties of the Institutional Review Board (IRB) where prisoners are involved in the research. HHS-funded research involving prisoners as subjects may not proceed until the Office for Human Research Protections (OHRP) issues approval, in writing, as required by 45 CFR 46.306(a)(2). In addition, OHRP Guidance on the Involvement of Prisoners in Research may be found at:
http://ohrp.osophs.dhhs.gov/humansubjects/guidance/prisoner.htm

b. HHS Waiver for Epidemiological Research Involving Prisoners as Subjects

On June 20, 2003 the Secretary of HHS waived the applicability of certain provisions of Subpart C of 45 CFR Part 46, (Additional DHHS Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects) to specific types of epidemiological research involving prisoners as subjects.

The applicability of 45 CFR 46.305(a)(1) and 46.306(a)(2) for certain epidemiological research conducted or funded by DHHS is waived when:

1. The sole purposes are:

   a) to describe the prevalence or incidence of a disease by identifying all cases, or
   b) to study potential risk factor associations for a disease, and

2. The Institution responsible for the conduct of the research certifies to the OHRP that the Institutional Review Board (IRB) approved the research and fulfilled its duties under 45 CFR 46.305(a)(2-7) and determined and documented that:

   a) the research presents no more than minimal risk, and
   b) no more than inconvenience to the prisoner-subjects, and
   c) prisoners are not a particular focus of the research.

For more information about this Waiver see http://www.hhs.gov/ohrp/special/prisoners/Prisoner waiver 6-20-03.pdf

(11) **Research Involving Human Fetal Tissue**

Human Fetal Tissue means tissue or cells obtained from a dead human fetus, including human embryonic stem cells, human pluripotent stem cells and human embryonic germ cells.

The governing federal statute is the Public Health Service Act, 42 U.S.C. 289g-1 and 289g-2. Implementing regulations and guidance for conducting research on human fetal tissue may be found at

45 CFR 46, Subpart B and http://grants1.nih.gov/grants/guide/notice-files/not93-235.html and any subsequent revisions to this NIH Guide to Grants and Contracts ("Guide") Notice.

By signing the face page of the proposal, the offeror (authorized institutional official) certifies that researchers using human fetal tissue are in compliance with 42 USC 289g-2. This statute specifically prohibits any person from knowingly acquiring, receiving, or transferring any human fetal tissue for valuable consideration. "Valuable consideration" is a concept similar to profit, and does not include reasonable payment for costs associated with the collection processing, preservation, storage, quality control or transportation of these tissues.

Research involving the transplantation of human fetal tissue must be conducted in accordance with applicable Federal, State and local law.

(12) **Research Involving Recombinant DNA Molecules (including Human Gene Transfer Research)**

Recombinant DNA Molecules are either 1) molecules that are constructed outside of living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell, or 2) DNA molecules that result from the replication of those described in 1).

The NIH Guidelines for Research Involving Recombinant DNA Molecules (http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html and the May 28, 2002 Notice, Compliance with the NIH Guidelines for Research Involving Recombinant DNA Molecules, at: (http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-02-052.html) and any subsequent revisions to the Guide Notice) stipulates biosafety and containment measures for recombinant DNA research and delineates critical, ethical principles and key safety reporting requirements for human gene transfer research (See Appendix M of the NIH Guidelines). These guidelines apply to both basic and clinical research studies.

The Recombinant DNA Advisory Committee (RAC) is charged with the safety of manipulation of genetic material through the use of recombinant DNA techniques. Prior to beginning any clinical trials involving the transfer of recombinant DNA to humans, the trial must be registered with the RAC. If this contract involves new protocols that contain unique and//or novel issues, the RAC must discuss them in a public forum and then the Institutional Biosafety Committee (IBC), the Institutional Review Board (IRB), and the project officer and contracting officer must approve the protocol prior to the start of the research.

Failure to comply with these requirements may result in suspension, limitation, or termination of NIH funding for any work related to Recombinant DNA Research or a requirement for the contracting officer's prior approval of any or all Recombinant DNA projects under any contract awarded from this solicitation. This includes the requirements of the Standing Institutional Biosafety Committee (IBC) (See http://www4.od.nih.gov/oba/IBC/IBCindexpg.htm).

As specified in Appendix M-1-C-4 of the NIH Guidelines, any serious adverse event must be reported immediately to the IRB, the IBC, the Office for Human Research Protections (if applicable), and the NIH Office for Biotechnology Activities (OBA), followed by the filing of a written report with each office/group and copies to the project officer and contracting officer. (http://www4.od.nih.gov/oba/rac/guidelines_02/Appendix_M.htm#_Toc7255836)

(13) **Human Embryonic Germ Cell (HEGC) Research**

1. Guidelines.

Research use of human embryonic germ cells derived from fetal tissue with Federal funds requires review of compliance with the NIH Guidelines for Research Using Human Pluripotent Stem Cells (http://stemcells.nih.gov/policy/guidelines.asp) (only the information regarding human embryonic germ cells is relevant). Embryonic germ cells are pluripotent stem cells derived from human embryos. See NIH Guide for Grants and Contracts Notice NOT-OD-02-049, requiring that offerors/contractors submit certain documents to the Human Pluripotent Stem Cell Review Group (HPSCRG), which will be reviewed in a public meeting. Research using human embryonic germ

cells may not be performed prior to approval by the HPSCRG.

All offerors should read the "NIH Guidelines" (http://stemcells.nih.gov/policy/guidelines.asp) if they either: (1) propose to respond to the Statement of Work requirements by conducting research that uses human embryonic germ cells or, (2) are responding to a Statement of Work that requires the use of human embryonic germ cells.

Offerors may obtain copies of these Guidelines from the website above or from the contact person listed in this solicitation.

2. Procedure for Review by Human Pluripotent Stem Cell Review Group (HPSCRG)

If, in response to the solicitation, the offeror proposes to use human embryonic germ cells, it must submit, as a separate attachment to its proposal, an original and two copies of the documentation and assurances that address the areas covered in the "Procedures for Submission of Compliance Documents to the Human Pluripotent Stem Cell Review Group (HPSCRG) for the Research Use of Human Embryonic Germ Cells," at:
(http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-02-049.html).
Prior to any award made under this solicitation, the documentation and assurances will be subject to review by the HPSCRG, which meets in a public meeting. No research involving the use of human embryonic germ cells may begin prior to HPSCRG approval.

Offerors are encouraged to review issues pertaining to informed consent processes described in Section II.B.2.b of the NIH Guidelines. Offerors should also review the March 19, 2002, DHHS Office of Human Research Protection's document titled "Guidance for Investigators and Institutional Review Boards Regarding Research Involving Human Embryonic Stem Cells, Germ Cells, and Stem Cell-Derived Test Articles," (http://stemcells.nih.gov/news/newsArchives/stemcell.pdf)

(14) **Human Embryonic Stem Cell (HESC) Research**

On August 9, 2001, the President announced the criteria that must be met for Federal funds to be used for research on existing human embryonic stem cell lines. These criteria were subsequently published by the NIH at: http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html. The following eligibility criteria must be met:

1. The derivation process (which commences with the removal of the inner cell mass from the blastocyst) must have already been initiated prior to August 9, 2001;
2. Prior to August 9, 2001, the embryo from which the stem cell line was derived no longer had the possibility of development as a human being;
3. The stem cells must have been derived from an embryo that was created for reproductive purposes;
4. The embryo was no longer needed for these purposes;
5. Informed consent must have been obtained for the donation of the embryo;
6. No financial inducements were provided for the donation of the embryo.

To facilitate research using human embryonic stem cells, the NIH has established a Human Embryonic Stem Cell Registry ("the NIH Registry") that lists the human embryonic stem cells that meet the eligibility criteria. This registry is available at: http://stemcells.nih.gov/registry/.

Research involving the derivation of new stem cells from human embryos or the use of human embryonic stem cells that are not listed on the NIH Human Embryonic Stem Cell Registry may not be conducted with Federal funding.

If a particular human embryonic stem cell line has not been required by the Statement of Work, an offeror proposing research involving human embryonic stem cells must cite a human embryonic stem cell line that is listed in the NIH Registry in its proposal.

(15) **Data and Safety Monitoring in Clinical Trials**

All offerors are directed to the full text of the NIH Policies regarding Data and Safety Monitoring and Reporting of Adverse Events that are found in the NIH Guide for Grants and Contracts Announcements at the following web sites:

http://grants.nih.gov/grants/guide/notice-files/not98-084.html
http://grants.nih.gov/grants/guide/notice-files/not99-107.html
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html

All offerors receiving an award under this solicitation must comply with the NIH Policy cited in these NIH Announcements and any other data and safety monitoring requirements found elsewhere in this solicitation.

The following is a brief summary of the Data and Safety Monitoring and Adverse Event Reporting Requirements:

Data and Safety Monitoring is required for every clinical trial. Monitoring must be performed on a regular basis and the conclusions of the monitoring reported to the Project Officer.

The type of data and safety monitoring required will vary based on the type of clinical trial and the potential risks, complexity and nature of the trial. A plan for data and safety monitoring is required for all clinical trials. A general description of a monitoring plan establishes the overall framework for data and safety monitoring. It should describe the entity that will be responsible for the monitoring, and the policies and procedures for adverse event reporting. Phase III clinical trials generally require the establishment of a Data Safety Monitoring Board (DSMB). The establishment of a DSMB is optional for Phase I and Phase II clinical trials.

The DSMB/Plan is established at the time the protocol is developed and must be approved by both the Institutional Review Board (IRB) and the Government and in place before the trial begins. If the protocol will be developed under the contract awarded from this solicitation, a general description of the data and safety monitoring plan must be submitted as part of the proposal and will be reviewed by the scientific review group (Technical Evaluation Panel, (TEP)) convened to evaluate the proposal. If the protocol is developed and is included as part of the submitted proposal, a complete and specific data and safety monitoring plan must be submitted as part of the proposal.

Monitoring Plans, at a minimum, must include the prompt reporting of adverse events to the IRB, the NIH Office of Biotechnology Activities (OBA), and the Food and Drug Administration (FDA). Also, in the plan you should describe the frequency of reporting of the conclusions of the monitoring activities. The overall elements of each plan may vary depending on the size and complexity of the trial. The NIH Policy for Data and Safety Monitoring at http://grants.nih.gov/grants/guide/notice-files/not98-084.html describes examples of monitoring activities to be considered.

The frequency of monitoring will depend upon potential risks, complexity, and the nature of the trial; therefore a number of options for monitoring trials are available. These can include, but are not limited to, monitoring by a:

- Principal Investigator (required)
- Independent individual /Safety Officer
- Designated medical monitor
- Internal Committee or Board with explicit guidelines
- Data and Safety Monitoring Board (DSMB - required for multisite trials)
- Institutional Review Board (IRB - required)

For multi-site Phase I and Phase II trials, a central reporting entity that will be responsible for preparing timely summary reports of adverse events for distribution among sites and IRBs should be considered.

Organizations with a large number of clinical trials may develop standard monitoring plans for Phase I and Phase II trials. In this case, such organizations may include the IRB-approved monitoring plan as part of the proposal submission.

(16) **Care of Live Vertebrate Animals**

a. The following notice is applicable when contract performance is expected to involve care of live vertebrate animals:

Notice to Offerors of Requirement for Compliance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals (Revised 1986, Reprinted 2000)

The Public Health Service (PHS) Policy on Human Care and Use of Laboratory Animals establishes a number of requirements for research activities involving animals. Before a PHS award may be made to an applicant organization, the organization shall file, with the Office of Extramural Research (OER), Office of Laboratory Animal Welfare (OLAW), National Institutes of Health (NIH), PHS, a written Animal Welfare Assurance which commits the organization to comply with the provisions of the PHS Policy on Humane Care and Use of Laboratory Animals by Awardee Institutions, the Animal Welfare Act, and the Guide for the Care and Use of Laboratory Animals prepared by the Institute of Laboratory Animal Resources. In accordance with the PHS Policy on Humane Care and Use of Laboratory Animals by Awardee Institutions, applicant organizations must establish a committee, qualified through the experience and expertise of its members, to oversee the institution's animal program, facilities and procedures. No PHS award involving the use of animals shall be made unless the Animal Welfare Assurance has been approved by OER, OLAW. Prior to award, the Contracting Officer will notify Contractor(s) selected for projects that involve live vertebrate animals that an Animal Welfare Assurance is required. The Contracting Officer will request that OER, OLAW negotiate an acceptable Animal Welfare Assurance with those Contractor(s). For further information, OER, OLAW, may be contacted at Rockledge Center I - Suite 1050, 6705 Rockledge Drive, Bethesda, MD 20817, (301) 496-7163, ext 234. FAX copies are of the PHS Policy are available at (301) 402-2803. This policy is also available on the internet at http://www.grants.nih.gov/grants/olaw/olaw.htm.

b. The following information must be included in the offerors technical proposal:

- identification of the species and approximate number of animals to be used;
- rationale for involving animals, and for the appropriateness of the species and numbers used;
- a complete description of the proposed use of the animals;
- a description ofprocedures designed to assure that discomfort and injury to animals will be limited to that which is unavoidable in the conduct of scientifically valuable research, and that analgesic, anesthetic, and tranquilizing drugs will be used where indicated and appropriate to minimize discomfort and pain to animals; and
- a description of any euthanasia method to be used.

c. If an Animal Assurance is already in place, the offeror's proposal shall include:

-The Animal Welfare Assurance number.
-The date last certified by OLAW. (i.e. assurance letter from OLAW)
-Evidence of recent AAALAC Accreditation.

(17) **Possession, Use and Transfer of Select Biological Agents or Toxins**

Notice to Offerors of Requirements of: 42 CFR Part 73, Possession , Use, and Transfer of Select Agents and Toxins (relating to public health and safety):
(http://www.cdc.gov/od/sap/42_cfr_73_final_rule.pdf);

7 CFR Part 331, Possession, Use, and Transfer of Select Agents and Toxins (relating to plant health or plant products) (http://www.aphis.usda.gov/programs/ag_selectagent/FinalRule3-18-05.pdf); and, 9 CFR Part 121, Possession, Use, and Transfer of Select Agents and Toxins (relating to human and animal health, animal health or animal products) (http://www.aphis.usda.gov/programs/ag_selectagent/FinalRule3-18-05.pdf) - March 18, 2005.

These regulations implement the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, and the Agricultural Bioterrorism Protection Act of 2002. They are designed to improve the ability of the United States Government to prevent, prepare for, and respond to bioterrorism and other public health emergencies. These regulations establish requirements regarding registration, security risk assessments, safety plans, security plans, emergency response plans, training, transfers, record keeping, inspections, and notifications.

Listings of HHS select agents and toxins, and overlap select agents or toxins as well as information about the registration process for domestic institutions, are available on the Select Agent Program Web site at http://www.cdc.gov/od/sap/ and http://www.cdc.gov/od/sap/docs/salist.pdf. Listings of USDA select agents and toxins as well as information about the registration process for domestic institutions are available on the APHIS/USDA website at http://www.aphis.usda.gov/programs/ag_selectagent/index.html and http://www.aphis.usda.gov/programs/ag_selectagent/ag_bioterr_forms.html. For foreign institutions, see the NIAID Select Agent Award information (http://www.niaid.nih.gov/ncn/clinical/default_biodefense.htm).

If the proposed contract will not involve Select Agents, the offeror must include a statement in its technical proposal that the work does not now nor will it in the future (i.e. throughout the life of the award) involve Select Agents.

Domestic Institutions

For prime or subcontract awards to domestic institutions that possess, use, and/or transfer Select Agents under this contract, the domestic institution must:

- include details about the select agent in their technical proposal, including the quantity proposed to be used during contract performance.

- comply with 42 CFR part 73, 7 CFR part 331 and/or 9 CFR part 121 at: http://www.aphis.usda.gov/programs/ag_selectagent/FinalRule3-18-05.pdf, as required, before using NIH funds for research involving Select Agents. No NIH funds can be used for research involving Select Agents if the final registration certificate is denied.

Foreign Institutions

For prime or subcontract awards to foreign institutions that possess, use, and/or transfer Select Agents under this contract, the foreign institution must:

- include details about the select agent in their technical proposal, including the quantity proposed to be used during contract performance.

- when requested during negotiations, provide information satisfactory to the NIAID/NIH that safety, security, and training standards equivalent to those described in 42 CFR part 73, 7 CFR part 331, and/or 9 CFR part 121 at: http://www.aphis.usda.gov/programs/ag_selectagent/FinalRule3-18-05.pdf for U.S. institutions are in place and will be administered on behalf of all Select Agent work under the resulting contract. The process for making this determination includes inspection of the foreign laboratory facility by an NIAID representative. During this inspection, the foreign institution must provide the following information: concise summaries of safety, security, and training plans; names of all individuals at the foreign institution who will have access to the Select Agents and procedures for ensuring that only approved and appropriate individuals, in accordance with institution procedures, will have access to the Select Agents under the contract; and copies of or links to any

applicable laws, regulations, policies, and procedures applicable to that institution for the safe and secure possession, use, and/or transfer of select agents.

An NIAID-chaired committee of U.S. federal employees (including representatives of NIH grants/contracts and scientific program management, CDC , Department of Justice and other federal intelligence agencies, and Department of State) will ultimately assess the results of the facility inspection, the regulations, policies, and procedures of the foreign institution for equivalence to the U.S. requirements described in 42 CFR part 73, 7 CFR part 331, and/or 9 CFR part 121 at:
http://www.aphis.usda.gov/programs/ag_selectagent/FinalRule3-18-05.pdf.
The committee will provide recommendations to the DEA Director, NIAID. The DEA Director will make the approval decision and notify the Contracting Officer. The Contracting Officer will inform the prime contractor of the approval status of the foreign institution. No NIH funds can be used for research involving Select Agents at a foreign institution until NIAID grants this approval.

(a) **Sharing Research Data**

*[Note: This policy applies to **all** NIH contracts, regardless of dollar value, that are expected to generate research data.]*

The NIH endorses the sharing of final research data to expedite the translation of research results into knowledge, products, and procedures to improve human health. This contract is expected to generate research data. Therefore, the offeror must submit a plan in its technical proposal for data sharing or state why data sharing is not possible. If data sharing is limited, the offeror should explain such limitations in its data sharing plan. NIH's data sharing policy may be found at the following Web site:

http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html

[If the resultant contract is part of a collaborative program involving multiple sites, the data sharing will be governed by a dissemination plan to be developed jointly following award. Offerors must include in their proposals a statement of willingness to work collaboratively after award with the other funded sites to prepare a joint dissemination plan. Coordinating Center proposals should describe methods to coordinate the dissemination planning and implementation. The Coordinating Center must include a budget and justification for any additional costs of this collaborative effort.]

(18) **Information Technology Systems Security**

IMPORTANT NOTE TO OFFERORS: The following information shall be addressed in a separate section of the Technical Proposal entitled, "Information Security."

The Statement of Work (SOW) requires the successful offeror to develop or access Federal automated information systems. Pursuant to the DHHS Information Security Program Policy (http://www.hhs.gov/read/irmpolicy/FINALHHSInformationSecurityProgramP.doc), the following requirements apply:

(a) Information Type

[x] Administrative, Management and Support Information:

[ ] Mission Based Information:

(b) Security Categories and Levels

Confidentiality	Level:	**[x]** Low	**[ ]** Moderate	**[ ]** High
Integrity	Level:	**[x]** Low	**[ ]** Moderate	**[ ]** High
Availability	Level:	**[x]** Low	**[ ]** Moderate	**[ ]** High
Overall	**Level:**	**[x] Low**	**[ ] Moderate**	**[ ] High**

(c) Position Sensitivity Designations

Prior to award, the Government will determine the position sensitivity designation for each contractor employee that the successful offeror proposes to work under the contract. For proposal preparation purposes, the following designations apply:

[ ] Level 6: Public Trust - High Risk (Requires Suitability Determination with a BI). Contractor employees assigned to a Level 6 position are subject to a Background Investigation (BI).

[ ] Level 5: Public Trust - Moderate Risk (Requires Suitability Determination with NACIC, MBI or LBI). Contractor employees assigned to a Level 5 position with no previous investigation and approval shall undergo a National Agency Check and Inquiry Investigation plus a Credit Check (NACIC), a Minimum Background Investigation (MBI), or a Limited Background Investigation (LBI).

[x] Level 1: Non Sensitive (Requires Suitability Determination with an NACI). Contractor employees assigned to a Level 1 position are subject to a National Agency Check and Inquiry Investigation (NACI).

Upon award, the contractor will be required to submit a roster of all IT staff working under the contract. The Government will determine the appropriate level of suitability investigation required for each staff member.

Contractor employees who have met investigative requirements within the past five years may only require an updated or upgraded investigation.

(d) Systems Security Plan

The offeror's proposal must:

(1) Include a detailed plan of its present and proposed systems security programs commensurate with the size and complexity of the requirements of the Statement of Work. Offerors must use:
NIH Systems Security Plan Template (detailed) at:
http://irm.cit.nih.gov/security/secplantemp.doc; or
NIH Systems Security Plan Outline (outline only) at:
http://irm.cit.nih.gov/nihsecurity/Security_Plan_Outline.doc.

OR

(1) Include a plan commensurate with the size and complexity of the requirements of the Statement of Work. The minimum areas to be addressed include, but are not limited to administrative, technical, and physical security as follows:

(i) Security Awareness Training
(ii) Logical Access Control
-Network (ex: firewall)
-System (ex: network OS, tcp wrappers, SSH)
-Application (ex: S-LDAP, SSL)
-Remote Access (ex: VPN)
-Monitoring and support (ex: IDS, pager, NOC)
(iii) Protection against data loss
-OS security (ex: patch management, configuration)
-Application security (ex: patch management)
-Database security
-Back-up and recovery
-Fault tolerance, high availability
(iv) Malicious Code Protection (ex: Antivirus, filtering of e-mail attachments, etc)
(v) Physical Security

-Access control (ex: locks, guards)
-Power conditioning and/or UPS
-Air conditioning
-Fire protection

Include an acknowledgment of its understanding of the security requirements.
Provide similar information for any proposed subcontractor developing or accessing an AIS.

The SSP that the offeror must submit with its proposal shall be finalized in coordination with the Project Officer no later than 90 calendar days after contract award.

(e) Information Systems Security Training

DHHS policy requires contractors receive security training commensurate with their responsibilities for performing work under the terms and conditions of their contractual agreements.

The successful offeror will be responsible for assuring that each contractor employee has completed the NIH Computer Security Awareness Training course(http://irtsectraining.nih.gov/) prior to performing any contract work, and on an annual basis thereafter, during the period of performance of the contract. The successful offeror shall maintain a listing of all individuals who have completed this training and shall submit this listing to the Project Officer.

Additional security training requirements commensurate with the position may be required as defined in NIST Special Publication 800-16, Information Technology Security Training Requirements (http://csrc.nist.gov/publications/nistpubs/800-16/800-16.pdf). This document provides information about information security training that may be useful to potential offerors.

c. BUSINESS PROPOSAL INSTRUCTIONS

(1) Basic Cost/Price Information

The business proposal must 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 basic elements of the proposed cost or price. These elements will include, as applicable, direct labor, fringe benefits, travel, materials, subcontracts, purchased parts, shipping, indirect costs and rate, fee, and profit.

(2) Proposal Cover Sheet

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

1. Solicitation, contract, and/or modification number;
2. Name and address of Offeror;
3. Name and telephone number of point of contact;
4. Name, address, and telephone number of Contract Administration Office, (if available);
5. Name, address, and telephone number of Audit Office (if available);
6. Proposed cost and/or price; profit or fee (as applicable); and total;
7. 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.
8. Date of submission; and
9. Name, title and signature of authorized representative.

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.

(3) Information Other than Cost or Pricing Data

a) The information submitted shall consist of data to permit the Contracting Officer and authorized representatives to determine price reasonableness or cost realism, e.g., information to support an analysis of material costs (when sufficient information on labor and overhead rates is already available), or information on prices and quantities at which the offeror has previously sold the same or similar items.

Any information submitted must support the price proposed. Include sufficient detail or cross references to clearly establish the relationship of the information provided to the price proposed. Support any information provided by explanations or supporting rational as needed to permit the Contracting Officer and authorized representative to evaluate the documentation.

[Unless otherwise stated in this solicitation, the information may be submitted in the offeror's own format.]

(4) Requirements for Cost or Pricing Data or Information Other than Cost and Pricing Data [FAR Clause 52.215-20 (October 1997)]

(a) Exceptions from cost or pricing data.

(1) In lieu of submitting cost or pricing data, offerors may submit a written request for exception by submitting the information described in the following subparagraphs. The Contracting Officer may require additional supporting information, but only to the extent necessary to determine

whether an exception should be granted, and whether the price is fair and reasonable.

(i) Identification of the law or regulation establishing the price offered. If the price is controlled under law by periodic rulings, reviews, or similar actions of a governmental body, attach a copy of the controlling document, unless it was previously submitted to the contracting office.

(ii) Commercial item exception. For a commercial item exception, the offeror shall submit, at a minimum, information on prices at which the same item or similar items have previously been sold in the commercial market that is adequate for evaluating the reasonableness of the price for this acquisition. Such information may include--

(A) For catalog items, a copy of or identification of the catalog and its date, or the appropriate pages for the offered items, or a statement that the catalog is on file in the buying office to which the proposal is being submitted. Provide a copy or describe current discount policies and price lists (published or unpublished), e.g., wholesale, original equipment manufacturer, or reseller. Also explain the basis of each offered price and its relationship to the established catalog price, including how the proposed price relates to the price of recent sales in quantities similar to the proposed quantities;

(B) For market-priced items, the source and date or period of the market quotation or other basis for market price, the base amount, and applicable discounts. In addition, describe the nature of the market;

(C) For items included on an active Federal Supply Service Multiple Award Schedule contract, proof that an exception has been granted for the schedule item.

(2) The offeror grants the Contracting Officer or an authorized representative the right to examine, at any time before award, books, records, documents, or other directly pertinent records to verify any request for an exception under this provision, and the reasonableness of price. For items priced using catalog or market prices, or law or regulation, access does not extend to cost or profit information or other data relevant solely to the offeror's determination of the prices to be offered in the catalog or marketplace.

(b) Requirements for cost or pricing data. If the offeror is not granted an exception from the requirement to submit cost or pricing data, the following applies:

(1) The offeror shall prepare and submit cost or pricing data and supporting attachments in accordance with Table 15-2 of FAR 15.408.

(2) As soon as practicable after agreement on price, but before contract award (except for unpriced actions such as letter contracts), the offeror shall submit a Certificate of Current Cost or Pricing Data, as prescribed by FAR 15.406-2.

(End of provision)

Alternate I (October 1997). As prescribed in 15.408(l), substitute the following paragraph (b)(1) for paragraph (b)(1) of the basic provision:

(b)(1) The offeror shall submit cost or pricing data and supporting attachments in the following format:

The format specified in paragraph L.2.c.(4) Cost and Pricing Data, subparagraph 3. Formats for Submission of Line Item Summaries shall be used for the submission cost information. Submission of all other cost or pricing data shall be in accordance with Table 15-2 in FAR 15.408.

(5) **Salary Rate Limitation in Fiscal Year 2006**

Offerors are advised that pursuant to P.L. 109-149, no NIH Fiscal Year 2006 (October 1, 2005 - September 30, 2006) funds may be used to pay the direct annual salary of an individual through any contract awarded as a result of this solicitation at a rate in excess of the Executive Schedule, Level I* (direct salary is exclusive of Overhead, Fringe Benefits and General and Administrative expenses, also referred to as "indirect cost" or "facilities and administrative (F&A) costs"). Direct salary has the same meaning as the term "institutional base salary." An individual's direct salary (or institutional base salary) is the annual compensation that the contractor pays for an individual's appointment whether that individual's time is spent on research, teaching, patient care or other activities. Direct salary (or institutional base salary) excludes any income that an individual may be permitted to earn outside of duties to the contractor.

This does not preclude the offeror from absorbing that portion of an employee's annual salary (plus the dollar amount for fringe benefits and associated indirect costs) that exceeds a rate of the Executive Schedule, Level I*. The salary rate limitation set by P.L. 109-149 applies only to Fiscal Year 2006 funds, however, salary rate ceilings for subsequent years may be included in future DHHS appropriation acts. Multi-year contracts awarded pursuant to this solicitation may be subject to unilateral modifications by the Government if an individual's annual salary exceeds any salary rate ceiling established in future appropriations acts. The Executive Schedule, Level I* annual salary rate limit also applies to individuals proposed under subcontracts, however it does not apply to consultants. P.L. 109-149 states in pertinent part:

> "None of the funds appropriated in this Act for the National Institutes of Health, the Agency for Healthcare Research and Quality, and the Substance Abuse, and Mental Health Services Administration shall be used to pay the salary of an individual through a grant or other extramural mechanism at a rate in excess of Executive Level I*."

LINK TO EXECUTIVE SCHEDULE SALARIES: http://www.opm.gov/oca/06tables/indexSES.asp

***Note to Offerors:** The current Fiscal Year Executive Level I Salary Rate should be adhered to in the preparation of your proposal. All costs associated with any resultant contract award shall be in compliance with the current Fiscal Year 2006 Executive Level I Salary rates.*

(6) **Small Business Subcontracting Plan**

If the proposed contract exceeds a total estimated cost of $500,000 for the entire period of performance, the apparent successful offeror shall be required to submit an acceptable subcontracting plan in accordance with the terms of the clause entitled "Small Business Subcontracting Plan," FAR Clause No. 52.219-9, incorporated herein by reference in the Solicitation, Attachment to this RFP is an example of such a plan.

a) THIS PROVISION DOES NOT APPLY TO SMALL BUSINESS CONCERNS.

b) The term "subcontract" means any agreement (other than one involving an employer-employee relationship) entered into by a Federal Government prime contractor or subcontractor calling for supplies or services required for the performance of the original contract or subcontract. This includes, but is not limited to, agreements/purchase orders for supplies and services such as equipment purchase, copying services, and travel services.

c) The offeror understands that:

(1) No contract will be awarded unless and until an acceptable plan is negotiated with the Contracting Officer which plan will be incorporated into the contract, as a material part thereof.

(2) An acceptable plan must, in the determination of the Contracting Officer, provide the maximum

practicable opportunity for Small Businesses, Small Disadvantaged Businesses, Women-Owned Small businesses, HubZone Small Businesses, Veteran-Owned Small Businesses, and Service Disabled Veteran-Owned Small Businesses to participate in the performance of the contract.

(3) If a subcontracting plan acceptable to the Contracting Officer is not negotiated within the time limits prescribed by the contracting activity and such failure arises out of causes within the control and with the fault or negligence of the offeror, the offeror shall be ineligible for an award. The Contracting Officer shall notify the Contractor in writing of the reasons for determining a subcontracting plan unacceptable early enough in the negotiation process to allow the Contractor to modify the plan within the time limits prescribed.

(4) Prior compliance of the offeror with other such subcontracting plans under previous contracts will be considered by the Contracting Officer in determining the responsibility of the offeror for award of the contract.

(5) It is the offeror's responsibility to develop a satisfactory subcontracting plan with respect to Small Business Concerns, Small Disadvantaged Business Concerns, Women-Owned Small Business Concerns, HubZone Small Business Concerns, Veteran-Owned Small Business Concerns, and Service Disabled Veteran-Owned Small Business Concerns that each such aspect of the offeror's plan will be judged independent of the other.

(6) The offeror will submit, as required by the Contracting Officer, subcontracting reports in accordance with the instructions thereon, and as further directed by the Contracting Officer. Subcontractors will also submit these reports to the Government's Contracting Officer or as otherwise directed, with a copy to the prime Contractor's designated small and disadvantaged business liaison.

d) Each plan must contain the following:

(1) Goals, expressed in terms of percentages of total planned subcontracting dollars, for the use of Small, Small Disadvantaged, Women-Owned, HUBZone, Veteran-Owned, and Service Disabled Veteran-Owned Small Business Concerns as subcontractors.

(2) A statement of total dollars planned to be subcontracted. A statement of total dollars to be subcontracted to each of the following type of small business concerns: Small, Small Disadvantaged, Women-Owned, HUBZone, Veteran-Owned, and Service Disabled Veteran-Owned Small Businesses.

(3) A description of the principal types of supplies and services to be subcontracted with an identification of which supplies and services are expected to be subcontracted to Small, Small Disadvantaged, Women-Owned, HUBZone, Veteran-Owned, and/or Service Disabled Veteran-Owned Small Business Concerns.

(4) A description of the method used to develop the subcontracting goals.

(5) A description of the method used to identify potential sources for solicitation purposes.

(6) A statement as to whether or not indirect costs were included in establishing subcontracting goals. If they were, a description of the method used to determine the proportionate share of indirect costs to be incurred with Small, Small Disadvantaged, Women-Owned, HUBZone, Veteran-Owned, and Service Disabled Veteran-Owned Small Businesses.

(7) The name of the individual employed by the offeror who will administer the offeror's subcontracting program and a description of his/her duties.

(8) A description of the efforts the offeror will make to assure that Small, Small Disadvantaged, Women-Owned, HUBZone, Veteran-Owned, and Service Disabled Veteran-Owned Small

Businesses have an equitable chance to compete for subcontracts.

(9) Assurances that the offeror will include in all subcontracts the contract clause "Utilization of Small Business Concerns." Assure that all subcontractors, other than small businesses, in excess of $500,000 adopt a plan similar to the plan agreed upon by the offeror.

(10) Assurances that the offeror (and any required subcontractors) will cooperate in studies or surveys as required and submit required reports (SF 294 and SF 295) to the Government.

(11) List the types of records the offeror will maintain to demonstrate procedures that have been adopted to comply with the requirement and goals in the plan, including establishing source lists. Also, the offeror shall describe its efforts to locate Small, Small Disadvantaged, Women-Owned, HUBZone, Veteran-Owned, and Service Disabled Veteran-Owned Small Businesses and award subcontracts to them.

For additional information about each of the above elements required to be contained the subcontracting plan, see FAR Clause 52.219-9, Small Business Subcontracting Plan, and the Sample Subcontracting Plan which is provided as an attachment to this RFP in SECTION J.

HHS expects each procuring activity to establish minimum subcontracting goals for all procurements. The anticipated minimum goals for this RFP are as follows:

23% for Small Business.
5% for Small Disadvantaged Business.
5% for Women-Owned Small Business.
3% for HUBZone Small Business.
3% for Veteran-Owned Small Business and Service-Disabled Veteran-Owned Small Business.

(7) **HUBZone Small Business Concerns**

Small Business offerors located in underutilized business zones, called "HUBZones," will be evaluated in accordance with FAR Clause 52.219-4, NOTICE OF PRICE EVALUATION PREFERENCE FOR HUBZONE SMALL BUSINESS CONCERNS, which is incorporated by reference in ARTICLE I.3. of this solicitation. Qualified HUBZone firms are identified in the Small Business Administration website at http://www.sba.gov/hubzone.

(8) **Extent of Small Disadvantaged Business Participation**

In accordance with FAR Subpart 15.304(c)(4), the extent of participation of Small Disadvantaged Business (SDB) concerns in performance of the contract in the authorized NAICS Subsectors shall be evaluated in unrestricted competitive acquisitions expected to exceed $500,000 ($1,000,000 for construction) subject to certain limitations (see FAR 19.1202-1 and 19.1202-2(b). The dollar amounts cited above include any option years/option quantities that may be included in this solicitation. The definition of a "small disadvantaged business" is cited in FAR 19.001.

The factor entitled “Extent of Small Disadvantaged Business Participation” as set forth under the Evaluation Criteria in Section M shall be used for evaluation purposes.

The Department of Commerce determines, on an annual basis, by Subsectors, as contained in the North American Industry Classification System (NAICS) code, and region, if any, the authorized SDB procurement mechanisms and applicable factors (percentages). TheNAICS codes can be found at:
http://www.sba.gov/size

The Department of Commerce website for the annual determination for NAICS codes* is:
http://www.arnet.gov/References/sdbadjustments.htm.

**Note: Public Law 103-355 which authorized the SDB Price Evaluation Adjustment (PEA) and associated percentages/factors expired on December 9, 2004, therefore, the percentages shown at this website are no longer applicable.*

Offerors shall include with their offers, SDB targets, expressed as dollars and percentages of total contract value, in each of the applicable, authorized NAICS Subsector(s). The applicable authorized NAICS Subsector(s) for this project is (are) identified elsewhere in this RFP. A total target for SDB participation by the prime contractor, that includes any joint ventures and team members, shall be provided as well as a total target for SDB participation by subcontractors. In addition, offerors must provide information that describes their plans for meeting the targets set forth in their proposal. **This information shall be provided in one clearly marked section of the Business Proposal, which shall describe the extent of participation of SDB concerns in the performance of the contract.**

If the evaluation factor in this solicitation includes an SDB evaluation factor or subfactor that considers the extent to which SDB concerns are specifically identified, the SDB concerns considered in the evaluation shall be listed in any resultant contract. Offerors should note that addressing the extent of small disadvantaged business participation **is not in any way intended to be a substitute** for submission of the subcontracting plan, if it is required by this solicitation. An example of the type of information that might be given (in addition to the narrative describing the plan for meeting the targets) follows:

EXAMPLE

Targets for SDB Participation - NAICS Subsector 223

	SDB Percentage of Total Contract Value	**SDB Dollars**
Total Contract Value- $1,000,000	25%	$250,000
SDB Participation by Prime	10%	$100,000
(Includes joint venture partners and team arrangements)*		
SDB Participation by subcontractors	15%	$150,000

*Note: FAR Subpart 9.6 defines “Contractor team arrangements” to include two or more companies forming a partnership or joint venture to act as a potential prime contractor, or a potential prime contractor who agrees with one or more companies to have them act as its subcontractors on a specific contract or acquisition program. For purposes of evaluation of the SDB participation factor, FAR 19.1202-4 requires that SDB joint ventures and teaming arrangements at the prime level be presented separately from SDB participation by subcontractors.

(9) **Qualifications of the Offeror**

You are requested to submit a summary of your "General Experience, Organizational Experience Related to this RFP, Performance History and Pertinent Contracts."

a) **General Experience**

General experience is defined as general background, experience and qualifications of the offeror. A discussion of proposed facilities which can be devoted to the project may be appropriate.

b) **Organizational Experience Related to the RFP**

Organizational experience is defined as the accomplishment of work, either past or on-going, which is comparable or related to the effort required by this RFP. This includes overall offeror or corporate experience, **but not** the experience and/or past performance of individuals who are proposed as personnel involved with the Statement of Work in this RFP.

c) **Performance History**

Performance history is defined as meeting contract objectives within **delivery** and **cost schedules** on efforts, either past or on-going, which is comparable or related to the effort required by this RFP.

d) **Pertinent Contracts**

Pertinent contracts is defined as a listing of each related contract completed within the last three years or currently in process. The listing should include: 1) the contract number; 2) contracting agency; 3) contract dollar value; 4) dates contract began and ended (or ends); 5) description of contract work; 6) explanation of relevance of work to this RFP; 7) actual delivery and cost performance versus delivery and cost agreed to in the contract(s). For award fee contracts, separately state in dollars the base fee and award fee available and the award fee actually received. The same type of organizational experience and past performance data should be submitted.

e) **Pertinent Grants**

List grants supported by the Government that involved similar or related work to that called for in this RFP. Include the grant number, involved agency, names of the grant specialist and the Science Administrator, identification of the work, and when performed.

You are cautioned that omission or an inadequate or inaccurate response to this very important RFP requirement could have a negative effect on the overall selection process. Experience and past performance are factors which are relevant to the ability of the offerors to perform and are considered in the source selection process.

f) **Submission of Electronic Funds Transfer Information with Offer, FAR Clause 52.232-38**, (May 1999)

The offeror shall provide, with its offer, the following information that is required to make payment by electronic funds transfer (EFT) under any contract that results from this solicitation. This submission satisfies the requirement to provide EFT information under paragraphs (b)(1) and (j) of the clause at 52.232-34, Payment by Electronic Funds Transfer--Other than Central Contractor Registration.

(1) The solicitation number (or other procurement identification number).
(2) The offeror's name and remittance address, as stated in the offer.
(3) The signature (manual or electronic, as appropriate), title, and telephone number of the offeror's official authorized to provide this information.
(4) The name, address, and 9-digit Routing Transit Number of the offeror's financial agent.
(5) The offeror's account number and the type of account (checking, savings, or lockbox).
(6) If applicable, the Fedwire Transfer System telegraphic abbreviation of the offeror's financial agent.
(7) If applicable, the offeror shall also provide the name, address, telegraphic abbreviation, and 9-digit Routing Transit Number of the correspondent financial institution receiving the wire transfer payment if the offeror's financial agent is not directly on-line to the Fedwire and, therefore, not the receiver of the wire transfer payment.

g) **Financial Capacity**

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.

h) **Incremental Funding**

An incrementally funded cost-reimbursement contract is a contract in which the total work effort is to be performed over a multiple year period and funds are allotted, as they become available, to cover discernible phases or increments of performance. The incremental funding technique allows for contracts to be awarded for periods in excess of one year even though the total estimated amount of funds expected to be obligated for the contract are not available at the time of the contract award. If this requirement is specified elsewhere in this RFP, the offeror shall submit a cost proposal for each year. In addition, the following provisions are applicable:

HHSAR 352.232-75, Incremental Funding (January 2001)

(a) It is the Government's intention to negotiate and award a contract using the incremental funding concepts described in the clause entitled Limitation of Funds. Under the clause, which will be included in the resultant contract, initial funds will be obligated under the contract to cover the first year of performance. Additional funds are intended to be allotted to the contract by contract modification, up to and including the full estimated cost of the contract, to accomplish the entire project. While it is the Government's intention to progressively fund this contract over the entire period of performance up to and including the full estimated cost, the Government will not be obligated to reimburse the Contractor for costs incurred in excess of the periodic allotments, nor will the Contractor be obligated to perform in excess of the amount allotted.

(b) The Limitation of Funds clause to be included in the resultant contract shall supersede the Limitation of Cost clause found in the General Provisions.

(End of provision)

i) **Facilities Capital Cost of Money**, FAR 52.215-16, (June 2003)

(This is applicable if you are a commercial organization.)

(a) Facilities capital cost of money will be an allowable cost under the contemplated contract, if the criteria for allowability in FAR 31.205-10(b) are met. One of the allowability criteria requires the prospective Contractor to propose facilities capital cost of money in its offer.

(b) If the prospective Contractor does not propose this cost, the resulting contract will include the clause Waiver of Facilities Capital Cost of Money.

(End of Provision)

If the offeror elects to claim this cost, the offeror shall specifically identify or propose it in the cost proposal for the contract by checking the appropriate box below.

[ ] The prospective Contractor has specifically identified or proposed facilities capital cost of money in its cost proposal and elects to claim this cost as an allowable cost under the contract. Submit Form CASB-CMF (see FAR 31.205-10).

[ ] The prospective Contractor has not specifically identified or proposed facilities capital cost of money in its proposal and elects not to claim it as an allowable cost under the contract.

(9) **Subcontractors**

If subcontractors are proposed, please include a commitment letter from the subcontractor detailing:

a) Willingness to perform as a subcontractor for specific duties (list duties).

b) What priority the work will be given and how it will relate to other work.
c) The amount of time and facilities available to this project.
d) Information on their cognizant field audit offices.
e) How rights to publications and patents are to be handled.
f) A complete cost proposal in the same format as the offeror's cost proposal.

Note: Organizations that plan to enter into a subcontract with an educational concern under a contract awarded under this RFP should refer to the following Web Site for a listing of clauses that are required to be incorporated in Research & Development (R&D) subcontracts with educational institutions: http://ocm.od.nih.gov/contracts/rfps/FDP/FDPclausecover.htm

(10) **Proposer's Annual Financial Report**

A copy of the organization's most recent annual report must be submitted as part of the business proposal.

(11) **Representations and Certifications - SECTION K**

One copy of SECTION K (which includes FAR Clause 52.204-8 Annual Representations and Certifications) shall be completed and be signed by an official authorized to bind your organization. Additionally, a completed copy of SECTION K shall be submitted from any proposed subcontractor. SECTION K can be found at: http://rcb.cancer.gov/rcb-internet/wkf/sectionk.pdf

(12) **Travel Costs/Travel Policy**

a) **Travel Costs - Commercial**

Costs for lodging, meals, and incidental expenses incurred by Contractor personnel shall be considered to be reasonable and allowable to the extent they do not exceed on a daily basis the per diem rates set forth in the Federal Travel Regulations, General Services Administration (GSA). Therefore, if travel costs are applicable and proposed by offerors, please be advised that they shall be calculated using the per diem rate schedule as established by GSA. Reimbursement of travel costs under any contract awarded from this RFP shall be in accordance with FAR 31.205-46.

b) **Travel Policy**

One copy of the offeror's (and any proposed subcontractor's) written travel policy shall be included in the business proposal (original only). If an offeror (or any proposed subcontractor) does not have a written travel policy, the offeror shall so state.

(13) **Certification of Visas for Non-U.S. Citizens**

Proposed personnel under research projects are not required to be citizens of the United States. However, if non-U.S. citizens are proposed under a contract to be performend in the United States and its outlying areas, then the offeror must indicate in the proposal that these individuals have the required visas.

SECTION M - EVALUATION FACTORS FOR AWARD

(1) GENERAL

Selection of an offeror for contract award will be based on an evaluation of proposals against four factors. The factors in order of importance are: technical, cost, past performance and Small Disadvantaged Business (SDB) participation. Although technical factors are of paramount consideration in the award of the contract, past performance, cost/price and SDB participation are also important to the overall contract award decision. All evaluation factors other than cost or price, when combined, are significantly more important than cost or price. In any case, the Government reserves the right to make an award(s) to that offeror whose proposal provides the best overall value to the Government.

The evaluation will be based on the demonstrated capabilities of the prospective Contractors in relation to the needs of the project as set forth in the RFP. The merits of each proposal will be evaluated carefully. Each proposal must document the feasibility of successful implementation of the requirements of the RFP. Offerors must submit information sufficient to evaluate their proposals based on the detailed criteria listed below.

(2) HUMAN SUBJECT EVALUATION

This research project involves human subjects. NIH Policy requires:

(a) Protection of Human Subjects from Research Risks

The offeror's proposal must address the involvement of human subjects and protections from research risk relating to their participation in the proposed research plan, or provide sufficient information on the research subjects to allow a determination by NCI that a designated exemption is appropriate.

If you claim that this research should be considered exempt from coverage by the Federal Regulations at 45 CFR 46, the proposal should address why you believe it is exempt, and under which exemption it applies.

The reviewers will evaluate the proposal with regard to four issues: Risks to Human Subjects, Adequacy of Protection Against Risks, Potential Benefits of the Proposed Research to the Subjects and Others, and Importance of the Knowledge to be Gained. See Section L for a complete discussion of what is required to be addressed for each of these issues. Based on the response to this criterion, this section of the proposal may be rated "unacceptable" (i.e., concerns are identified as to the protections described against risk to human subjects or no discussion is found regarding protections against risk to human subjects) or "acceptable." If the reviewers find that this portion of the proposal is "unacceptable" they will provide a narrative supporting their finding.

If the Government includes your proposal in the competitive range (for competitive proposals), or if the Government holds discussions with the selected source (for sole source acquisitions), you will be afforded the opportunity to address the concerns raised by the reviewers. You will be able to further discuss and/or clarify your position until submission of your Final Proposal Revision (FPR). Once discussions are closed with the submission of your FPR, if your proposed plan for the protection of human subjects from research risks is still found to be unacceptable, then your proposal may not be considered further for award.

(b) Women and Minorities

Women and members of minority groups and their subpopulations must be included in the study population of research involving human subjects, unless a clear and compelling rationale and justification are provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. In addition, for NIH-Defined Phase III clinical trials, all proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to detect significant differences in intervention effect (see NIH Guide

http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm, Definitions - Significant Difference) by sex/gender, racial/ethnic groups, and relevant subpopulations, if applicable, unless the Government has specified that this solicitation involves a sex/gender specific study or a single or limited number of minority population groups. The proposal also must include one of the following plans:

- Plans to conduct valid analysis to detect significant differences in intervention effect among sex/gender and/or racial/ethnic subgroups when prior studies strongly support these significant differences among subgroups, OR

- Plans to include and analyze sex/gender and/or racial/ethnic subgroups when prior studies strongly support no significant differences in intervention effect between subgroups (representation of sex/gender and/or racial/ethnic groups as subject selection criterion is not required; however, inclusion and analyses are encouraged), OR

- Plans to conduct valid analyses of the intervention effect in sex/gender and/or racial/ethnic subgroups (without requiring high statistical power for each subgroup) when the prior studies neither support nor negate significant differences in intervention effect between subgroups.

Also, the proposal must address the proposed outreach programs for recruiting women and minorities as participants.

Reviewers will consider the areas covered here and in Section L of the solicitation in narrative form in their evaluation. Some of the issues they will evaluate include:

- whether the plan proposed includes minorities and both genders in adequate representation
- how the offeror addresses the inclusion of women and members of minority groups and their subpopulations in the development of a proposal that is appropriate to the scientific objectives of the solicitation
- the description of the proposed study populations in terms of sex/gender and racial/ethnic groups and the rationale for selection of such subjects
- if exclusion is proposed, that the rationale is appropriate with respect to the health of the subjects and/or to the purpose of the research.
- In addition, for gender exclusion, the reviewers will examine the rationale to determine if it is because:

    - the purpose of the research constrains the offeror's selection of study participants by gender (e.g., uniquely valuable stored specimens or existing datasets are single gender; very small numbers of subjects are involved; or
    - overriding factors dictate selection of subjects); or
    - gender representation of specimens or existing datasets cannot be accurately determined, and this does not compromise the scientific objectives of the research.

- For minority group exclusion, the reviewers will examine the rationale to determine if those minority groups are excluded because:

    - inclusion of those groups would be inappropriate with respect to their health,;or
    - inclusion of those groups would be inappropriate with respect to the purpose of the research.

- For NIH-defined Phase III clinical trials, reviewers will also consider whether there is an adequate description of plans to conduct analyses to detect significant differences of clinical or public health importance in intervention effect(s) by sex/gender and/or racial ethnic subgroups when the intervention effect(s) is expected in the primary analyses, or if there is an adequate description of plans to conduct valid analyses of the intervention effect in subgroups when the intervention effect(s) is not expected in the primary analyses.

If you determine that inclusion of women and minority populations is not feasible, you must submit a detailed rationale and justification for exclusion of one or both groups from the study population with the

technical proposal. The Government will review the rationale to determine if it is appropriate with respect to the health of the subjects and/or the purpose of the research

Based on the evaluation of the response to this criterion, this section of the proposal may be rated "unacceptable" (i.e., no discussion can be found regarding the proposed gender/minority inclusion plans, or concerns are identified as to the gender or minority representation, or the proposal does not adequately address limited representation of one gender or minority; or the plan is not in accordance with NIH policy guidelines) or "acceptable." See Section L of the solicitation for the requirements of women/minorities inclusion. If the reviewers find that this portion of the proposal is "unacceptable" they will provide a narrative supporting their finding.

If the Government includes your proposal in the competitive range (for competitive proposals), or if the Government holds discussions with the selected source (for sole source acquisitions), you will be afforded the opportunity to address the concerns raised by the reviewers. You will be able to further discuss and/or clarify your position until submission of your Final Proposal Revision (FPR). Once discussions are closed with the submission of your FPR, if your proposed plan for the inclusion/exclusion of women and minorities is still found to be unacceptable, then your proposal may not be considered further for award.

(c) **Children**

Children (i.e. individuals under the age of 21) must be included in all human subject research unless there are clear and compelling reasons not to include them.

Your proposal must include a description of plans for including children. If you plan to exclude children from the required research, your proposal must present an acceptable justification for the exclusion. If you determine that exclusion of a specific age range of child is appropriate, your proposal must also address the rationale for such exclusion. Also, the plan must include a description of the expertise of the investigative team for dealing with children at the ages included, of the appropriateness of the available facilities to accommodate the children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose/objective of the solicitation. Also, see Section L of the solicitation for further specific requirements on inclusion of children.

Based on the reviewers' evaluation of the offeror's response, this section of the proposal may be rated "unacceptable" (i.e., no discussion can be found regarding the proposed inclusion plans for children; or concerns are identified as to the offeror's response regarding the inclusion of children; or the plan is not in accordance wit h NIH policy guidelines) or "acceptable." If the reviewers find that this portion of the proposal is "unacceptable" they will provide a narrative supporting their finding.

If the Government includes your proposal in the competitive range (for competitive proposals), or if the Government holds discussions with the selected source (for sole source acquisitions), you will be afforded the opportunity to address the concerns raised by the reviewers. You will be able to further discuss and/or clarify your position until submission of your Final Proposal Revision (FPR). Once discussions are closed with the submission of your FPR, if your proposed plan for the inclusion of children is still found to be unacceptable, then your proposal may not be considered further for award.

If the information provided in your proposal about the inclusion of children is rated "unacceptable" and the Government includes your proposal in the competitive range (for competitive proposals), or if the Government holds discussions with the selected source (for sole source acquisitions), you will be afforded the opportunity to further discuss, clarify or modify your plan during discussions and in your Final Proposal Revision (FPR). If your plan for inclusion of children is still considered "unacceptable" by the Government after discussions, your proposal may not be considered further for award.

(d) **Data and Safety Monitoring**

The offeror's proposal must include a general description of the Data and Safety Monitoring Plan for all clinical trials. The principles of data and safety monitoring require that all biomedical and behavioral clinical trails be monitored to ensure the safe and effective conduct of human subjects research, and to

recommend conclusion of the trial when significant benefits or risks are identified or if it is unlikely that the trial can be concluded successfully. Risks associated with participation in research must be minimized to the extent practical and the method and degree of monitoring should be commensurate with risk. Additionally, all plans must include procedures for adverse event reporting. Finally, generally, for Phase III clinical trials, the establishment of a Data and Safety Monitoring Board (DSMB) is required, whereas for Phase I and II clinical trials, the establishment of a DSMB is optional. The reviewers will rely on the Statement of Work and Section L in the solicitation, as well as any further technical evaluation criteria in this Section M, as applicable, for the solicitation's specific requirements for data and safety monitoring.

As a part of the evaluation for proposals, the reviewers will consider the acceptability of the proposed data and safety monitoring plan with respect to the potential risks to human participants, complexity of study design, and methods for data analysis. Based on the evaluation of the response to this criterion, this section of the proposal may be rated “unacceptable” (i.e., concerns are identified as to the adequacy of the monitoring plan or no discussion can be found regarding the proposed monitoring plans) or “acceptable.” If the reviewers find that this portion of the proposal is "unacceptable" they will provide a narrative supporting their finding.

If the Government includes your proposal in the competitive range (for competitive proposals), or if the Government holds discussions with the selected source (for sole source acquisitions), you will be afforded the opportunity to address the concerns raised by the reviewers. You will be able to further discuss and/or clarify your position until submission of your Final Proposal Revision (FPR). Once discussions are closed with the submission of your FPR, if your proposed plan for data and safety monitoring is still found to be unacceptable, then your proposal may not be considered further for award.

(3) **MANDATORY QUALIFICATION CRITERIA**

The mandatory qualification criteria establish conditions that must be met **at the time of receipt of the Original Proposal submission** in the Office of Acquisitions, NIAID, in order for your proposal to be considered any further for award.

Listed below are the mandatory qualification criteria. **The offeror must include all information that documents and/or supports the Mandatory Qualification Criteria in one clearly marked section at the front of the Technical Proposal.** Technical Proposals that are determined by the Project Officer and Contracting Officer not to meet the Mandatory Qualification Criteria will not be submitted for peer review and will not be considered any further for award.

Mandatory Qualification Criteria:

Documentation must be provided to verify that the proposed anthrax vaccine candidate meets the following minimum development status criteria:

a. As purified Protective antigen (PA) has been shown to be efficacious against B. anthracis spore challenge in animal models, the proposed vaccine must contain a PA component. The PA component may be proteinaceous or nucleotide-encoded.

   Required documentation: The offeror must provide, in this section of the Technical Proposal, a letter on official letterhead certifying that the proposed vaccine contains a PA component. In addition, the letter must be signed by an official legally authorized to bind the organization.

b. Should the final vaccine presentation/inoculation strategy include a novel device, a pre-Investigational Device Exemption (pre-IDE) filed for the device with the FDA or an Investigational New Drug Application (IND) filed with another investigational vaccine product using the proposed device must be currently filed with the FDA.

   Required documentation: A copy of the documentation showing the filing with FDA must be provided in this section of the Technical Proposal.

c. Data and results from a proof-of-concept study of the vaccine candidate in an anthrax spore challenge animal model which has demonstrated vaccine efficacy.

Required documentation: This may be in the form of a final study report or a peer-reviewed publication and must be provided in this section of the Technical Proposal.

JUSTIFICATION: By placing these Mandatory Qualification Criteria in this solicitation, the initial risk of selecting a product with unknown potential is reduced and ensures that the Government secures the best value for its limited product development funding and meets the urgent public health needs for this vaccine development effort.

(4) EVALUATION OF OPTIONS

It is anticipated that any contract(s) awarded from this solicitation will contain option provision(s) and period(s). In accordance with FAR Clause 52.217-5, Evaluation of Options. (July 1990), the Government will evaluate offers for award purposes by adding the total price for all options to the total price for the basic requirement, except when it is determined in accordance with FAR 17.206(b) not to be in the Government's best interests. Evaluation of options will not obligate the Government to exercise the option(s).

(5) **TECHNICAL EVALUATION CRITERIA**

The evaluation criteria are used by the technical evaluation committee when reviewing the technical proposals. The criteria below are listed in the order of relative importance with weights assigned for evaluation purposes.

OFFERORS AND REVIEWERS ARE ADVISED TO REFER TO APPENDIX A - Additional Technical Proposal Instructions - OF THIS SOLICIATION PACKAGE FOR GUIDANCE AND INFORMATION RELATED TO THE PREPARATION OF TECHNICAL PROPOSALS.

CRITERIA	**WEIGHT**
CRITERION 1: TECHNICAL APPROACH/METHODOLOGY	**55**

a. Candidate Anthrax Vaccine

1) Soundness, adequacy, and feasibility of the proposed candidate anthrax vaccine to fulfill the third generation anthrax vaccine objectives of long-term stability and/or storage at ambient temperatures; rapid immune responses with two doses; and amenability for rapid mass immunization including self-administration or administration of vaccine by non-technical personnel.

2) Soundness, adequacy, and feasibility of the documentation and data supporting the selection of the proposed vaccine candidate with respect to the following:

   a) the results of any completed studies indicating superior safety/reactogenicity profile relative to the anthrax vaccine currently licensed in the U.S.;
   b) the results of any completed studies on formulation, immunogenicity and ability to protect against lethal challenge of B. anthracis spores;
   c) prior human use and non-clinical safety of any proposed new adjuvant (not currently in a licensed vaccine);
   d) if applicable, additional/enhanced benefit of added antigen component(s) in conjunction with PA;

3) Soundness, adequacy and feasibility of the documentation that describes the offeror's anthrax vaccine development program with respect to the following:

   a) current status of Drug Substance (DS) and Final Drug Product (FDP) processes;

b) status of assays, in-process/release assays including potency, and serological/efficacy endpoint assay(s);
c) available stability data;
d) non-clinical study data; and
e) the Quality Assurance/Quality Control Program

4) Soundness, adequacy and feasibility of the data and other information documenting the completion by the offeror of any milestone.

b. <u>Vaccine Development Plan</u>

1) Manufacturing

a) Soundness, adequacy, thoroughness, and feasibility of the proposed technical approach and methods for manufacturing processes, product characterization and release assays, technology transfer for pilot-lot to large-scale transition for both DS and FDP, process and assay development and validation, consistency lot production, and testing of cGMP DS and cGMP FDP.

b) Adequacy, appropriateness and feasibility of the associated timelines for completion.

2) Non-clinical Studies

a) Soundness, adequacy, thoroughness and feasibility of the proposed safety/toxicity studies for supporting an Investigational New Drug (IND) application.
b) Soundness, adequacy, thoroughness and feasibility of the proposed aerosol spore challenge studies in the rabbit and the non-human primate (NHP) models to support the "Animal Rule" and future pivotal studies to identify correlates of protection based on the non-clinical and clinical data.
c) Soundness, adequacy, thoroughness and feasibility of the proposed assays for analyzing serological immune responses to determine immune correlates.

CRITERION 2: FACILITIES, OTHER RESOURCES, SAFETY AND TRAINING **15**

Adequacy, suitability and availability of safe facilities for the development, manufacturing, and non-clinical testing of a vaccine suitable for use under an IND as specified in the Statement of Work, including:

a. Compliance of the product manufacturing facilities for both DP and FDP with cGMP.

b. Compliance of the non-clinical facilities with GLP.

c. Adequate biocontainment facilities, safety procedures, and staff with the required training, experience and expertise to operate the facilities and conduct the studies in accordance with the Biosafety Level (BSL) 2 and 3 guidelines, and in accordance with DHHS regulations regarding the transfer of Select Agents (42 CFR Part 72).

d. Facilities for the housing and care of laboratory animals, including veterinary coverage, the physical plant housing animals and laboratories, safety procedures, and expertise and training of the technical staff employed.

e. Capacity of all facilities to perform required testing in a timely and efficient manner with the resources dedicated to the project.

CRITERION 3: QUALIFICATIONS OF SCIENTIFIC AND TECHNICAL PERSONNEL **15**

Appropriateness, adequacy, and relevance of the documented training, expertise, experience and availability (based on percent effort devoted to this project) of proposed scientific and technical staff of the offeror and any proposed subcontractors in relation to their specific duties and responsibilities, as follows:

a. Principal Investigator (PI)

Qualifications of the proposed PI to lead, direct and coordinate all contract activities, including activities carried out by subcontractors. This includes: appropriate knowledge and expertise in advanced bacterial vaccine development; prior successful IND submissions to the FDA and completion of preclinical and clinical vaccine studies; and the capacity to monitor progress, access performance, identify performance problems and implement corrective actions.

b. Key Scientific and Technical Personnel

1) Qualifications and ability to conduct the range of vaccine production activities, assays, and non-clinical and clinical studies.

2) Qualifications and experience with products of a similar nature regulated by the FDA, and the regulatory requirements that govern the production of cGMP materials and to conduct testing in compliance with GLP and GCP.

c. Other Scientific and Technical Personnel

1) Qualifications and experience of other scientific and technical personnel.

2) Experience and expertise of the offeror's Quality Assurance (QA) and Quality Control (QC) personnel

CRITERION 4: PROJECT MANAGEMENT **15**

a. Adequacy and feasibility of the plan for overall project organization, staffing, and management, including the management of any consultants and subcontractors, to meet the production and non-clinical testing milestones; appropriateness of the proposed mix and balance of key personnel in relation to their specific responsibilities and time commitments.

b. Adequacy and completeness of the plan for PI communication and interaction with the Contracting Officer and the Project Officer and for PI communication, monitoring, and management of the project.

c. Adequacy, appropriateness and completeness of the project management systems and quality control methods to ensure the effective initiation, implementation, and conduct of contract requirements, and to monitor, track and report Contractor and subcontractor costs and performance.

d. Appropriateness of the qualifications, experience and expertise of proposed administrative staff with respect to the financial management and reporting, and the execution, management and reporting of subcontracts.

CRITERION 5: OPTION 1: Phase 1 Clinical Trial **10**

a. Soundness, appropriateness, adequacy, and feasibility of the proposed Phase 1 clinical trial design, timelines and plans for the recruitment and retention of study participants.

b. Capability to implement and provide oversight for clinical trials as demonstrated by the Quality Management Plan, the Clinical Monitoring Plan, the Safety Oversight Plan, and the Data Management Plan.

c. Adequacy and feasibility of the plans and procedures to:
   1) prepare, submit, and update an IND,
   2) keep NIAID apprised of progress and all communications with the FDA,
   3) ensure that NIAID may co-monitor or provide for independent audits of the clinical studies.

d. Qualifications and experience of the Principal Investigator, regulatory staff, scientific and technical staff to adequately conduct and manage the clinical testing as required in the Statement of Work Option 1; knowledge and experience with the regulatory requirements that govern the clinical testing in compliance with GCP; qualifications and experience with products of a similar nature regulated by the FDA.

e. Adequacy, completeness and feasibility of the plan to manage the clinical trial, including consultants and/or subcontractors to meet the overall clinical testing as required in the Statement of Work Option 1, and to monitor, track, and report cost and performance to the Project Officer.

f. Adequacy and availability of proposed clinical facilities, equipment and other resources for conducting the clinical trial in compliance with Federal regulatory requirements and Good Clinical Practice (GCP).

CRITERION 6: OPTION 2: Phase 2 Clinical Trial(s) **10**

a. Soundness, appropriateness, adequacy, and feasibility of the proposed Phase 2 clinical trial design(s), timelines and plans for the recruitment and retention of study participants.

b. Capability to implement and provide oversight for clinical trials as demonstrated by the Quality Management Plan, the Clinical Monitoring Plan, the Safety Oversight Plan, and the Data Management Plan.

c. Adequacy and feasibility of the plans and procedures to:
   1) update an IND,
   2) keep NIAID apprised of progress and all communications with the FDA,
   3) ensure that NIAID may co-monitor or provide for independent audits of the clinical studies.

d. Qualifications and experience of the Principal Investigator, regulatory staff, scientific and technical staff to adequately conduct and manage the clinical testing as required in the Statement of Work Option 2; knowledge and experience with the regulatory requirements that govern the clinical testing in compliance with GCP; qualifications and experience with products of a similar nature regulated by the FDA.

e. Adequacy, completeness and feasibility of the plan to manage the clinical trial, including consultants and/or subcontractors to meet the overall clinical testing as required in the Statement of Work Expansion Option 2, and to monitor, track, and report cost and performance to the Project Officer.

f. Adequacy and availability of proposed clinical facilities, equipment and other resources for conducting the clinical trial in compliance with Federal regulatory requirements and Good Clinical Practice (GCP).

TOTAL POSSIBLE POINTS: **120**

(6) PAST PERFORMANCE FACTOR

An evaluation of offerors' past performance information will be conducted prior to any communications with offerors leading to establishment of the competitive range. However, this evaluation will not be conducted on any offeror whose proposal will not be admitted to the competitive range on the basis of the results of the evaluation of factors other than past performance.

The evaluation will be based on information obtained from references provided by the offeror, other relevant past performance information obtained from other sources known to the Government, and any information supplied by the offeror concerning problems encountered on the identified contracts and corrective action taken.

The government will assess the relative risks associated with each offeror. Performance risks are those associated with an offeror's likelihood of success in performing the acquisition requirements as indicated by that offeror's record of past performance.

The assessment of performance risk is not intended to be a product of a mechnaical or mathematical analysis of an offeror's performance on a list of contracts but rather the product of subjective judgement by the Government after it considers relevant information.

When assessing performance risks, the Government will focus on the past performance of the offeror as it relates to all acquisition requirements, such as the offeror's record of performing according to specifications, including standards of good workmanship; the offeror's record of controlling and forecasting costs; the offeror's adherence to contract schedules, including the administrative aspects of performance; the offeror's reputation for reasonable and cooperative behavior and commitment to customer satisfaction; and generally, the offeror's business-like concern for the interest of the customer.

The Government will consider the currency and relevance of the information, source of the information, context of the data, and general trends in the offeror's performance.

The lack of a relevant performance record may result in an unknown performance risk assessment, which will neither be used to the advantage nor disadvantage of the offeror.

(7) EXTENT OF SMALL DISADVANTAGED BUSINESS PARTICIPATION

SDB participation will not be scored, but the Government’s conclusions about overall commitment and realism of the offeror’s SDB Participation targets will be used in determining the relative merits of the offeror’s proposal and in selecting the offeror whose proposal is considered to offer the best value to the Government.

The extent of the offeror’s Small Disadvantaged Business Participation Targets will be evaluated before determination of the competitive range. Evaluation of SDB participation will be assessed based on consideration of the information presented in the offeror’s proposal. The Government is seeking to determine whether the offeror has demonstrated a commitment to use SDB concerns for the work that it intends to perform.

Offers will be evaluated on the following sub-factors:

(a) Extent to which SDB concerns are specifically identified
(b) Extent of commitment to use SDB concerns
(c) Complexity and variety of the work SDB concerns are to perform
(d) Realism of the proposal
(e) Past performance of offerors in complying with subcontracting plan goals for SDB concerns and monetary targets for SDB participation
(f) Extent of participation of SDB concerns in terms of the value of the total acquisition.

SOLICITATION ATTACHMENTS INCLUDED WITH THE RFP

The following pages include Attachments applicable to this RFP as specified in SECTION J - List of Attachments

PACKAGING AND DELIVERY OF THE PROPOSAL

PAPER SUBMISSION: The paper copy is the official copy for recording timely receipt of proposals.

SUBMISSION OF PROPOSALS BY FACSIMILE OR E-MAIL IS **NOT** ACCEPTABLE.

A. EXTERNAL PACKAGE MARKING:

In addition to the address cited below, mark each package as follows:

"**RFP NO. NIH-NIAID-DMID-07-05**
TO BE OPENED BY AUTHORIZED GOVERNMENT PERSONNEL ONLY"

B. PAPER COPIES and CD-Rom to:

If Hand Delivery or Express Service	If using U.S. Postal Service
Ross Kelley Contracting Officer Office of Acquisitions, DEA, NIAID, NIH 6700-B Rockledge Drive, Room 3214, MSC 7612 Bethesda, Maryland 20817	Ross Kelley Contracting Officer Office of Acquisitions, DEA, NIAID, NIH 6700-B Rockledge Drive, Room 3214, MSC 7612 Bethesda, Maryland 20892-7612

NOTE: All material sent to this office by Federal Express should be sent to the Hand Carried Address.

NOTE: The U.S. Postal Service's "Express Mail" does not deliver to the hand delivered (20817 zip code) address. Any package sent to this address via this service will be held at a local post office for pick-up. THE GOVERNMENT IS NOT RESPONSIBLE FOR PICKING UP ANY MAIL AT A LOCAL POST OFFICE. If a proposal is not received at the place, date, and time specified herein, it will be considered a "late proposal," in accordance with HHSAR 352.215-70, Late Proposals and Revisions (NOV 1986).

C. NUMBER OF COPIES:

TOTAL PAGE COUNT DOES NOT INCLUDE: Title and Back Page; NIH-2043; Table of Contents; Section Dividers that do not contain information other than title of Section.

PAGES THAT ARE 2-SIDED WILL COUNT AS 2 PAGES.

FORMATTING AND LAYOUT:
Use your usual word processing and spreadsheet programs to prepare and format the technical and business proposals. *If documents are submitted using Adobe .pdf, the document should be submitted using a* ***.pdf searchable*** *format.*

- Type size must be 10 to 12 points.
- Type spacing should be no more than 15 characters per inch. Within a vertical inch, there must be no more than six lines of text.
- Print margins must be at least one inch on each edge of the paper.
- Print setup should be single-sided on standard letter size paper (8.5 x 11" in the U.S., A4 in Europe).
- Proposals shall NOT include links to Internet Web site addresses (URLs) or otherwise direct readers to alternate sources of information.

CREATING AND NAMING ELECTRONIC FILES:

1. A separate CD should be submitted for the Technical Proposal and Business Proposal information. *Offerors who submit both Technical and Business Proposals on the same CD will be required to resubmit them on separate CDs.*
2. Files on CDs should be named using the following format:

Company name / RFP number / technical / ** /date

** if multiple files are submitted for the technical proposal, please include the name of the section in the file name.

EXAMPLE: XYX Company/07-05/Technical/Approach/9-18-06

Company name / RFP number / business / ** / date

** if multiple files are submitted for the business proposal, please include the name of the section in the file name.

EXAMPLE: XYX Company/07-05/Business/Staffing/9-18-06

THE NUMBER OF COPIES AND APPLICABLE PAGE LIMITATIONS REQUIRED OF EACH PART OF YOUR PROPOSAL ARE AS SPECIFIED BELOW.

PAGES IN EXCESS OF THIS LIMITATION WILL BE REMOVED FROM THE PROPOSAL AND EXCESS PAGES WILL NOT BE PROVIDED TO THE REVIEWERS TO BE READ OR EVALUATED.

OFFERORS MUST CERTIFY THAT THE INFORMATION IN THE PAPER AND ELECTRONIC COPIES IS EXACTLY THE SAME.

Document	Number of Copies	Page Limits
Technical Proposal and all Appendices	**PAPER** One (1) unbound SIGNED ORIGINAL. Five (5) unbound COPIES **ELECTRONIC FILES ON CD** Twenty (20) Compact Disks containing an electronic copy of the Technical Proposal (including all Appendices)	**Not to Exceed 200 pages**
Business Proposal	**PAPER** One (1) unbound SIGNED ORIGINAL. Five (5) unbound COPIES **ELECTRONIC FILES ON CD** Four (4) Compact Disks containing an electronic copy of the Business Proposal	N/A
Breakdown of Proposed Estimated Cost using Electronic Cost Proposal EXCEL Workbook	This Attachment to the Business Proposal should be submitted as a separate EXCEL file on the Business Proposal Compact Disk. **See Section J, Attachment entitled Breakdown of Proposed Estimated Costs (plus Fee) with Excel Spreadsheet to access the Excel Workbook.**	N/A

PROPOSAL INTENT RESPONSE SHEET

RFP No.: NIH-NIAID-DMID-07-05
RFP Title: "DEVELOPMENT OF A THIRD GENERATION ANTHRAX VACCINE"

Please review the attached Request for Proposal. Furnish the information requested below and return this page by **July 19, 2006**. Your expression of intent is not binding but will greatly assist us in planning for proposal evaluation.

[ ] DO INTEND TO SUBMIT A PROPOSAL
[ ] DO NOT INTEND TO SUBMIT A PROPOSAL FOR THE FOLLOWING REASONS:

Company/Institution Name (print): _____
Address (print): _____
_____
_____
_____

Project Director's Name (print): _____
Title (print): _____
Signature/Date: _____
Telephone Number and E-mail Address (print clearly):
_____
_____

***Name of individual to whom electronic proposal instructions should be sent:**

Name: _____
Title: _____
E-Mail Address: _____
Telephone Number: _____

Names of Collaborating Institutions and Investigators (include Subcontractors and Consultants) (print):
_____
_____
_____
_____
(Continue list on a separate page if necessary)

RETURN VIA FAX OR E-MAIL TO:
OA, NIAID, NIH
Room 3214
6700-B Rockledge Drive, MSC 7612
Bethesda, MD 20892-7612
Attn: Ross Kelley
RFP-NIH-NIAID- DMID-07-05
FAX# (301) 480-4675
Email : RKelleyt@niaid.nih.gov

ATTACHMENT 2

BACKGROUND

Development of a Third Generation Anthrax Vaccine
RFP NIH-NIAID-DMID-07-05

The National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH) supports research related to the basic understanding of microbiology and immunology leading to the development of vaccines, therapeutics, and medical diagnostics for the prevention, treatment, and diagnosis of infectious diseases. The NIAID Division of Microbiology and Infectious Diseases (DMID) supports a comprehensive extramural research program focused on the prevention and control of diseases caused by virtually all infectious agents (with the exception of the human immunodeficiency virus). This includes basic research, such as studies of microbial biology and physiology; applied research, including the development of vaccines, therapeutics and medical diagnostics; and clinical studies to evaluate experimental drugs and vaccines.

Bacillus anthracis (B. anthracis), the etiologic agent of anthrax, is a facultative anaerobic, spore-forming bacterium that can cause human disease via the gastrointestinal, cutaneous, or inhalation (pulmonary) routes. Clinical manifestations of disease differ with route -- the inhalation route being the most lethal. With an anthrax inhalation exposure, the incubation period usually varies from 12 hours to five or more days depending upon the dose received. The initial clinical signs and symptoms are nonspecific and may include malaise, headache, fever, nausea, and vomiting. These non-specific signs and symptoms are followed by a sudden onset of respiratory distress with dyspnea, stridor, cyanosis, and chest pain. The onset of respiratory distress is followed by shock and death with close to 100% mortality.

Recent threats posed by the use of infectious agents as weapons of biological warfare have generated increased concern for the safety of the general American populace. The ability to generate very large quantities of anthrax spores using basic microbiological techniques combined with the ability of these agents to be disseminated by aerosolization has made anthrax a primary bioterrorist and military threat. With the deliberate exposure of citizens of the United States, including postal workers and other Government employees to *B. anthracis* spores in 2001, there is an urgent need to stockpile appropriate and effective medical countermeasures to protect all U.S. citizens from the morbidity and mortality associated with infection from these instruments of terror.

A priority has been placed on post-exposure prophylaxis (PEP) for emergency civilian usage where exposure or suspected exposure to anthrax spores would be immediately treated with antibiotic therapy in conjunction with an approved regimen of anthrax vaccine. This combination therapy is based on the premise that germinated spores would be eliminated by antibiotic therapy while spores undergoing latent germination, which is known to occur after cessation of antibiotic therapy, would be eliminated by a protective immune response generated by the vaccine.

The only anthrax vaccine currently licensed in the United States, Biothrax™ (Emergent Biosolutions; Gaithersburg, Maryland), consists of filtered *B. anthracis* culture supernatant treated with formalin and formulated with an aluminum adjuvant. This vaccine is currently administered subcutaneously as a six-dose regimen. The predominant means of protection provided by this vaccine is thought to be antibodies generated against the protective antigen (PA) molecule.

A 2002 Institute of Medicine (IOM) report, The Anthrax Vaccine: Is It Safe? Does It Work?, Strom, B.L. et. al., Editors, National Academies Press, 2002 (http://www.iom.edu/CMS/3795/4324.aspx) recommended that research should be pursued and encouraged to develop other possible anthrax vaccine products that can be produced more consistently and that are less reactogenic than AVA (BioThrax™). Based on this premise, the second generation anthrax vaccine platform consists of aluminum adjuvanted recombinant PA (rPA) in a liquid form delivered intramuscularly via syringe. As a single recombinant protein suspension, this formulation is subject to many of the limitations of other recombinant products including degradation over time, required refrigeration for storage, and multiple immunizations to generate high antibody titers.

This solicitation will support the development and testing of third generation anthrax vaccine candidates which build upon the second generation vaccine, resulting in properties desirable for a biodefense vaccine to be stored in the Strategic National Stockpile (SNS). These properties include long-term stability (i.e., 3 years or longer) at room temperature, the ability to generate a protective immune response in one or two doses, and the ability to be safely self-administered and/or rapidly inoculated into large numbers of people. Anthrax vaccine candidates eligible for support under this solicitation shall possess all or some of these properties while maintaining a safety profile superior to the currently U.S. licensed anthrax vaccine and an equivalent immunogenicity and efficacy profile as the rPA-Alhydrogel based vaccine. Novel formulations/final vaccine presentation, new delivery platforms, adjuvants other than aluminum, and inclusion of antigens in addition to PA may be components of candidate vaccines.

NIAID anticipates making one or more awards under this Request for Proposal (RFP). The contract or contracts awarded under this solicitation will contain a base period of three years and will have two Options. If exercised, Option 1 will require the Contractor to design and conduct a Phase 1 dose escalating clinical trial in healthy subjects ages 18 to 40. In addition, if exercised, Option 2 will require the Contractor to design and conduct up to two Phase 2 clinical trials in healthy subjects ages 18 to 55. The exercise of these Options may result in expanding the scope of work and extending the period of performance by up to four years.

The NIAID is aware that no single organization or institution may have the expertise and facilities required to perform all parts of the Statement of Work. Therefore, it may be necessary for the Contractor to subcontract a portion of the work. The Contractor shall be responsible for ALL work performed under this contract, including that performed by any subcontractor.

STATEMENT OF WORK

Development of a Third Generation Anthrax Vaccine
RFP NIH-NIAID-DMID-07-05

OVERALL OBJECTIVE AND SCOPE

OBJECTIVE

The objective of this contract is to advance the development and testing of an anthrax vaccine candidate that possesses characteristics that shall improve upon the second generation anthrax vaccines. Such characteristics include the following:

1. Long-term stability of final product: Final product shall be suitable for storage in the Strategic National Stockpile (SNS). The vaccine shall be stable for extended periods of storage (i.e., 3 years or longer) at ambient/room temperature.
2. Rapid immune response: Final product shall need no more than two doses to elicit a protective response.
3. Ease of vaccine inoculation: Final product shall possess properties to enable rapid administration to large numbers of people following a bioterror incident and, therefore, shall utilize a platform that shall allow non-technical persons to perform inoculations or self-administration.

The contract shall support the development and testing of anthrax vaccine candidates possessing any one or all of the characteristics listed above, while maintaining a safety profile superior to the currently licensed anthrax vaccine. The Contractor shall advance anthrax vaccine development and methods for novel formulations/final vaccine presentation, new delivery platforms, adjuvants other than aluminum, and inclusion of additional antigens.

For the purposes of this contract, the anthrax vaccine must contain, in part, a Protective antigen (PA) component, as PA has been shown to be efficacious against *B. anthracis* spore challenge in animal models and has progressed through a proof-of-concept efficacy study in a relevant spore challenge animal model. Additionally, if the Contractor plans to use novel devices/technologies to facilitate vaccine dosing, a pre-Investigational Device Exemption (pre-IDE) must be filed for the device with the U.S. Food and Drug Administration (FDA), or an Investigational New Drug Application (IND) must be filed with the FDA for another investigational vaccine product using the proposed device.

***NOTE**: While the contract will provide funds to support the development of a Final Drug Product (FDP) to be adapted to a novel device, the contract will NOT provide funds for the development of a novel device.*

The base contract shall encompass the development, manufacturing, characterization, and non-clinical testing of the vaccine candidate based on defined milestones and timelines. Options for Phase 1 and Phase 2 Clinical Trial(s) may be exercised at the discretion of the Government.

SCOPE OF WORK

The work to be performed shall include:

a. manufacture of Drug Substance (DS) lots and Filled/Finished Final Drug Product (FDP) under current Good Manufacturing Practice (cGMP) using pilot-scale production processes;
b. qualification of all process, release, characterization, stability indicating, and serological assays;
c. conduct of a stability program for manufactured material;
d. performance of pre-clinical safety and toxicity studies, aerosol challenge efficacy studies in the rabbit using general-use prophylaxis (GUP) and post-exposure prophylaxis (PEP) models, and a PEP aerosol challenge study in a non-human primate (NHP) model;
e. submission of a Letter of Cross-Reference to Center for Biologics Evaluation and Research (CBER)/FDA to Contractor Master File or Investigational New Drug (IND) application;
f. delivery of 2,000 doses of FDP to DMID/NIAID; and
g. submission of a feasibility plan for transitioning to a large-scale manufacture platform and detailed path to submission of a Biologics License Application (BLA).
h. Options 1 and 2 for Clinical Trials.

   Option 1. Design and conduct a dose escalating Phase 1 clinical trial in healthy subjects ages 18 to 40.

   Option 2. Design and conduct up to two Phase 2 clinical trials in healthy subjects ages 18 to 55.

TECHNICAL REQUIREMENTS

Independently and not as an agent of the Government, the Contractor shall 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 below and shall be responsible for ALL work performed under this contract including that performed by any subcontractor. Specifically, the Contractor shall:

1. PRODUCT DEVELOPMENT MILESTONES

Milestone 1. Manufacture of Drug Substance (DS)

a. Manufacturing Runs -- Perform a minimum of three successful manufacturing runs of drug substance (DS) at pilot-lot scale using cGMP to generate clinical grade material suitable for use in Phase 1 and 2 clinical trials. If FDP contains more than one antigen, one successfully-released lot of DS shall comprise manufacture of all antigen components at pilot scale. For purposes of this contract, pilot-scale DS fermentation is defined as a minimum of 30 liter (L) fermentor working volume and/or sufficient DS to fill 2,000 doses of FDP. Pilot lot processes utilized must be transferable to a large-scale process with minimal, if any, defined modifications.

   1) *Within 9 months of contract award*, complete and release a clinical grade DS component lot.

2) *Within 11 months of contract award*, complete and release a minimum of two additional cGMP DS component lots. All process and product specifications must be defined for the third lot using qualified or validated assays.

b. Batch Records -- Submit Batch Records, as requested by the Project Officer. Provide for Project Officer on-site review of Batch Records when directed by the Project Officer. Submit a Certificate of Analysis (CoA) for each released lot, and a DS Process Development Report following completion of the three released lots. Completion of Milestone 1 shall be based on the Project Officer determination, through review of the CoAs for released material, associated Batch Records, and the DS Process Development Report, that the released material has been manufactured under cGMP and is suitable for use in Phase 1 and 2 clinical trials.

Milestone 2. Stability Program

a. Stability Program -- *Within 9 months of contract award* and upon completion of the first DS component lot, initiate a stability program that shall extend throughout the duration of the contract award. All released lots of DS, FDP, and vaccine diluent are required to be on stability testing throughout the contract period of performance. Additionally, if novel adjuvants/immune stimulators (not in a licensed product) are utilized, these must be a part of the stability program. The stability program shall include real-time and accelerated stability testing for DS, FDP, and novel adjuvants/immune stimulators. Assays used in the stability program must be stability indicating.

b. Stability Data Reports -- Submit Monthly Stability Data Reports to the Project Officer indicating, at a minimum, appearance, purity, pH, and potency for DS and FDP; and in addition, concentration for DS and sterility for FDP.

Milestone 3. Qualification of Assays

a. Product Characterization -- *Within 10 months of contract award*, develop/obtain, characterize and qualify product characterization and in-process/release assays, including a potency test(s), serological assays to assess host immunologic responses to vaccine (must include anti-PA ELISA , PA Toxin Neutralization Assay [TNA], and if applicable, assays to assess serological responses to additional vaccine antigens), and all required assay reagents. Immunological assays developed/obtained shall be applied in support of the CBER/FDA "Animal Rule" as outlined in 21 CFR 601.91(a)(1-4). Some qualified reference reagents may be available from the NIAID Biodefense and Emerging Infections Research Resources Repository (see http://www3.niaid.nih.gov/Biodefense/Research/resources.htm#repos).

b. Assay Protocols and Final Assay Qualification Reports – *Within 10 months of contract award* submit these Reports to the Project Officer for review and approval. Completion of Milestone 3 shall be determined by the Project Officer's acceptance of the Final Assay Qualification Reports for all assays.

Milestone 4. Formulation and Fill of Final Drug Product (FDP)

a. Final Drug Product -- Formulate, fill, finish and release a minimum of three successful cGMP grade FDP lots. Formulated vaccine must be in the presentation intended for final clinical use, long-term stability, and licensure. *[Note: For purposes of this contract, one lot FDP is defined as a minimum of 2,000 final doses per single run.]*

   1) *Within 11 months of contract award*, formulate, fill, finish and release one lot of clinical grade cGMP FDP.

   2) *Within 14 months of contract award*, formulate, fill, finish and release two additional lots of clinical grade cGMP FDP.

b. Batch Records -- Submit Batch Records, as requested by the Project Officer. Provide for Project Officer on-site review of Batch Records when directed by the Project Officer. Submit a CoA for each released lot, and a FDP Process Development Report *following completion of the three released lots*. Completion of Milestone 4 shall be based on the Project Officer determination, through review of the submitted CoAs for released material and associated Batch Records, and the FDP Process Development Report that the released material is suitable for use in Phase 1 and 2 clinical trials.

Milestone 5. Pre-clinical Safety and Toxicity Study(ies).

a. Safety and Toxicity Study(ies) -- *Within 12 months of contract award*, initiate a Good Laboratory Practice (GLP) safety and toxicity study(ies). The number and type of safety and toxicity studies to be performed shall be dependent on CBER/FDA requirements for supporting a Contractor-filed IND and a Phase 1 clinical trial using the vaccine candidate.

   1) Draft Pre-clinical Safety and Toxicity Protocol(s) -- *Within 10 months of contract award*, develop and submit, for Project Officer review, a Draft Pre-clinical Safety and Toxicity Protocol(s) and provide the rationale for proposed study design(s) and animal species selected.

   2) Final Pre-clinical Safety and Toxicity Protocol(s) – *Project Officer will provide comments within 14 calendar days. Within 30 calendar days of receipt of Project Officer comments*, revise the Draft Pre-clinical Safety and Toxicity Protocol(s) as necessary, and submit the Final Pre-clinical Safety and Toxicity Protocol(s) to the Project Officer. The Contractor must be in receipt of Project Officer written approval of the Final Pre-clinical Safety and Toxicity Protocol(s) prior to study initiation.

   3) Discussions with CBER/FDA -- Conduct discussions with CBER/FDA with respect to the design and number of the proposed pre-clinical safety and toxicity study(ies) proposed. Provide documentation, in the form of written minutes of interactions with the FDA, that these discussion have taken place and concurrence has been received from CBER/FDA indicating that a successful outcome of the proposed study(ies) would be supportive for the filing of an IND.

4) Conduct the Pre-clinical Safety and Toxicity Study(ies) in accordance with the approved Final Protocol(s).

b. Final Pre-clinical Safety and Toxicity Study Report(s) -- *Within 60 calendar days after completion of the Pre-clinical Safety and Toxicity Study(ies)*, prepare and submit, for Project Officer review and approval, a Final Pre-clinical Safety and Toxicity Study Report(s). Completion of Milestone 5 shall be based on delivery of the Final Pre-clinical Safety and Toxicity Study Report(s) and acceptance of the Report(s) by the Project Officer.

Milestone 6. Non-clinical General-Use Prophylaxis (GUP) Study(ies) in the Rabbit Model.

a. Aerosol Anthrax Spore-challenge Study(ies) -- *Within twelve (12) months of contract award*, initiate one or more aerosol anthrax spore-challenge study(ies) in the rabbit model using a GUP regimen to determine the efficacy and immunogenicity of the vaccine candidate.

1) Guidelines -- Unless otherwise directed by the Project Officer, adhere to the guidelines established by DMID/NIAID, in collaboration with an Interagency Animal Studies Group (IASG) comprised of Government members from the FDA and the Department of Defense (DOD) and non-Government consultants, for an aerosol spore-challenge rabbit model for GUP to define immune correlates of protection in support of the CBER/FDA "Animal Rule" as outlined in 21 CFR 601.91(a)(1-4). See http://www3.niaid.nih.gov/Biodefense/Research/products.htm#b for model overview.

2) Draft Non-clinical Rabbit GUP Protocol(s) -- *Within 10 months of contract award*, develop and submit a Draft Non-clinical Rabbit GUP Protocol(s) and provide the rationale for proposed study design(s) to the Project Officer.

3) Final Non-clinical Rabbit GUP Protocol -- *Within 30 calendar days of receipt of Project Officer comments*, revise the Draft Non-clinical Rabbit GUP Protocol as necessary and submit the Final Protocol for Project Officer approval. The Contractor must be in receipt of the Project Officer's written approval of the Final Protocol prior to study initiation.

4) Conduct the Non-clinical GUP studies in accordance with the approved Final Protocol.

5) Summary Interim Non-clinical Rabbit GUP Report -- *Within 14 weeks of study initiation*, prepare and submit a Summary Interim Non-clinical Rabbit GUP Report, for Project Officer review and approval, containing at a minimum, post-challenge survival data, and all raw and analyzed data available up to the post-challenge survival time point.

6) Final Rabbit GUP Report(s) -- *Within 30 calendar days after completion of the approved Non-clinical Rabbit GUP study(ies)*, prepare and submit a Final Rabbit GUP Report(s) to the Project Officer. Completion of Milestone 6 shall be based on

delivery of the Non-clinical Rabbit GUP Study Report(s) and Project Officer determination of the acceptability of the Final Report(s).

Milestone 7. Non-clinical Post-Exposure Prophylaxis (PEP) Study in the Rabbit Model.

a. Aerosol Anthrax Spore-challenge PEP Study -- *Within 14 months of contract award*, initiate an aerosol anthrax spore-challenge PEP study in the rabbit model to determine if the candidate vaccine provides added value over antibiotic use alone in this animal model when used in conjunction with antibiotic therapy using a post-exposure regimen.

1) Guidelines -- Unless otherwise directed by the Project Officer, adhere to the guidelines established by DMID/NIAID, in collaboration with the IASG, for an aerosol spore-challenge rabbit model for PEP to define immune correlates of protection in support of the CBER/FDA "Animal Rule" as outlined in 21 CFR 601.91(a)(1-4). See http://www3.niaid.nih.gov/Biodefense/Research/products.htm#b for model overview.

2) Draft Non-clinical Rabbit PEP Protocol -- *Within 12 months of contract award*, develop and submit, for Project Officer review, a Draft Non-clinical Rabbit PEP Protocol and provide the rationale for the proposed study design(s).

3) Final Non-clinical Rabbit PEP Protocol -- *Within 30 calendar days of Project Officer review*, revise the Draft Protocol as necessary, and submit the Final Non-clinical Rabbit PEP Protocol for Project Officer approval. Project Officer written approval of the Final Protocol shall be required prior to study initiation.

4) Conduct the Non-clinical PEP study in accordance with the approved Final Protocol.

5) Summary Interim Non-clinical Rabbit PEP Report -- *Within 8 weeks of study initiation*, prepare and submit, for Project Officer review and approval, a Summary Interim Non-clinical Rabbit PEP Report containing, at a minimum, post-challenge survival data, and all raw and analyzed data available up to the post-challenge survival time point.

6) Final Non-clinical Rabbit PEP Study Report(s) -- *Within 30 calendar days after completion of the approved study,* prepare and submit a Final Non-clinical Rabbit PEP Study Report(s). Completion of Milestone 7 shall be based on delivery of the Non-clinical Rabbit PEP Study Report(s) and Project Officer determination of the acceptability of the Final Study Report(s).

Milestone 8. Non-clinical Data and CMC Information.

a. Submission of Non-clinical Data and CMC Information -- *Within 18 months of contract award*, submit to the Project Officer all chemistry, manufacturing, and controls (CMC) information, and non-clinical information necessary to support a Government-held IND; or submit to CBER/FDA a Letter of Cross-Reference to the Contractor IND or Master File.

b. Use of Data -- The NIAID and/or the Contractor may use data developed during performance of this contract for consultations with the FDA in planning subsequent product development and/or clinical studies.

c. Completion of Milestone 8 shall be based on submission and Project Officer acceptance of CMC information and non-clinical data, or a copy of the Letter of Cross Reference.

Milestone 9. Non-clinical Post-Exposure Prophylaxis (PEP) Study in a Non-Human Primate (NHP) Model.

a. Aerosol Anthrax Spore-challenge PEP Study -- *Within 18 months of contract award*, initiate an aerosol anthrax spore-challenge PEP study in a NHP model to determine if the candidate vaccine provides added value when used in conjunction with antibiotic therapy over antibiotic use alone in this animal model .

1) Guidelines -- Unless otherwise requested by the Project Officer, adhere to the guidelines established by DMID/NIAID, in collaboration with the IASG, for an aerosol spore-challenge NHP model for PEP to define immune correlates of protection in support of the CBER/FDA "Animal Rule" as outlined in 21 CFR 601.91(a)(1-4). See http://www3.niaid.nih.gov/Biodefense/Research/products.htm#b for model overview.

2) Draft Non-Clinical NHP PEP Protocol -- *Within 16 months of contract award*, develop and submit, for Project Officer review, a Draft Non-clinical NHP PEP Protocol and provide the rationale for the proposed study design.

3) Final Non-clinical NHP PEP Protocol -- *Within 30 calendar days of Project Officer review*, revise the Draft Protocol as necessary, and submit the Final Non-clinical NHP PEP Protocol for Project Officer approval. Project Officer approval of the Final Protocol shall be required prior to study initiation.

4) Conduct the Non-clinical NHP PEP study in accordance with the approved Final Protocol.

5) Summary Interim Non-clinical NHP PEP Report -- *Within 8 weeks of study initiation*, prepare and submit, for Project Officer review and approval, a Summary Interim Non-clinical NHP PEP Report containing at a minimum, post-challenge survival data, and all raw and analyzed data available up to the post-challenge survival time point.

6) Final Non-clinical NHP PEP Study Report(s) -- *Within 30 calendar days after completion of the approved study*, prepare and submit a Final Non-clinical NHP PEP Study Report. Completion of Milestone 9 shall be based on delivery of the Non-clinical NHP PEP Study Report and Project Officer determination of the acceptability of the Final Study Report.

Milestone 10. Delivery of Vaccine to NIAID.

Within 24 months of contract award, deliver to DMID/NIAID repository contractor a minimum of 2,000 clinical doses of FDP. Delivered vaccine must be from more than one FDP lot.

a. Shipping Validation Report – *Within 30 calendar days prior to shipment of vaccine material*, prepare and submit for Project Officer review and approval, a Shipping Validation Report.

b. Delivery of Vaccine Material -- *Upon Project Officer approval of the Shipping Validation Report*, deliver the following vaccine material:

1) the 2,000 cGMP vaccine doses;
2) a CoA for each FDP lot included in the 2,000 vaccine doses;
3) a quantity of cGMP manufactured diluent sufficient for performing dose-ranging clinical studies with the 2,000 vaccine doses; and
4) any novel device(s) utilized for vaccine inoculation.

c. Completion of Milestone 10 shall be based on Project Officer's written concurrence that all deliverables have been shipped under cGMP conditions and successfully received by DMID/NIAID.

Milestone 11. Development Plan for Biological License Application (BLA).

a. Integrative Development Plan -- Prepare an integrative Development Plan that details the manufacturing, non-clinical, clinical and regulatory strategies to be applied to the candidate vaccine for filing BLAs for PEP and GUP indications. The Integrative Development Plan shall consist of the following components:

1) The Manufacturing Development Plan Component shall include:

a) current methods for pilot-scale manufacturing, product characterization and release,
b) current methods for technology transfer for pilot-lot to large-scale transition for both DS and FDP,
c) proposed timelines up to manufacture of consistency lots for FDP, and
d) a validation plan for all associated assays.

2) The Non-Clinical Development Plan Component shall include:

a) proposed study designs for additional animal safety and toxicity studies and pivotal animal immunogenicity and efficacy studies necessary to establish a correlate of protection to satisfy Emergency-Use Authorization requirements (http://www3.niaid.nih.gov/Biodefense/Research/products.htm) and the CBER/FDA "Animal Rule" as outlined in 21 CFR 601.91(a)(1-4), and

b) a description of the immunological assays to be validated and used to define efficacy endpoint(s) and proposed timelines for the completion of all non-clinical studies.

3) The Clinical and Regulatory Development Plan Component shall include:

a) a synopsis of a dose-escalating Phase 1 and formulation and regimen Phase 2 clinical trials in healthy adult subjects,
b) a synopsis of additional studies beyond initial Phase 1 and 2 clinical trials required for a BLA, including Phase 2 studies involving vulnerable populations (i.e. children, the elderly), Phase 3 safety trials, and post-marketing studies,
c) an associated regulatory strategy,
d) a data management plan,
e) a statistical monitoring plan,
f) a safety monitoring plan for each clinical trial, and
g) proposed timelines for protocol development, protocol implementation, study completion and analysis of final study data.

b. Submit the Integrative Development Plan to the Project Officer for review and approval *within 30 months after contract award*. Completion of Milestone 11 shall be based on Project Officer written approval of the Integrative Development Plan.

2. **MANUFACTURING AND NON-CLINICAL BIOCONTAINMENT FACILITIES, SAFETY AND TRAINING**

a. Provide facilities for the development, manufacturing, and testing of the vaccine candidate, including product manufacturing facilities, both DS and FDP, that are compliant with current Good Manufacturing Practices (cGMPs) and the capacity to perform required tasks. All facilities shall be available for manufacturing and testing sufficient to complete Milestones 1 and 4 with required resources dedicated to the project.

b. For non-clincal testing of the vaccine candidate provide safe biocontainment facilities and resources and conduct work in accordance with the Biosafety in Microbiology and Biomedical Laboratories (BMBL) Guidelines, Centers for Disease Control and Prevention and the National Institutes of Health, fourth edition, HHS Publication No. (CDC) 93-8395 published by the U.S. Government Printing Office, May 1999, Stock Number 017-040-0547-4.

c. Provide staff with the required level of training, experience and expertise to operate the facilities and conduct the studies in accordance with the Biosafety Level (BSL) 2 and 3 guidelines (http://bmbl.od.nih.gov/) where appropriate.

d. Provide training, protective garments, equipment and monitoring to assure safe handling of potentially hazardous microorganisms and toxins for all personnel working with *B. anthracis* or organisms producing these anthrax toxins, including staff of any subcontractors, and ensure implementation of prompt corrective actions for any identified safety problems.

e. Where applicable, conduct work in accordance with DHHS regulations regarding the transfer of Select Agents (42 CFR Part 72).

f. Where applicable, follow the Federal Guidelines for Research Involving Recombinant DNA molecules (http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html).

3. **ANIMAL CARE AND USE**

a. Acquisition and Selection of Laboratory Animals

The decision of which animal species is to be used and any requirements for specific-pathogen free (SPF) animals shall be made jointly by the Project Officer and the Contractor with the Project Officer having final approval authority.

b. Housing and Care of Laboratory Animals and Maintenance of Animal Records

1) Provide well-equipped and maintained facilities with necessary biohazard containment capabilities, using appropriate biosafety procedures to care for and handle animals receiving aerosol anthrax spore challenge. Animals may be housed in BSL-2 biohazard containment facilities until exposure to anthrax spores. Exposure of animals to anthrax spores and housing of animals following exposure to anthrax spores shall follow biocontainment practices for laboratory animals as described in the Biosafety in Microbiological and Biomedical Laboratories (BMBL) guidelines (http://bmbl.od.nih.gov/).

2) Comply with the Public Health Service Policy on Humane Care and Use of Laboratory Animals. This policy may be accessed at http://grants1.nih.gov/grants/olaw/references/phspol.htm.

3) Provide care and routine health surveillance for laboratory animals. The veterinary and animal care staff shall perform and record observations, including each animal's health status and any treatments received, and euthanize animals according to humane procedures approved by the Contractor's Institutional Animal Care and Use Committee (IACUC).

4) Provide for on-call veterinary coverage of the animal facility 24 hours a day, seven days a week, and provide at least daily observation of the health status of each animal, including weekends and holidays.

5) Provide standard technical and veterinary assistance, as needed, for the performance of routine procedures, such as inoculation and bleeding of the selected laboratory animals. Provide veterinary capability for the performance of post-mortem examinations.

6) Provide and manage a security system to prevent unauthorized entry into the animal care facility.

7) Ensure appropriate oversight and monitoring of animal care facilities, equipment, services and procedures carried out under subcontract.

4. **QUALITY ASSURANCE/QUALITY CONTROL**

Develop and implement a Quality Assurance/Quality Control plan to ensure that the manufacturing and testing of vaccine candidate and the data generated meet all FDA Good Manufacturing Practices (GMP) (http://www.fda.gov/cber/) and Good Laboratory Practices (GLP) (http://www.fda.gov/ora/compliance_ref/bimo/glp/default.htm) regulatory standards. This plan shall include standard operating procedures for

establishing and maintaining the QA/QC process and demonstrated remediation to address problems as they occur.

a. A draft of this plan shall be *submitted to the Project Officer within 15 calendar days of contract award*.

b. The Project Officer will provide comments to the Contractor *within 15 calendar days of receipt of the draft plan*.

c. The Contractor shall submit a Final QA/QC Plan, which incorporates the Project Officer's comments, *within 15 calendar days after the Project Officer's comments are received*.

5. **MEETINGS AND CONFERENCES**

a. Progress Review Meetings/Teleconferences

1) Participate in and prepare materials for regular meetings and teleconferences to coordinate and oversee contract activities as requested by the Project Officer.

2) At a minimum, meetings shall include one Contractor visit every three months, for two days, to meet with the Project Officer and other Project Officer-designated NIAID staff in Bethesda, Maryland.

3) Agendas shall be provided to the Project Officer for approval *within two calendar days prior to the Meeting/Conference*

4) Meeting/Conference minutes shall be provided to the Project Officer approval within three calendar days following each Meeting/Conference.

5) Provide read-ahead documents to the Project Officer.

6) Progress review activities shall include bi-weekly teleconferences of all Contractors and subcontractors with Project Officer to discuss study designs, progress, problems and obstacles and approaches to overcoming problems and obstacles.

7) Other meetings with the Contractor may be held to discuss proposed modifications to study designs and/or timelines; meetings with individual Contractors and other HHS officials to discuss the technical, regulatory, and ethical aspects of the research and development program.

8) Provide data, reports, and presentations to groups of outside experts and Government personnel, as required by the Project Officer, in order to facilitate review of contract activities.

b. Site Visits/Technical Audits

The Project Officer and/or Project Officer's designee(s) will perform on-site visits and/or technical audits at Contractor and subcontractor sites. At a minimum, up to

six, two-day site visits/technical audits will be conducted annually throughout the contract performance period.

c. FDA Meetings

The Project Officer and Project Officer's designees shall be granted permission by the Contractor to be an observer at all FDA meetings and teleconferences related to any activities being performed as part of this contract including work performed by subcontractors and collaborators.

6. SCIENTIFIC AND TECHNICAL TEAM

Provide all expertise needed to complete the contract milestones including: development, manufacturing, characterization, testing, and regulatory activities of the vaccine candidate. The team must provide strong scientific leadership, as well as significant experience and expertise in the management, design and execution of a research and development program focused on product development, manufacturing, and testing in vertebrate animals. The team shall include the following:

a. A Principal Investigator qualified to lead, direct and coordinate all contract activities, including activities carried out by subcontractors. This includes appropriate knowledge and expertise in advanced bacterial vaccine development; prior successful IND submissions to the FDA and completion of preclinical and clinical vaccine studies; and the capacity to monitor progress, access performance, identify performance problems and implement corrective actions.

b. Experienced Quality Assurance/Quality Control (QA/QC) personnel

c. Key Scientific and Technical Personnel with the qualifications and abilities to conduct the range of vaccine production activities, assays, and non-clinical and clinical studies.

7. PROJECT MANAGEMENT

a. Overall Project Management

1) Provide for the overall management, integration and coordination of all contract activities carried out under each Option, including the management and coordination of activities carried out by subcontractors.

2) Provide a technical and administrative infrastructure to ensure the efficient planning, initiation, implementation, management and timely completion of all Option activities and requirements and effective communications with the Project Officer and the Contracting Officer.

3) The Principal Investigator shall be responsible for overall project management and communications, tracking, monitoring and reporting on project status and progress, and recommending modifications to project requirements and timelines.

4) This infrastructure shall also include personnel to coordinate contract and study specific activities and administrative staff with responsibility for financial management and financial reporting on all activities conducted by the Contractor and subcontractors.

b. Subcontract Execution, Management and Reporting

Manage the subcontracting activity and carry out the following for the Option activities to be conducted under subcontract:

1) manage any subcontracting activity for the clinical trial and ensure that the award and management of subcontracts is in accordance with FAR Clause 52.244-2.

2) execute and manage subcontracts, oversee the technical, administrative and operational activities of subcontractors, including auditing subcontractor facilities, services, and financial expenditures, and track deliverables and reporting requirements;

3) assess and provide quarterly technical reports on subcontractor performance and progress, identify and resolve problems with subcontractor performance.

4) ensure that subcontractor personnel, equipment and facilities are compliant with regulatory requirements in effect throughout the contract period of the Option.

5) 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.

6) perform all necessary transition and closeout functions on each subcontract.

[*END OF BASE PERIOD – STATEMENT OF WORK*]

8. OPTION 1: PHASE 1 CLINICAL TRIAL

Unless the Government excercises Option 1 this contract will only consist of paragraphs 1. through 7. of the Statement of Work.

Option 1: Design and conduct of a Phase 1 dose-escalating clinical trial in healthy subjects ages 18 to 40.

In the event that Government elects to exercise Option 1, the Contractor shall be required to carry out the functions specified below, and shall provide the necessary scientific, technical and management personnel and the clinical research facilities and other resources needed to perform these functions:

a. Protocol Development
b. Protocol Implementation
c. Protocol Oversight;
d. Quality Assurance/Quality Control
e. Scientific and Technical Personnel
f. Clinical Research Facilities and Resources
g. Meetings
h. Interim Data Report and Final Report

a. PROTOCOL DEVELOPMENT

1) Protocol Development Processes and Templates

In developing clinical protocols, adhere to DMID standardized protocol development processes and templates (http://www.niaid.nih.gov/dmid/clinresearch/#resources). The processes and requirements delineated below shall be implemented by the Contractor during the protocol development stage. The Contractor shall not proceed to the protocol implementation stage on all final clinical protocols until written approval by the Project Officer has been received.

2) Draft and Final Protocol

a) Draft Protocol -- *Within 45 calendar days of receipt of contract Modification signed by Contracting Officer to exercise Option 1*, develop and submit the Draft Protocol and associated materials for Project Officer review, using the DMID Study Product Protocol Template (http://www.niaid.nih.gov/dmid/clinresearch/protocol_template.doc) and the DMID Study Product Protocol Template: Working Shell (http://www.niaid.nih.gov/dmid/clinresearch/interventionalworkingshell.doc). Associated materials, in addition to the Draft Protocol, shall include: the statistical analysis plan (SAP); informed consent forms; case report forms (CRFs), safety monitoring plan; and Manual of Procedures. The Contractor shall develop the safety monitoring plan in collaboration with the Project Officer's clinical team, and the final safety monitoring plan shall be determined by the Project Officer.

b) Final Protocol -- Modify the Draft Protocol as necessary to address Project Officer comments, and *submit the Final Protocol within 4 weeks following receipt of Project Officer comments*. The protocol shall be considered final only upon receipt of written approval by the Project Officer.

3) Clinical Trial Timeline

Within 30 calendar days of receipt of contract Modification signed by Contracting Officer to exercise Option 1, a Clinical Trial Timeline shall be developed by the Contractor and approved by the Project Officer and shall delineate the time frames for the development of the Draft and Final Protocol, recruitment, intervention and follow-up of study participants, study completion, and analysis and publication of study data and results. The Contractor shall not implement the study prior to receipt of Project Officer's written approval of the Protocol Timeline.

b. **PROTOCOL IMPLEMENTATION**

1) Pre-Study Initiation Requirements

Prior to study initiation, the following requirements must be satisfied:

a) Human Subjects Requirements - Obtain and provide to the Project Officer and Contracting Officer documentation of local Institutional Review Board (IRB) approval to conduct the clinical trial for all participating clinical sites. Copies of Department of Health and Human Services (DHHS) regulations for the protection of human subjects, 45 CFR Part 46, are available from the Office for Human Research Protections (OHRP), Office of the Secretary (OS), DHHS –http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm. DMID policies, guidelines, templates and other important information regarding performing human subjects research are available at: http://www.niaid.nih.gov/dmid/clinresearch/.

b) 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/index.htm).

c) Study Investigator Meeting/Teleconference

(1) The Principal Investigator, clinical investigators and clinical study personnel who will be performing the clinical trial shall participate in a study initiation meeting and/or teleconference to be organized by the Contractor prior to study initiation.

(2) DMID clinical personnel reserve the right to attend the meeting/teleconference.

(3) The meeting/teleconference shall serve to review protocol specifications, requirements and procedures, target enrollment, and approved protocol timelines.

(4) Summaries of major discussion and action items shall be prepared by the Contractor and submitted to the Project Officer *within one week after completion of the meeting/teleconference*.

2) Study Product Requirements

Responsibility for investigational product accountability shall include the following, as applicable:

a) accurate records documenting supply of test article;
b) date and amount of test article dispensed to each subject;
c) amount of test article used and verified during a monthly physical inventory;
d) preservation and validation of cold chain including records to verify cold chain for all materials stored at other than room temperature;
e) packaging and labeling of test article in compliance with applicable labeling regulations;
f) transport of investigational products to clinical area; and
g) documentation that all participating clinical sites have received the appropriate supply of the investigational product.

3) Clinical Trial Conduct

Conduct the clinical trial 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 approved clinical protocol and the Manual of Procedures.

4) Protocol Tracking Reports

Develop and implement tracking procedures for reporting enrollment status and for the follow-up of study participants. In addition, prepare and submit Protocol Tracking Reports as part of the Monthly Technical Progress Reports during the active enrollment phase.

5) Protocol Amendments and Other Clinical Trial Modifications

a) Recommend to the Project Officer, amendments to the clinical protocol, the Manual of Procedures and the informed consent documents, including a written description of the proposed amendments/modifications and their rationale. All such amendments and modifications shall require written approval by the Project Officer prior to implementation. The Project Officer may also recommend amendments.

b) Obtain and provide documentation of IRB approval to the Project Officer and Contracting Officer for protocol amendments prior to implementation.

6) Data Management and Quality Control

Retain primary responsibility for data management and quality control functions carried out under this contract and any subcontract, including:

a) Developing and operating a data management system to maintain up-to-date information on all clinical and laboratory data.

b) Developing and implementing standards and procedures for the entry and quality control of study data to ensure that clinical data are accurate, complete and entered in a timely fashion.

c) Providing training in the use of the data management system for clinical site personnel prior to study implementation.

d) Managing data and address queries in accordance with DMID source document guidelines (www.niaid.nih.gov/dmid/clinresearch/sourcedocumentationstandards.pdf).

c. **PROTOCOL OVERSIGHT**

1) Investigational New Drug (IND) Sponsorship

Serve as the IND sponsor and assume responsibility for all IND-related activities and requirements, including:

a) preparation of materials for and requesting, scheduling and participating in all meetings and teleconferences with the CBER/FDA pre- and post-IND submission;
b) arranging meetings and teleconferences with the FDA that include the Project Officer and other DMID staff as designated by the Project Officer;
c) preparation and submission of the IND;
d) preparation and submission of all FDA required documentation to CBER/FDA in sufficient time to initiate a Phase 1 clinical trial during the third performance year of the base contract following CBER/FDA review and approval by the Project Officer;
e) provision to the Project Officer of copies of all FDA correspondence and meeting/teleconference minutes;
f) preparation and submission of the Annual IND Report to the FDA;
g) preparation and submission of an Interim Data Study Report containing safety and immunogenicity raw data and statistically analyzed results *up to four weeks following the final vaccine dose*; and
h) preparation and submission of the Final Clinical Study Report 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 and the Project Officer *within one 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/aprqtr/21cfr312.23.htm and link for final report http://a257.g.akamaitech.net/7/257/2422/01apr20051500/edocket.access.gpo.gov/cfr_2005/aprqtr/21cfr312.64.htm).

2) Safety Oversight

a) Contractor Safety Oversight Requirements

(1) Implement the approved safety oversight plan, including, at a minimum, provision for an Independent Safety Monitor and back-up monitor for all participating clinical sites identified by the Contractor and approved by the Project Officer.

(2) The charter and membership of any Contractor-constituted safety oversight structure is required to be approved by the Project Officer.

b) DMID Safety Oversight Structure

(1) DMID, in conjuction with the Contractor, shall establish a Safety Oversight Structure for the clinical trial, independent of the Principal Investigator. The Safety Oversight Structure shall operate in a manner consistent with DMID Safety Oversight Guidances (http://www.niaid.nih.gov/dmid/clinresearch/), and shall accommodate the risk and complexity of the clinical trial.

(2) Present the clinical protocol, safety data, and interim and final study data to the DMID Safety Oversight Structure. The Project Officer will have approval of data format.

c) Serious Adverse Event Reporting

(1) The information contained in the DMID Serious Adverse Event (SAE) Report Form must be included in the Contractor's SAE Report Form. It is recommended that the Contractor use the DMID SAE Report Form located at http://www.niaid.nih.gov/dmid/clinresearch/.

(2) Submit SAE Reports to the DMID Office of Clinical Research Affairs (OCRA), according to the Clinical Terms of Award (http://www.niaid.nih.gov/ncn/pdf/clinterm.pdf).

(3) Report SAE events to OCRA within 24 hours following Contractor notification of event.

d) Clinical Site Monitoring

(1) Perform clinical site monitoring/auditing 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 GCP, the clinical protocol and applicable regulatory requirements.

(2) Conduct an initiation visit by the Clinical Monitor prior to active recruitment.

(3) Conduct ongoing clinical site monitoring during the active recruitment, dosing, follow-up and close-out phases of the clinical trial.

(4) Identify performance problems and deficiencies through the clinical site monitoring function and for developing and implementing remedial actions to address all such performance problems and issues.

(5) Submit updated clinical monitoring reports on a monthly basis to the Project Officer.

e) System of Records

Design, implement and maintain a system of records for the clinical trial in compliance with the Privacy Act and the Confidentiality of Information Clauses contained within the contract.

d. **QUALITY ASSURANCE/QUALITY CONTROL(QA/QC)**

1) Quality Assurance/Quality Control Plan

a) QA/QC Control Plan -- Develop and implement a Quality Assurance/Quality Control plan to ensure that the conduct of the clinical trial and the data generated meet all FDA Good Clinical Practices (GCP) (http://www.fda.gov/oc/gcp/guidance.html) and DMID/NIAID regulatory standards (http://www.niaid.nih.gov/dmid/clinresearch/OP_QM001Rev0.pdf).

b) Draft QA/QC Control Plan – At the request of the Project Officer following the exercise of an Option, submit *a draft plan to the Project Officer within 30 calendar days.* The Project Officer will provide comments to the Contractor within two weeks of receipt of the draft plan.

c) Final QA/QC Control Plan – *At the request of the Project Officer and within 15 calendar days from receipt of the Project Officers comments,* submit a final plan that incorporates the Project Officer's comments. This plan shall include standard operating procedures for establishing and maintaining the QA/QC process and demonstrated remediation to address problems as they occur.

2) Audits

Audits may be requested by the Project Officer to assure that Contractor and/or subcontractor facilities and all planned procedures meet FDA regulations and guidance for Good Clinical Practices (GCP) and/or Good Laboratory Practices (GLP). Ensure that all Contractor and/or subcontractor records and staff are available for such audits.

e. **SCIENTIFIC AND TECHNICAL PERSONNEL**

Provide appropriately trained and experienced personnel for the conduct and oversight of the clinical trial, including:

1) Clinical Trial Principal Investigator

The Clinical Trial Principal Investigator shall be licensed as a physician and shall ensure that active licensure is maintained for the entire period of performance of the trial, including each Option if exercised. The Principal Investigator must possess experience in the design and conduct of clinical trials for infectious diseases and specifically, clinical trials of candidate vaccines against infectious diseases.

2) Other Scientific/Technical Personnel

a) Physician investigators shall be licensed physicians; maintain active licensure for the entire period of clinical trial performance for each Option; and possess experience in the design and conduct of clinical trials of infectious diseases, particularly clinical trials of candidate vaccines against infectious diseases, and in the assessment of participants for study eligibility and safety post enrollment.

b) Clinical Research Study Staff, trained and experienced in Good Clinical Practices, including:

(1) nurse managers, study coordinators,
(2) clinical support staff,
(3) laboratory personnel,
(4) personnel with regulatory expertise, and
(5) data managers.

c) A Research Pharmacist proficient in all aspects of investigational product management.

d) Collaborating clinical investigators or consultants in other medical specialties when necessary to meet protocol-specific requirements.

e) Qualified personnel necessary to package, label, store under appropriate conditions, and track clinical specimens.

f. **CLINICAL RESEARCH FACILITIES AND RESOURCES**

Provide all necessary clinical research facilities and resources for the conduct of the clinical trial, including:

1) Outpatient Clinical Research Facilities at all participating clinical sites to accommodate enrollment, administration of investigational product, and follow-up of subject in accordance with the specific requirements of the approved protocol.

2) Clinical Laboratory Facilities to obtain and process clinical specimens and conduct protocol-required tests to determine participant eligibility and safety evaluations. For all such facilities, maintain current Clinical Laboratory Improvement Amendment certification (www.cms.hhs.gov/clia) and Joint Commission on

Accreditation of Healthcare Organizations approval (www.jcaho.org) or equivalent foreign organization.

3) Research Laboratory Facilities to process and store specimens and conduct protocol relevant cultures and/or immunologic assays. Ensure that work conforms to standards acceptable for IND and/or BLA submission (see http://www.niaid.nih.gov/dmid/clinresearch/#resources for guidance). Serological analysis performed must utilize standardized protocols, characterized reagents, and qualified or validated immunological assays for all human studies.

4) Research Pharmacy Facilities for the management of the investigational product, including Standard Operating Procedures and other appropriate procedures and policies to provide for appropriate storage of, and monitoring controlled access to the investigational product.

5) Clinical Trial Sites

   a) Solicit, negotiate, execute and manage subcontracts for the provision of clinical site personnel, services and facilities, including oversight of subcontractor performance.

   b) Clinical sites must:

      (1) Provide qualified clinical investigators, nurse managers, study coordinators, and other clinical research support staff.

      (2) Provide staff with experience and expertise in the conduct of clinical trials 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.

      (3) Provide staff with experience in the screening, recruitment and retention of study participants; access to healthy adult subjects; and research laboratory facilities, equipment and personnel for the conduct of protocol-specific tests and for the processing and storage of clinical specimens.

   c) Utilize the personnel, services and facilities of qualified clinical sites to provide access to and ensure enrollment of adequate numbers of study participants for the timely conduct and completion of the clinical trial.

g. **MEETINGS**

1) For each Option, sponsor all clinically-related meetings, including an Option Kick-Off Meeting, an Investigator Meeting, and site visits to clinical sites to assure GCP compliance throughout the clinical trial. The Project Officer, the Contracting Officer and other NIAID program staff may attend these meetings and site visits.

2) Incorporate progress review updates into the biweekly Contractor/Project Officer teleconferences and the Monthly Technical Progress Report.

h. **CLINICAL INTERIM STUDY REPORT AND FINAL REPORT**

1) A Clinical Interim Study Report containing safety and immunogenicity raw data and statistically analyzed results shall be submitted *within 45 days following analysis of interim trial data*.

2) A comprehensive Final Clinical Study Report shall be submitted *within three months following completion of the clinical trial*.

[END OF OPTION 1 - STATEMENT OF WORK]

9. **OPTION 2: Up to two Phase 2 Clinical Trials**

Unless the Government excercises Option 2 this contract will only consist of paragraphs 1. through 8. of the Statement of Work. This Option may be excercised up to two times.

Design and conduct of up to two Phase 2 clinical trials in healthy subjects ages 18 to 55 to optimize vaccine formulation and define a (Post-Exposure Prophylaxis) PEP regimen. Unless otherwise requested by the Project Officer, adhere to the guidelines established by DMID/NIAID, in collaboration with the IASG, for PEP emergency use of vaccines. See http://www3.niaid.nih.gov/Biodefense/Research/products.htm#b for information on human safety and immunogenicity requirements.

The Contractor shall be required to carry out the functions specified below, and shall provide the necessary scientific, technical and management personnel and the clinical research facilities and other resources needed to perform these functions:

a. Protocol Development
b. Protocol Implementation
c. Protocol Oversight
d. Quality Assurance/Quality Control
e. Scientific and Technical Personnel
f. Clinical Research Facilities and Resources
g. Meetings
h. Interim Data Report and Final Report

a. **PROTOCOL DEVELOPMENT**

1) Protocol Development Processes and Templates

In developing clinical protocols, adhere to DMID standardized protocol development processes and templates (http://www.niaid.nih.gov/dmid/clinresearch/#resources). The processes and requirements delineated below shall be implemented by the Contractor during the protocol development stage. The Contractor shall not proceed to the protocol implementation stage on all final clinical protocols until written approval by the Project Officer has been received.

2) Draft and Final Protocol

a) Draft Protocol -- *Within 45 calendar days of receipt of contract Modification signed by Contracting Officer to exercise Option 2*, develop and submit the Draft Protocol and associated materials for Project Officer review, using the DMID Study Product Protocol Template (http://www.niaid.nih.gov/dmid/clinresearch/protocol_template.doc) and the DMID Study Product Protocol Template: Working Shell (http://www.niaid.nih.gov/dmid/clinresearch/interventionalworkingshell.doc). Associated materials, in addition to the Draft Protocol, shall include: the statistical analysis plan (SAP); informed consent forms; case report forms (CRFs), safety monitoring plan; and Manual of Procedures. The Contractor shall develop the safety monitoring plan in collaboration with the Project

Officer's clinical team, and the final safety monitoring plan shall be determined by the Project Officer.

b) Final Protocol -- Modify the Draft Protocol as necessary to address Project Officer's comments and *submit the Final Protocol within 4 weeks following receipt of Project Officer's comments*. The protocol shall be considered final only upon receipt of written approval by the Project Officer.

3) Clinical Trial Timeline

Within 30 calendar days of receipt of contract Modification signed by Contracting Officer to exercise Option 2, a Clinical Trial Timeline shall be developed by the Contractor and approved by the Project Officer and shall delineate the time frames for the development of the Draft and Final Protocol, recruitment, intervention and follow-up of study participants, study completion, and analysis and publication of study data and results. The Contractor shall not implement the study prior to receipt of Project Officer's written approval of the Protocol Timeline.

b. **PROTOCOL IMPLEMENTATION**

1) Pre-Study Initiation Requirements

Prior to study initiation, the following requirements must be satisfied:

a) Human Subjects Requirements - Obtain and provide to the Project Officer and Contracting Officer documentation of local Institutional Review Board (IRB) approval to conduct the clinical trial for all participating clinical sites. Copies of Department of Health and Human Services (DHHS) regulations for the protection of human subjects, 45 CFR Part 46, are available from the Office for Human Research Protections (OHRP), Office of the Secretary (OS), DHHS –http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm. DMID policies, guidelines, templates and other important information regarding performing human subjects research are available at: http://www.niaid.nih.gov/dmid/clinresearch/.

b) 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/index.htm).

c) Study Investigator Meeting/Teleconference

(1) The Principal Investigator, clinical investigators and clinical study personnel who will be performing the clinical trial shall participate in a study initiation meeting and/or teleconference to be organized by the Contractor prior to study initiation.

(2) DMID clinical personnel reserve the right to attend the meeting/teleconference.

(3) The meeting/teleconference shall serve to review protocol specifications, requirements and procedures, target enrollment, and approved protocol timelines.

(4) Summaries of major discussion and action items shall be prepared by the Contractor and submitted to the Project Officer *within one week after completion of the meeting/teleconference.*

2) Study Product Requirements

Responsibility for investigational product accountability shall include the following, as applicable:

a) accurate records documenting supply of test article;
b) date and amount of test article dispensed to each subject;
c) amount of test article used and verified during a monthly physical inventory;
d) preservation and validation of cold chain including records to verify cold chain for all materials stored at other than room temperature;
e) packaging and labeling of test article in compliance with applicable labeling regulations;
f) transport of investigational products to clinical area; and
g) documentation that all participating clinical sites have received the appropriate supply of the investigational product.

3) Clinical Trial Conduct

Conduct the clinical trial 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 approved clinical protocol and the Manual of Procedures.

4) Protocol Tracking Reports

Develop and implement tracking procedures for reporting enrollment status and for the follow-up of study participants. In addition, prepare and submit Protocol Tracking Reports as part of the Monthly Technical Progress Reports during the active enrollment phase.

5) Protocol Amendments and Other Clinical Trial Modifications

a) Recommend to the Project Officer, amendments to the clinical protocol, the Manual of Procedures and the informed consent documents, including a written description of the proposed amendments/modifications and their rationale. All such amendments and modifications shall require written approval by the Project Officer prior to implementation. The Project Officer may also recommend amendments.

b) Obtain and provide documentation of IRB approval to the Project Officer and Contracting Officer for protocol amendments prior to implementation.

6) Data Management and Quality Control

Retain primary responsibility for data management and quality control functions carried out under this contract and any subcontract, including:

a) Developing and operating a data management system to maintain up-to-date information on all clinical and laboratory data.

b) Developing and implementing standards and procedures for the entry and quality control of study data to ensure that clinical data are accurate, complete and entered in a timely fashion.

c) Providing training in the use of the data management system for clinical site personnel prior to study implementation.

d) Managing data and address queries in accordance with DMID source document guidelines (www.niaid.nih.gov/dmid/clinresearch/sourcedocumentationstandards.pdf).

c. **PROTOCOL OVERSIGHT**

1) Investigational New Drug (IND) Sponsorship

Serve as the IND sponsor and assume responsibility for all IND-related activities and requirements, including:

a) preparation of materials for and requesting, scheduling and participating in all meetings and teleconferences with the CBER/FDA pre- and post-IND submission;
b) arranging meetings and teleconferences with the FDA that include the Project Officer and other DMID staff as designated by the Project Officer;
c) preparation and submission of the IND;
d) preparation and submission of all FDA required documentation to CBER/FDA in sufficient time to initiate a Phase 1 clinical trial during the third performance year of the base contract following CBER/FDA review and approval by the Project Officer;
e) provision to the Project Officer of copies of all FDA correspondence and meeting/teleconference minutes;
f) preparation and submission of the Annual IND Report to the FDA;
g) preparation and submission of an Interim Data Study Report containing safety and immunogenicity raw data and statistically analyzed results *up to four weeks following the final vaccine dose*; and
h) preparation and submission of the Final Clinical Study Report 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 and the Project Officer *within one 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/aprqtr/21cfr312.23.htm and link for final report http://a257.g.akamaitech.net/7/257/2422/01apr20051500/edocket.access.gpo.gov/cfr_2005/aprqtr/21cfr312.64.htm).

2) Safety Oversight

a) Contractor Safety Oversight Requirements

(1) Implement the approved safety oversight plan, including, at a minimum, provision for a Data Safety Monitoring Board (DSMB) for all participating clinical sites identified by the Contractor and approved by the Project Officer.

(2) The charter and membership of any Contractor-constituted safety oversight structure is required to be approved by the Project Officer.

b) DMID Safety Oversight Structure

(1) DMID, in conjuction with the Contractor, shall establish a Safety Oversight Structure for the clinical trial, independent of the Principal Investigator. The Safety Oversight Structure shall operate in a manner consistent with DMID Safety Oversight Guidances (http://www.niaid.nih.gov/dmid/clinresearch/), and shall accommodate the risk and complexity of the clinical trial.

(2) Present the clinical protocol, safety data, and interim and final study data to the DMID Safety Oversight Structure. The Project Officer will have approval of data format.

c) Serious Adverse Event Reporting

(1) The information contained in the DMID Serious Adverse Event (SAE) Report Form must be included in the Contractor's SAE Report Form. It is recommended that the Contractor use the DMID SAE Report Form located at http://www.niaid.nih.gov/dmid/clinresearch/.

(2) Submit SAE Reports to the DMID Office of Clinical Research Affairs (OCRA), according to the Clinical Terms of Award (http://www.niaid.nih.gov/ncn/pdf/clinterm.pdf).

(3) Report SAE events to OCRA within 24 hours following Contractor notification of event.

d) Clinical Site Monitoring

(1) Perform clinical site monitoring/auditing 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 GCP, the clinical protocol and applicable regulatory requirements.

(2) Conduct an initiation visit by the Clinical Monitor prior to active recruitment.

(3) Conduct ongoing clinical site monitoring during the active recruitment, dosing, follow-up and close-out phases of the clinical trial.

(4) Identify performance problems and deficiencies through the clinical site monitoring function and for developing and implementing remedial actions to address all such performance problems and issues.

(5) Submit updated clinical monitoring reports on a monthly basis to the Project Officer.

e) System of Records

Design, implement and maintain a system of records for the clinical trial in compliance with the Privacy Act and the Confidentiality of Information Clauses contained within the contract.

d. **QUALITY ASSURANCE/QUALITY CONTROL(QA/QC)**

1) Quality Assurance/Quality Control Plan

a) QA/QC Control Plan -- Develop and implement a Quality Assurance/Quality Control plan to ensure that the conduct of the clinical trial and the data generated meet all FDA Good Clinical Practices (GCP) (http://www.fda.gov/oc/gcp/guidance.html) and DMID/NIAID regulatory standards (http://www.niaid.nih.gov/dmid/clinresearch/OP_QM001Rev0.pdf).

b) Draft QA/QC Control Plan – At the request of the Project Officer following the exercise of an Option, submit *a draft plan to the Project Officer within 30 calendar days.* The Project Officer will provide comments to the Contractor within two weeks of receipt of the draft plan.

c) Final QA/QC Control Plan – *At the request of the Project Officer and within 15 calendar days from receipt of the Project Officers comments,* submit a final plan that incorporates the Project Officer's comments. This plan shall include standard operating procedures for establishing and maintaining the QA/QC process and demonstrated remediation to address problems as they occur.

2) Audits

Audits may be requested by the Project Officer to assure that Contractor and/or subcontractor facilities and all planned procedures meet FDA regulations and guidance for Good Clinical Practices (GCP) and/or Good Laboratory Practices (GLP). Ensure that all Contractor and/or subcontractor records and staff are available for such audits.

e. **SCIENTIFIC AND TECHNICAL PERSONNEL**

Provide appropriately trained and experienced personnel for the conduct and oversight of the clinical trial, including:

1) Clinical Trial Principal Investigator

The Clinical Trial Principal Investigator shall be licensed as a physician and shall ensure that active licensure is maintained for the entire period of performance of the trial, including each Option if exercised. The Principal Investigator must possess experience in the design and conduct of clinical trials for infectious diseases and specifically, clinical trials of candidate vaccines against infectious diseases.

2) Other Scientific/Technical Personnel

a) Physician investigators shall be licensed physicians; maintain active licensure for the entire period of clinical trial performance for each Option; and possess experience in the design and conduct of clinical trials of infectious diseases, particularly clinical trials of candidate vaccines against infectious diseases, and in the assessment of participants for study eligibility and safety post enrollment.

b) Clinical Research Study Staff, trained and experienced in Good Clinical Practices, including:

(1) nurse managers, study coordinators,
(2) clinical support staff,
(3) laboratory personnel,
(4) personnel with regulatory expertise, and
(5) data managers.

c) A Research Pharmacist proficient in all aspects of investigational product management.

d) Collaborating clinical investigators or consultants in other medical specialties when necessary to meet protocol-specific requirements.

e) Qualified personnel necessary to package, label, store under appropriate conditions, and track clinical specimens.

f. **CLINICAL RESEARCH FACILITIES AND RESOURCES**

Provide all necessary clinical research facilities and resources for the conduct of the clinical trial, including:

1) Outpatient Clinical Research Facilities at all participating clinical sites to accommodate enrollment, administration of investigational product, and follow-up of subject in accordance with the specific requirements of the approved protocol.

2) Clinical Laboratory Facilities to obtain and process clinical specimens and conduct protocol-required tests to determine participant eligibility and safety evaluations. For all such facilities, maintain current Clinical Laboratory Improvement Amendment certification (www.cms.hhs.gov/clia) and Joint Commission on

Accreditation of Healthcare Organizations approval (www.jcaho.org) or equivalent foreign organization.

3) Research Laboratory Facilities to process and store specimens and conduct protocol relevant cultures and/or immunologic assays. Ensure that work conforms to standards acceptable for IND and/or BLA submission (see http://www.niaid.nih.gov/dmid/clinresearch/#resources for guidance). Serological analysis performed must utilize standardized protocols, characterized reagents, and qualified or validated immunological assays for all human studies.

4) Research Pharmacy Facilities for the management of the investigational product, including Standard Operating Procedures and other appropriate procedures and policies to provide for appropriate storage of, and monitoring controlled access to the investigational product.

5) Clinical Trial Sites

   a) Solicit, negotiate, execute and manage subcontracts for the provision of clinical site personnel, services and facilities, including oversight of subcontractor performance.

   b) Clinical sites must:

      (1) Provide qualified clinical investigators, nurse managers, study coordinators, and other clinical research support staff.

      (2) Provide staff with experience and expertise in the conduct of clinical trials 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.

      (3) Provide staff with experience in the screening, recruitment and retention of study participants; access to healthy adult subjects; and research laboratory facilities, equipment and personnel for the conduct of protocol-specific tests and for the processing and storage of clinical specimens.

   c) Utilize the personnel, services and facilities of qualified clinical sites to provide access to and ensure enrollment of adequate numbers of study participants for the timely conduct and completion of the clinical trial.

g. **MEETINGS**

1) For each Option, sponsor all clinically-related meetings, including an Option Kick-Off Meeting, an Investigator Meeting, and site visits to clinical sites to assure GCP compliance throughout the clinical trial. The Project Officer, the Contracting Officer and other NIAID program staff may attend these meetings and site visits.

2) Incorporate progress review updates into the biweekly Contractor/Project Officer teleconferences and the Monthly Technical Progress Report.

h. **CLINICAL INTERIM STUDY REPORT AND FINAL REPORT**

1) A Clinical Interim Study Report containing safety and immunogenicity raw data and statistically analyzed results shall be submitted *within 45 days following analysis of interim trial data*.

2) A comprehensive Final Interim Study Report shall be submitted *within three months following completion of the clinical trial*.

[END OF OPTION 2 - STATEMENT OF WORK]

REPORTING REQUIREMENTS AND DELIVERABLES

Development of a Third Generation Anthrax Vaccine
RFP NIH-NIAID-DMID-07-05

A. **Technical Reports**

In addition to those reports required by the other terms of this contract, the Contractor shall prepare and submit the following reports in the manner stated below and in accordance with ARTICLE F.1. DELIVERIES of this contract:

The Contractor shall submit to the Contracting Officer and to the Project Officer technical progress reports covering the work accomplished during each reporting period. These reports are subject to the technical inspection and requests for clarification by the Project Officer. These reports shall be brief and factual and prepared in accordance with the format described below.

Format of Cover page: All reports shall include a cover page prepared in accordance with the following format:

- Contract Number and Project Title
- Period of Performance Being Reported
- Contractor's Name and Address
- Author(s)
- Date of Submission
- Delivery Address

1. Monthly Technical Progress Reports

Each Report shall include the following specific information:

a) SECTION I - An introduction covering the purpose and scope of the contract effort.

b) SECTION II –Document the results of work done during the period covered for each milestone. Each milestone section should also include a summary paragraph of accomplishments/issues for the time period covered in the report. These reports shall be in sufficient detail to explain comprehensively the results achieved. The description shall include pertinent data and/or graphs in sufficient detail to explain any significant results achieved and preliminary conclusions resulting from analysis and scientific evaluation of data accumulated to date under the project for each milestone. Monthly updates of all data generated for DS and FDP lots on stability shall be included. Also to be included in the report is a summary of work proposed for the next reporting period for each milestone. Preprints and reprints of papers and abstracts shall be submitted with Monthly Reports. If Option 1 or Option 2 are funded, Protocol Tracking Reports shall also be included. All work performed and materials utilized shall be linked to the associated costs. Cost breakdown shall be reported by a cost breakdown of Direct Labor, Direct Materials, Subcontracts, Consultants, Travel, etc.

c) SECTION III - Substantive performance: a description of current technical or substantive performance and any problems encountered and/or which may exist along with proposed corrective action. This requires an explanation of any difference between planned progress and actual progress, reasons for differences that have occurred, and if behind planned progress, an outline of corrective action to be taken. Estimated and actual costs shall be provided for each task and milestone performed during the reporting period. The current status of each milestone or sub-task shall be displayed on an updated Gantt chart as a component of the Monthly Technical Progress Report.

d) The last Monthly Report for Year 1 shall include a summary (not to exceed 200 words) of salient results achieved during the first year of the contract.

e) A Monthly Report will not be required for the period when the Final Report is due.

2. Milestone Reports

Milestone Reports shall be provided to the Contracting Officer and the Project Officer within 30 days of completion of each Milestone unless otherwise agreed upon by the Principal Investigator and the Project Officer. The Milestone Report shall detail work done for each milestone, as well as issues and solutions that occurred during the performance of each milestone.

3. Annual Technical Progress Report for Clinical Research Study Populations

The Contractor shall submit information about the inclusion of women and members of minority groups and their subpopulations for each study being performed under this contract. The contractor shall submit this information in the format indicated in the attachment entitled, "Inclusion Enrollment Report," which is set forth in Section J of this contract. The contractor also shall use this format, modified to indicate that it is a final report, for reporting purposes in the final report. The contractor shall submit the report in accordance with ARTICLE F.1. DELIVERIES of this contract. The final report shall be due on/before the completion date of the contract.]

In addition, the NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research, Amended, October, 2001 applies. The Guidelines may be found at the following website:
http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm

Include a description of the plans to conduct analyses, as appropriate, by sex/gender and/or racial/ethnic groups in the clinical trial protocol as approved by the IRB, and provide a description of the progress in the conduct of these analyses, as appropriate, in the annual progress report and the final report. If the analysis reveals no subset differences, a brief statement to that effect, indicating the subsets analyzed, will suffice. The Government strongly encourages inclusion of the results of subset analysis in all publication submissions. In the final report, the contractor shall include all final analyses of the data on sex/gender and race/ethnicity.

4. Final Report

Final Report: On/before the completion date of the contract, the Contractor shall submit a comprehensive Final Report to detail and document the results of the entire contract work for the period covered. The Final Report shall also contain an executive summary for activities performed under the contract. The format described for the Monthly Technical Progress Reports shall be used for the Final Report. The Final Report shall be in sufficient detail to explain comprehensively the methods used and the results achieved. Specifically the Final Report shall summarize each milestone effort and discuss each deliverable within the corresponding milestone. Preprints and reprints not submitted previously shall be submitted as an appendix. The Final Report shall include a summary (not to exceed 200 words) of Salient Results achieved during the performance of the contract.

Draft Final Report: The Contractor shall provide the Project Officer and Contracting Officer with a copy of the Final Report in **draft** form 45 calendar days prior to the completion date of the contract. The Project Officer will review the draft Final Report and provide the Contractor with comments within 15 calendar days after receipt. The Final Report shall be corrected by the Contractor, if necessary and the final version delivered as specified in the above paragraph.

B. **Technical Reports Distribution and Delivery Schedule**

Satisfactory performance of the final contract shall be deemed to occur upon performance of the work described in Article C.1. and upon delivery and acceptance by the Contracting Officer, or the duly authorized representative, of the following items in accordance with the stated delivery schedule.

The items specified below, will be required to be delivered F.O.B. Destination as set forth in FAR 52.247-35, F.O.B. DESTINATION, WITHIN CONSIGNEES PREMISES (APRIL 1984), and in accordance with and by the date(s) specified below and any specifications stated in SECTION D, PACKAGING, MARKING AND SHIPPING, of the contract:

Item	Deliverable	Recipient & Number of Copies	Report Due Dates
1.	Monthly Technical Progress Report	1 Copy to PO 1 Original to CO Plus: Electronic (either e-mail or CD) to both PO and CO	The first report is due on/before _____, and shall include any fractional part of the initial month. Thereafter, reports are due on/before the 15th of the month following each monthly reporting period.
2.	Milestone Reports	1 Copy to PO 1 Original to CO Plus: Electronic (either e-mail or CD) to both PO and CO	Submitted within 30 calendar days of completion of each Milestone.

3.	Annual Technical Progress Report for Clinical Research Study Populations	1 Copy to PO 1 Original to CO Plus: Electronic (either e-mail or CD) to both PO and CO	The first report is due on/before _____. Thereafter, the report shall be due on or before the 30th of the month following each annual reporting period. The Final Clinical Research Study Populations Report shall be due on/before _____.
4.	Annual Utilization Report	1 Copy to CO	Due on/before the 30th of the month following each anniversary date of the contract.
5.	Final Invention Statement	1 Copy to CO	Due on/before completion date of the contract.
6.	All reports and documentation including the invention disclosure report, the confirmatory license, and the government support certification	1 Copy - OPERA	As required by FAR Clause 52.227-11.
7.	Draft Final Report and Summary of Salient Results	1 Copy to PO 1 Original to CO Plus: Electronic (either e-mail or CD) to both PO and CO	Due 45 calendar days prior to the completion date of the contract. Project Officer should return comments within 15 calendars days after receipt of draft Final Report.
8.	Final Report and Summary of Salient Results	1 Copy to PO 1 Original to CO Plus: Electronic (either e-mail or CD) to both PO and CO	Due on/before the completion date of the contract.

C. **Other Reports and Deliverables:**

In addition to the above reports, the following are considered deliverables under this contract:

1. Source Code and Object Code

   Unless otherwise specified herein, the Contractor shall deliver to the United States government, upon the completion date of the contract, all source code and object code developed, modified, and/or enhanced under this contract.

2. Other reports and deliverables identified in the Statement of Work, as detailed below:

Item	Deliverable	SOW Paragraph Reference	Recipients & Number of Copies	Deliverable Due Date(s)
1.	Batch Production Records	Milestone 1, para. b. Milestone 4. para. b.	Project Officer	As requested by the Project Officer
2.	Certificate of Analysis (CoA)	Milestone 1, para. b. Milestone 4. para. b.	Project Officer	For each released lot.
3.	Drug Substance (DS) Process Development Report	Milestone 1, para. b.	Project Officer	Following completion of the three released lots.
4.	Stability Data Reports	Milestone 2. para. b.	Project Officer	Monthly
5.	Assay Protocols and Final Assay Qualification Reports	Milestone 3. para. b.	Project Officer	Within 10 months of contract award
6.	Final Drug Product (FDP) Process Development Report	Milestone 4. para. b.	Project Officer	Following completion of the three released lots.
7	Draft Pre-clinical Safety and Toxicity Protocol(s)	Milestone 5. para. a.1)	Project Officer	Within 10 months of contract award.
8.	Final Pre-clinical Safety and Toxicity Protocol(s)	Milestone 5. para. a.2.	Project Officer	Within 30 calendar days of receipt of Project Officer comments.
9.	Written minutes of interactions with the FDA	Milestone 5. para. a.3.	1 copy to PO 1 copy to NIAID regulatory designee	Following discussions with CBER/FDA. As transcripts become available.
10.	Draft Non-clinical Rabbit GUP Protocol(s)	Milestone 6. para. a.2)	Project Officer	Within 10 months of contract award.
11.	Final Non-clinical Rabbit GUP Protocol(s)	Milestone 6. para. a.3)	Project Officer	Within 30 calendar days of receipt of Project Officer comments.
12.	Summary Interim Non-clinical Rabbit GUP Report	Milestone 6. para. a.5)	Project Officer	Within 14 weeks of study initiation
13.	Final Rabbit GUP Report(s)	Milestone 6. para. a.6)	Project Officer	Within 30 calendar days after completion of the approved Non-clinical Rabbit GUP study(ies).
14.	Draft Non-clinical Rabbit PEP Protocol	Milestone 7. para. a.2)	Project Officer	Within 12 months of contract award.
15.	Final non-clinical Rabbit PEP Protocol	Milestone 7. para. a.3)	Project Officer	Within 30 calendar days of Project Officer review.
16.	Summary Interim Non-clinical Rabbit PEP Report	Milestone 7. para. a.5)	Project Officer	Within 8 weeks of study initiation.

17.	Final Non-clinical Rabbit PEP Study Report(s)	Milestone 7. para. a.6)	Project Officer	Within 30 calendar days after completion of the approved study(ies).
18.	Submission of Non-clinical Data and chemistry, manufacturing and controls (CMC) information -- OR— Letter of Cross-Reference to the Contractor IND or Master File	Milestone 8. para. a.	1 copy to PO 1copy to NIAID regulatory designee	Within 18 months of contract award.
19.	Draft Non-clinical NHP PEP Protocol	Milestone 9. para. a.2)	Project Officer	Within 16 months of contract award.
20.	Final Non-clinical NHP PEP Protocol	Milestone 9. para. a.3)	Project Officer	Within 30 calendar days of Project Officer review.
21.	Summary Interim Non-clinical NHP PEP Report	Milestone 9. para. a.5)	Project Officer	Within 8 weeks of study initiation.
22.	Final Non-clinical NHP PEP Study Report(s)	Milestone 9. para. a.6)	Project Officer	Within 30 calendar days after completion of the approved study(ies).
23.	Shipping Validation Report	Milestone 10., para. a.	Project Officer	Within 30 calendar days of shipment of vaccine material.
24.	Delivery of Vaccine Material: • 2,000 cGMP vaccine doses • CoA for each FDP lot • Quantity of cGMP manufactured diluent • Any novel device(s)	Milestone 10. para. b.1) thru b.4)	John Kudrick Fischer Bioservices DMID-CAR 687-A, Lofstrand Lane Rockville, MD 20850	Within 24 months of contract award. Upon Project Officer approval of the Shipping Validation Report
25.	Integrative Development Plan	Milestone 11. para. B.	Project Officer	Within 30 months of contract award.
26.	Draft Quality Assurance/Quality Control (QA/QC) plan.	Item 4.	Project Officer	Within 15 calendar days of contract award
27.	Final QA/QC plan.	Item 4.	Project Officer	With 15 calendar days following receipt of Project Officer's comments
28.	Meeting and Conference Agendas.	Item 5.	Project Officer	Within 2 calendar days prior to Meeting/Conference
29.	Meeting and Conference Minutes.	Item 5.	Project Officer	Within 3 calendar days following Meeting/Conference

30.	Draft Protocol and associated materials including Statistical Analysis Plan (SAP) Investigator Brochure (IB) and Updates, and a Manual of Procedures.	Options -- para. 8.a.2)a) & 9.a.2)a)	1 copy to PO 1 copy to ORA 1 copy to PO's clinical designee	Within 45 calendar days of receipt of contract Modification signed by Contracting Officer that exercises Option.
31.	Final Protocol and associated materials including Statistical Analysis Plan (SAP) Investigator Brochure (IB) and Updates, and a Manual of Procedures.	Options -- para. 8.a.2)b) & 9.a.2)b)	1 copy to PO 1 copy to ORA 1 copy to PO's clinical designee	Within 4 weeks following receipt of Project Officer comments
32.	Clinical Trial Timeline	Options -- para. 8.a.3). & 9.a.3)	1 copy to PO 1 copy to ORA 1 copy to PO's clinical designee	Within 30 calendar days of receipt of contract Modification signed by Contracting Officer that exercises Option.
33.	Summaries of major discussion and action items	Options -- para. 8.g.1) & 2) & 9.g)1) & 2)	1 copy to PO 1 copy to ORA 1 copy to PO's clinical designee	Within 1 week after completion of the meeting/teleconference.
34.	Documentation of IRB approval	Options -- para. 8.b.1)a) & 5) & 9.b.1)a) & 5)	1 copy to PO 1 copy to ORA 1 copy to PO's clinical designee 1 copy to CO	Prior to implementation of clinical trial.
35.	Document related to IND-related activities.	Options -- para. 8.c.1)a) thru h) & 9.c.1)a) thru h)	1 copy to PO 1 copy to ORA 1 copy to PO's clinical designee	As indicated in this paragraph of the SOW.
36.	Clinical Monitoring Reports	Options -- para. 8.c.2)d)(5) & 9.c.2)d)(5).	1 copy to PO 1 copy to PO's clinical designee 1 copy to ORA	Monthly
37.	Draft QA/QC Control Plan	Options – para. 8.d.1)b) & 9.d.1)b)	1 copy to PO 1 copy to ORA 1 copy to PO's clinical designee	At the request of the Project Officer following the exercise of an Option
38.	Final QA/QC Control Plan	Options – Para. 8.d.1)c) & 9.d.1)c)	1 copy to PO 1 copy to ORA 1 copy to PO's clinical designee	At the request of the Project Officer following the exercise of an Option

39.	Clinical Interim Study Report containing safety and immunogenicity data and a comprehensive final report	Options – para. 8.h.1) & 9.h.1)	1 copy to PO 1 copy to ORA 1 copy to PO's clinical designee	Within 45 days following analysis of interim trial data.
40.	Final Clinical Study Report containing safety and immunogenicity data and a comprehensive final report	Options – para. 8.h.2) & 9.h.2)	1 copy to PO 1 copy to ORA 1 copy to PO's clinical designee	Within three months following completion of the clinical trial.

Copies of reports shall be sent to the following addresses:

NIAID Project Officer:
Office of Biodefense Research Affairs, DMID, NIAID, NIH
6610 Rockledge Drive, Room, MSC 6604
Bethesda, MD 20892-6604

Office of Regulatory Affairs (ORA):
Office of Regulatory Affairs, DMID, NIAID, NIH
6610 Rockledge Drive, Room 6035, MSC 6604
Bethesda, MD 20892-6604

NIAID Contracting Officer:
Office of Acquisitions, DEA, NIAID, NIH
6700-B Rockledge Drive, Room 3214, MSC 7612
Bethesda, MD 20892-7612

OPERA:
Office of Extramural Inventions and Technology Resources Branch
OPERA, NIH
6705 Rockledge Drive, Room 1040 A, MSC 7980
Bethesda, Maryland 20892-7980

APPENDIX A

"DEVELOPMENT OF A THIRD GENERATION ANTHRAX VACCINE"
RFP NIH-NIAID-DMID-07-05

ADDITIONAL TECHNICAL PROPOSAL INSTRUCTIONS
FORMAT FOR TECHNICAL PROPOSAL – TABLE OF CONTENTS

It is strongly recommended that offerors use the following template as the Table of Contents for the Technical Proposal. All information presented in the Technical Proposal should be presented in the order specified below.

The following additional Technical Proposal instructions reflect the requirements of the RFP and are meant to provide additional instructions as well as a uniform format for Technical Proposals. The information requested in these instructions should be used as a guide for formatting and preparing the Technical Proposal. Offerors should follow the instructions in Section L of the solicitation and include the information requested in this appendix.

Offerors are advised to give careful consideration to the Statement of Work, all reference material, appendices and attachments, the technical evaluation criteria, and, the RFP as a whole, in the development of their Technical Proposals.

Offerors who propose subcontracts to perform portions of the Statement of Work should clearly identify the specific tasks for which they plan to utilize subcontractors, as well as the method and level of integration between the prime contractor and all proposed subcontractor(s), and the expected advantages of such an approach.

Offerors are reminded that the total page limitation for the Technical Proposal is 200 pages, including all appendices and attachments.

PAGES IN EXCESS OF THIS LIMITATION WILL BE REMOVED FROM THE PROPOSAL AND THESE EXCESS PAGES WILL NOT BE PROVIDED TO THE REVIEWERS TO BE READ OR EVALUATED.

TECHNICAL PROPOSAL – TABLE OF CONTENTS

SECTION 1

A. PROPOSAL TITLE PAGE. Include RFP title and number, name of organization, DUNS number, proposal part, and identify if the proposal is an original or copy.
B. PROJECT OBJECTIVES, NIH FORM 1688
C. GOVERNMENT NOTICE FOR HANDLING PROPOSALS
D. TABLE OF CONTENTS
E. PROPOSAL SUMMARY AND DATA RECORD (NIH-2043)
F. MANDATORY QUALIFICATION CRITERIA

The Mandatory Qualification Criteria, identified in SECTION M of this solicitation, must be met at the time of the Original Technical Proposal submission. Documentation to support compliance must be provided by the offeror and any proposed subcontractors. Offerors who fail to meet these criteria at the time of original proposal submission, will not have their proposals reviewed or considered further for award. All required documentation to demonstrate that you have met the Mandatory Qualification Criteria must be placed in a separate, clearly marked section of your Technical Proposal.

GENERAL INFORMATION

1. The time period for each of the milestones described in the Statement of Work are offered as Government estimates. The offeror may propose alternate timelines and milestones.

2. Some offerors may have already completed some of the tasks/milestones identified in the Statement of Work for the base period. The Technical Proposal must include sufficient detailed information regarding the extent and the status of cGMP production, all assays (development, qualified, validated), and non-clinical study data to support claims of completion and to allow for appropriate technical evaluation and cost consideration. If work has been completed using Government funding, reference the funding agency and the grant/contract number.

SECTION 2: TECHNICAL PROPOSAL OVERVIEW (maximum 3 pages)

Provide a brief description of the proposed research and development program, including:

1. A brief description of the candidate vaccine and the third generation anthrax vaccine objectives it is intended to address;
2. A Milestone summary delineating the scope of product development activities to be performed;
3. A Gantt chart that clearly defines the Milestones and timelines for each task to be performed;
4. A budget summary, in direct costs (labor, materials, subcontracts, consultants, etc.), for each milestone;
5. A description of the activities to be performed by the offeror and those that shall be provided by any proposed subcontractors, including the identification of the proposed subcontractors and a list of key personnel of the offeror and the proposed subcontractors with degrees and titles;
6. A brief description of the facilities and other resources to be made available by the offeror and any proposed subcontractors; and
7. The period of contract funding requested and the total budget for each year.

SECTION 3: TECHNICAL PLAN/APPROACH

1. **Vaccine Candidate and Testing/Production Capability**

    a. Vaccine Candidate: Describe the scientific basis for the selection of the vaccine candidate as it relates to the third generation anthrax vaccine objectives: long-term stability and/or storage at ambient temperatures; rapid immune responses with two doses; and/or amenability for rapid mass immunization including self-administration or administration of vaccine by non-technical personnel. This includes:

1) The scientific justification and rationale for the selection of properties to fulfill the third generation anthrax vaccine objectives.
2) A description of results from any completed studies demonstrating a superior safety/reactogenicity profile relative to the currently licensed anthrax vaccine.
3) A description of the results of any completed studies on formulation, their immunogenicity, and their ability to protect against lethal challenge of *B. anthracis* spores.
4) If a new adjuvant is proposed (not currently in a licensed vaccine), a description of prior use in humans and non-clinical safety data.
5) If an alternative to intramuscular injection via syringe is proposed for delivery, provide scientific justification and data for route and delivery platform.
6) If a novel device/technologies to facilitate vaccine dosing is proposed, provide a scientific justification for use of the device and results of studies which demonstrate its effectiveness.
7) Provide stability data, if available, for candidate vaccine and individual vaccine components.
8) If an antigen component(s) in addition to PA is included in the vaccine candidate, provide justification for use of the added component(s).

b. Testing/Production Capability: Describe the current status of the offeror's anthrax vaccine program. Provide detailed information regarding the extent and status of the following activities:

1) process development and scale-up production;
2) analytical, release, stability and serological assays; and
3) non-clinical study data.

c. Quality Assurance/Quality Control: Describe the offeror's and any proposed subcontractor's, current QA/QC Program to ensure manufacturing and testing meet FDA GMP and GLP regulatory standards.

d. Provide documentation for all tasks and Milestones that have been completed. If work has been completed using Government funding, reference the funding agency and the grant/contract number.

2. **Vaccine Development Plan**

a. Manufacturing (SOW Milestones 1, 2, 3 and 4)

1) Describe technical approaches and methods for pilot-scale manufacturing, product characterization and release, technology transfer for pilot-lot to large-scale transition for both DS and FDP, and testing of cGMP DC and cGMP FDP.
2) Provide timelines up to manufacture of consistency lots for FDP.
3) Provide a validation plan for all associated assays.
4) If methodology for drug substance production other than fermentation is proposed, provide documentation to indicate that current yield is at least of equivalent quantity as a 30 L fermentation process or sufficient for 2,000 doses of FDP.

b. Non-clinical Studies (SOW Milestones 5, 6, 7, 8 and 9)

1) Provide detailed synopses of all proposed non-clinical studies to evaluate safety/toxicity and immunogenicity, including the conduct of all FDA required IND enabling studies for the anthrax vaccine candidate. Describe the proposed approach to providing the NIAID with all relevant information and/or the ability to cross-reference a Master File that will support NIAID filing a Government-held IND.

2) Provide detailed study synopses for aerosol spore challenge studies in the rabbit and the non-human primate (NHP) models, including non-clinical general-use prophylaxis (GUP) studies in the rabbit model (Statement of Work - Milestone 6), non-clinical post-exposure prophylaxis (PEP) study in the rabbit model (Statement of Work - Milestone 7), and non-clinical PEP studies in a non-human primate model (Statement of Work - Milestone 9). Include the rationale for the proposed study designs and a discussion of the ability of the proposed study designs to generate supportive data for the CBER/FDA "Animal Rule" and for future pivotal studies to identify immune correlates of protection based on the non-clinical and clinical data.

SECTION 4: FACILITIES, OTHER RESOURCES, SAFETY AND TRAINING

Document the availability for the period of performance of the contract and the adequacy of facilities, equipment, space and other resources necessary to carry out the Statement of Work, including:

1. Location and features of facilities (lease or ownership information shall be provided).

2. Documentation of cGMP compliance for BDS and FDP facilities.

3. Identification and description of ALL support resources (including IT systems) which will be required to effectively complete the requirements of the contract.

4. Capacity to perform all required manufacturing and non-clinical testing in a timely and efficient manner with the resources dedicated to the project.

5. Access to required GLP laboratories and animal facilities with necessary biocontainment capabilities, including BSL-3 laboratory facilities for aerosol challenge studies.

6. Description of the level of biocontainment required for compliance with Select Agent Regulations in conjunction with each animal model and assay system used in the testing process. Describe safety training and implemention, and monitoring of safety procedures related to protection of personnel and the environment from chemical and biological hazards.

7. Documentation that animal testing laboratories have current certification from the NIH Office of Laboratory Animal Welfare (OLAW) (http://grants.nih.gov/grants/olaw/olaw.htm).

8. Procedures to be used for the care and housing of laboratory animals, the extent of appropriate veterinary coverage, the physical plant housing all animals and laboratories, the safety procedures in place, and the expertise and training of the technical staff employed.

SECTION 5: PERSONNEL

Provide the following documentation/information for the Principal Investigator and all proposed scientific and technical staff, including staff of the offeror and any proposed subcontractors. Limit the CV to 2-3 pages, provide selected references for publications relevant to the scope of requirements for the contract, include relevant ongoing projects, and limit previous experience to the past five (5) years.

1. **Principal Investigator**: Describe the experience, training, expertise, and qualifications, as well as percentage of effort, of the proposed Principal Investigator (PI) in planning, initiating, implementing, managing and coordinating the scope of functions to be carried out under the contract, including experience with projects of similar size and complexity. Include experience with leading and directing project activities either directly or indirectly through subcontracts. Identify and discuss problems encountered in meeting milestones and timelines for similar projects and describe how those problems were resolved. Describe the PI's scientific and technical expertise, training and experience in advanced product development activities and with products that are regulated by the FDA, in particular vaccine research and development for infectious diseases. Include a discussion of prior preclinical and clinical studies for successful submissions to the FDA.

2. **Key Scientific and Technical Personnel**: Describe the training, experience, education, and qualifications, as well as the percentage of the total time each will be committed to the project. Specify workloads/tasks that each will be performing, and document knowledge of and experience with the regulatory requirements that govern the production of cGMP materials and testing in compliance with GLP and GCP.

3. **Other Scientific and Technical Personnel**:

    a. Describe responsibilities and document the relevant experience, training and expertise of the Quality Assurance/Quality Control (QA/QC) personnel.

    b. Describe responsibilities and document the relevant experience, training and expertise of other personnel as needed to address the requirements of the Statement of Work.

SECTION 6: PROJECT MANAGEMENT

1. Provide a plan for project organization, staffing, and management in relation to the implementation, conduct, monitoring and completion of the milestones identified in the Statement of Work. Include a detailed description of the responsibilities and the level of effort for all proposed personnel who will be assigned to the contract, and an administrative framework indicating clear lines of authority and responsibility for all personnel. If consultants and/or subcontractors are to be used, include a plan to manage and coordinate consultant and/or subcontractor(s) efforts. Include a chart of the proposed organizational/management structure for the project.

2. Describe project management systems that will be used to track activities and to keep multiple activities on time and budget. The plan must include a description of the quality control methods that will be used to ensure the effective and efficient initiation, implementation, management, and oversight of contract requirements.

3. Outline how the PI will communicate and interact with the Contracting Officer and the Project Officer and how the PI will communicate, monitor, and manage the project both internally and externally (at subcontractor facilities).

SECTION 7: OPTIONS

1. **Option 1 – Phase 1 Clinical Trial**

   a. Option 1 Overview: Provide a brief overview that delineates the following:

      1) the overall clinical trial infrastructure, including Clinical Trial Principal Investigator and institution, participating clinical trial sites and clinical investigators, and clinical research facilities, including clinical research outpatient, clinical research laboratory, and clinical pharmacy facilities; and

      2) a summary of the major design features of the proposed clinical trial.

   b. Clinical Trial Concept Proposal

      Provide a Concept Proposal of no more than ten (10) pages addressing the following design features of the proposed Phase 1 clinical trial to evaluate safety and immunogenicity as follows:

      1) Objectives.
      2) Primary hypothesis.
      3) Study design including inclusion/exclusion criteria.
      4) Study population.
      5) Primary and secondary endpoints.
      6) Follow-up time for study subjects.
      7) Statistical methods and randomization. Include an algorithm for the method in which subjects are to be enrolled and randomized.
      8) Potential problems and obstacles in implementing the proposed clinical trial and strategies to overcome identified problems and obstacles.

      NOTE: The clinical trial design, as proposed, will be used in the evaluation of the scientific and technical merit, appropriateness and feasibility. The final clinical trial design and clinical protocol shall be subject to review, modification and approval by the Project Officer and the Contracting Officer if the Option is exercised.

   c. Clinical Trial Timeline and Plan for Recruitment and Enrollment

      1) Provide a timeline delineating all steps involved, including protocol development, initiation, completion of enrollment, study completion, and analysis and publication of final study results. Include a discussion of past experience in meeting timelines for projects of similar size and complexity, obstacles and problems encountered during the conduct of these projects, and how they were resolved.

2) Provide a plan for the recruitment and retention of the study participants and a description of potential problems and obstacles to achieving the required enrollment targets, as well as proposed solutions to overcome identified problems/obstacles.

d. Protocol-related Documents: Provide the following protocol-related documents, plans and forms. These materials will be used in the evaluation of the Technical Proposal and may not be the final documents approved post award if the Option is exercised.

1) Quality Management Plan
2) Clinical Monitoring Plan
3) Data Management Plan including processes and procedures for the collection, quality control and management of study data at the offeror's institution and all proposed clinical trial sites
4) Safety Oversight Plan (see http://www.niaid.nih.gov/dmid/clinresearch/)

e. IND-related Activities: Describe in detail how the offeror proposes to:

1) prepare, submit, and update an IND;
2) keep NIAID apprised of progress and all communications with the FDA; and
3) ensure that NIAID may co-monitor or provide for independent audits of the clinical studies.

f. Clinical Research Facilities and Resources: Describe and document the availability and adequacy of clinical research facilities, equipment and other resources for conducting the clinical trial in compliance with Federal regulatory requirements and GCP, including facilities for the screening, enrollment, treatment and follow-up of study participants, clinical laboratory facilities, and pharmacy facilities.

g. Organizational Experience: Describe previous organizational experience of the offeror and all proposed clinical trial sites in conducting clinical trials in compliance with Federal regulations.

h. Qualifications of Proposed Clinical Trial Personnel: Document the qualifications, experience, training and availability of the proposed clinical trial personnel for the offeror and of all proposed subcontractors and consultants, including scientific and technical, clinical and regulatory staff with experience in the conduct and management of the clinical trial; provide documentation of experience with products of a similar nature regulated by the FDA, and knowledge of and experience in complying with the regulatory requirements that govern clinical testing in compliance GCP.

i. Clinical Trial Management: Describe how the offeror will manage the clinical trial, including any consultants and subcontractors, to meet the overall clinical testing requirements; describe procedures to be used to monitor, track, and report cost and performance to the Project Officer and the Contracting Officer.

j. Provide a Technical Proposal Cost Summary *(See Section J, Attachments)* for Option 1 delineating, in direct costs, the proposed budget linked to the specific functions and tasks to be carried out with subtotals for: (i) protocol development, (ii) study initiation, (iii) protocol implementation and oversight, (iv) study completion, and (v)analysis and presentation of final study results.

2. **Option 2 – Phase 2 Clinical Trial(s)**

a. Option 2 Overview: Provide a brief overview that delineates the following:

1) the overall clinical trial(s) infrastructure, including Clinical Trial Principal Investigator and institution, participating clinical trial sites and clinical investigators, and clinical research facilities, including clinical research outpatient, clinical research laboratory, and clinical pharmacy facilities; and

2) a summary of the major design features of the proposed clinical trial(s).

b. Clinical Trial Concept Proposal

Provide a Concept Proposal of no more than ten (10) pages addressing the following design features of the proposed Phase 2 clinical trial(s) to evaluate safety and immunogenicity as follows:

1) Objectives.
2) Primary hypothesis.
3) Study design including inclusion/exclusion criteria.
4) Study population.
5) Primary and secondary endpoints.
6) Follow-up time for study subjects.
7) Statistical methods and randomization. Include an algorithm for the method in which subjects are to be enrolled and randomized.
8) Potential problems and obstacles in implementing the proposed clinical trial(s) and strategies to overcome identified problems and obstacles.

NOTE: The clinical trial design, as proposed, will be used in the evaluation of the scientific and technical merit, appropriateness and feasibility. The final clinical trial design(s) and clinical protocol(s) shall be subject to review, modification and approval by the Project Officer and the Contracting Officer if the Option is exercised.

c. Clinical Trial Timelines and Plan for Recruitment and Enrollment

1) Provide a timeline delineating all steps involved, including protocol development, initiation, completion of enrollment, study completion, and analysis and publication of final study results. Include a discussion of past experience in meeting timelines for projects of similar size and complexity, obstacles and problems encountered during the conduct of these projects, and how they were resolved.

2) Provide a plan for the recruitment and retention of the study participants and a description of potential problems and obstacles to achieving the required enrollment targets, as well as proposed solutions to overcome identified problems/obstacles.

d. Protocol-related Documents: Provide the following protocol-related documents, plans and forms. These materials will be used in the evaluation of the Technical Proposal and may not be the final documents approved post award if the Option is exercised.

1) Quality Management Plan
2) Clinical Monitoring Plan
3) Data Management Plan including processes and procedures for the collection, quality control and management of study data at the offeror's institution and all proposed clinical trial sites
4) Safety Oversight Plan (see http://www.niaid.nih.gov/dmid/clinresearch/)

e. IND-related Activities: Describe in detail how the offeror will:

1) update an IND,
2) keep NIAID apprised of progress and all communications with the FDA, and
3) ensure that NIAID may co-monitor or provide for independent audits of the clinical studies,

f. Clinical Research Facilities and Resources: Describe and document the availability and adequacy of clinical research facilities, equipment and other resources for conducting the clinical trial in compliance with Federal regulatory requirements and GCP, including facilities for the screening, enrollment, treatment and follow-up of study participants, clinical laboratory facilities, and pharmacy facilities.

g. Organizational Experience: Describe previous organizational experience of the offeror and all proposed clinical trial sites in conducting clinical trials in compliance with Federal regulations.

h. Qualifications of Proposed Clinical Trial Personnel: Document the qualifications, experience, training and availability of the proposed clinical trial personnel for the offeror and of all proposed subcontractors and consultants, including scientific and technical, clinical and regulatory staff with experience in the conduct and management of the clinical trial; provide documentation of experience with products of a similar nature regulated by the FDA, and knowledge of and experience in complying with the regulatory requirements that govern clinical testing in compliance GCP.

i. Clinical Trial Management: Describe how the offeror will manage the clinical trial, including any consultants and subcontractors, to meet the overall clinical testing requirements; describe procedures to be used to monitor, track, and report cost and performance to the Project Officer and the Contracting Officer.

j. Provide a Technical Proposal Cost Summary *(See Section J, Attachments)* for Option 2 delineating, in direct costs, the proposed budget linked to the specific functions and tasks to be carried out for (i) protocol development, (ii) study initiation, (iii) protocol implementation and oversight, (iv) study completion, and (v) analysis and presentation of final study results.

SECTION 7: DOCUMENTATION REQUIRED UNDER SECTION L OF THE SOLICITATION

Section L of the RFP provides minimum documentation requirements for the following items. The required information described in Section L should be assembled together, in the following clearly marked sections of the technical proposal. Refer to Section L of the RFP for specific requirements. Also read each section, below, carefully. In some cases, offerors may be asked to provide documentation which is in addition to the minimum requirements identified in Section L.

A. Human Subjects

Section L of the RFP specifies the minimum documentation requirements for Human Subjects use. All related documentation shall be included in the proposal in a clearly marked section. The Technical proposal shall document all information necessary to evaluate Human Subject use. The following information is essential:

1. Human Subjects

   Include plans for compliance with applicable domestic and international regulations on the use of human subjects (e.g. IRB submission and approval plans, consent procedures, etc.).

2. Also include, as applicable, documents relevant to the following:

   a. Notice to Offerors of Requirements of 45 CFR Part 46, Protection of Human Subjects (March 2005)
   b. Instructions to Offerors Regarding Protection of Human Subjects
   c. Collaborating Site(s)
   d. Required Education in the Protection of Human Research Participants
   e. Inclusion of Women and Minorities in Research Involving Human Subjects
   f. Inclusion of Children in Research Involving Human Subjects
   g. Data and Safety Monitoring in Clinical Studies
   h. Research Involving Human Fetal Tissue
   i. Research Involving Prisoners as Subjects
   j. Research Involving Recombinant DNA Molecules (including Human Gene Transfer Research)
   k. Human Embryonic Germ Cell (HEGC) Research
   l. Human Embryonic Stem Cell (HESC) Research
   m. HIV Antiretroviral Treatment Trials

B. Animal Welfare

Section L of the RFP specifies the minimum documentation requirements for Animal Welfare compliance. All related documentation should be included in the proposal in a clearly marked section. The Technical proposal shall document all information necessary to evaluate Animal welfare issues.

C. **Sharing Research Data (Plan)**

Section L of the RFP specifies the minimum documentation requirements for Data Sharing. All related documentation shall be included in the proposal in this clearly marked section. The Technical Proposal shall include a plan for Data Sharing as required by this RFP.

D. **Sharing of Model Organisms for Biomedical Research (Plan)**

Section L of the RFP specifies the minimum documentation requirements for Model Organism sharing. All related documentation shall be included in the proposal in this clearly marked section. The Technical Proposal shall include a plan for sharing Model Organisms as required by this RFP.

E. **Biohazard Safety**

The Technical Proposal shall include a plan for biohazard safety and security requirements.

F. **IT Systems Security**

Section L of the RFP specifies the minimum documentation requirements for IT Systems security. All related documentation shall be included in the proposal in this clearly marked section. The Technical Proposal shall include a plan for IT Systems security as required by this RFP.

APPENDIX B
Development of a Third Generation Anthrax Vaccine
RFP NIH-NIAID-DMID-07-05

ADDITIONAL BUSINESS PROPOSAL INSTRUCTIONS AND UNIFORM COST ASSUMPTIONS

In addition to the format requirements for the business proposal that are contained in Section L of the solicitation, the information provided in this appendix is intended to provide uniform cost assumptions and business clarifications.

Offerors are advised to give careful consideration to the statement of work, all reference material provided as appendices and attachments, and the technical evaluation criteria, and, the RFP as a whole, in the development of your proposal. The information requested in these instructions should be used as a guide for the development and formatting of your business proposal. Offerors should consider and include the information requested in this appendix, as well as **any other** information which will benefit the proposal.

BUSINESS PROPOSAL – TABLE OF CONTENTS

SECTION 1 – PROPOSAL SUMMARY AND DATA RECORD (Form NIH-2043)

SECTION 2 – COST OR PRICE SUPPORT

Section L of the RFP specifies the minimum documentation requirements for cost data and all cost related support. All related documentation should be included in the proposal in a clearly marked section.

SECTION 3 – UNIFORM COST ASSUMPTIONS

1) Technical Cost Assumptions

a. Overall Budget and Budgets by Milestone: It is anticipated that this contract will be awarded in phases aligned with the milestones identified in the Statement of Work. Consequently, Business Proposals must provide a breakdown by line item of cost, to include Direct Labor, Direct Materials, Subcontracts, Consultants, Travel, etc. for each milestone as well as a cost estimate by year for the entire project. The Business Proposal must include a detailed Gantt chart that provides timelines delineating each milestone with associated tasks and budget.

b. **Option 1**: A separate cost proposal must be submitted for Option 1 for the design and conduct of a Phase 1 dose escalating clinical trial in healthy adults. Business Proposals must provide a breakdown by line item of cost, to include Direct Labor, Direct Materials, Subcontracts, Consultants, Travel, Indirect Cost and Fee for each milestone associated with Option 1. The Business Proposal must include a detailed Gantt chart that provides timelines delineating each milestone with associated tasks and budget.

c. **Option 2**: A separate cost proposal must be submitted for Option 2 for the design and conduct of up to two Phase 2 clinical trials in healthy adults. Business Proposals must provide a breakdown by line item of cost, to include Direct Labor, Direct Materials, Subcontracts, Consultants, Travel, Indirect Cost and Fee for each milestone associated with Option 2 as well as a cost estimate by year for Option 2. The Business Proposal must include a detailed Gantt chart that provides timelines delineating each milestone with associated tasks and budget.

2) Travel and Site Visits

Assume one, two-day visit every three months to the NIAID in Bethesda, Maryland for two persons.

Assume a total of six, two-day site visits/technical audits annually to Contractor or subcontractor sites by NIAID or their representatives (three to four persons) to be conducted throughout the contract performance period. Include costs of supporting these visits, but not the costs of the independent auditors.

SECTION 4 - TABLE OF CONTENTS FOR DOCUMENTATION REQUIRED UNDER SECTION L OF THE SOLICITATION

1) Small Business Subcontracting Plan

Section L of the RFP specifies the minimum documentation requirements for completing a subcontracting plan. This plan should be turned in with the original proposal. All related documentation should be included in the proposal in a clearly marked section.

2) Extent of Small Disadvantaged Business Participation

Section L of the RFP specifies the minimum documentation requirements for small disadvantaged business utilization. This information should be turned in with the original proposal. All related documentation should be included in the proposal in a clearly marked section.

3) Past Performance Data, including references

Section L of the RFP specifies the minimum documentation requirements for providing past performance information. This information should be turned in with the original proposal. All related documentation shall be included in the proposal in a clearly marked section.

APPENDIX C: ADVANCE UNDERSTANDINGS

1. PUBLICATION AND PRESENTATION OF CONTRACT-GENERATED DATA AND FINDINGS

Any manuscript or scientific meeting abstract containing data generated under the contract shall be submitted to the Project Officer for review no less than 30 calendar days for manuscripts and 15 calendar days for abstracts before submission for publication or public presentation, respectively. NIAID contract support shall be acknowledged in all such publications. Preprints and reprints of papers and abstracts shall be submitted with the Monthly Technical Progress Reports.

2. ESSENTIAL MATERIALS AND RIGHTS THEREIN

The Contractor is responsible for the timely acquisition and delivery to the Government of all tangible materials and rights therein needed to perform the project, whether or not those materials and rights are set forth as a specific deliverable. The Contractor is also required to deliver to the Government any data and rights therein needed to perform the project. The Government is not required to obtain for the Contractor any proprietary rights, including intellectual property rights, or any materials needed by the Contractor to perform the project. The Contractor agrees that the project includes the development, manufacture, use and distribution of the vaccine.